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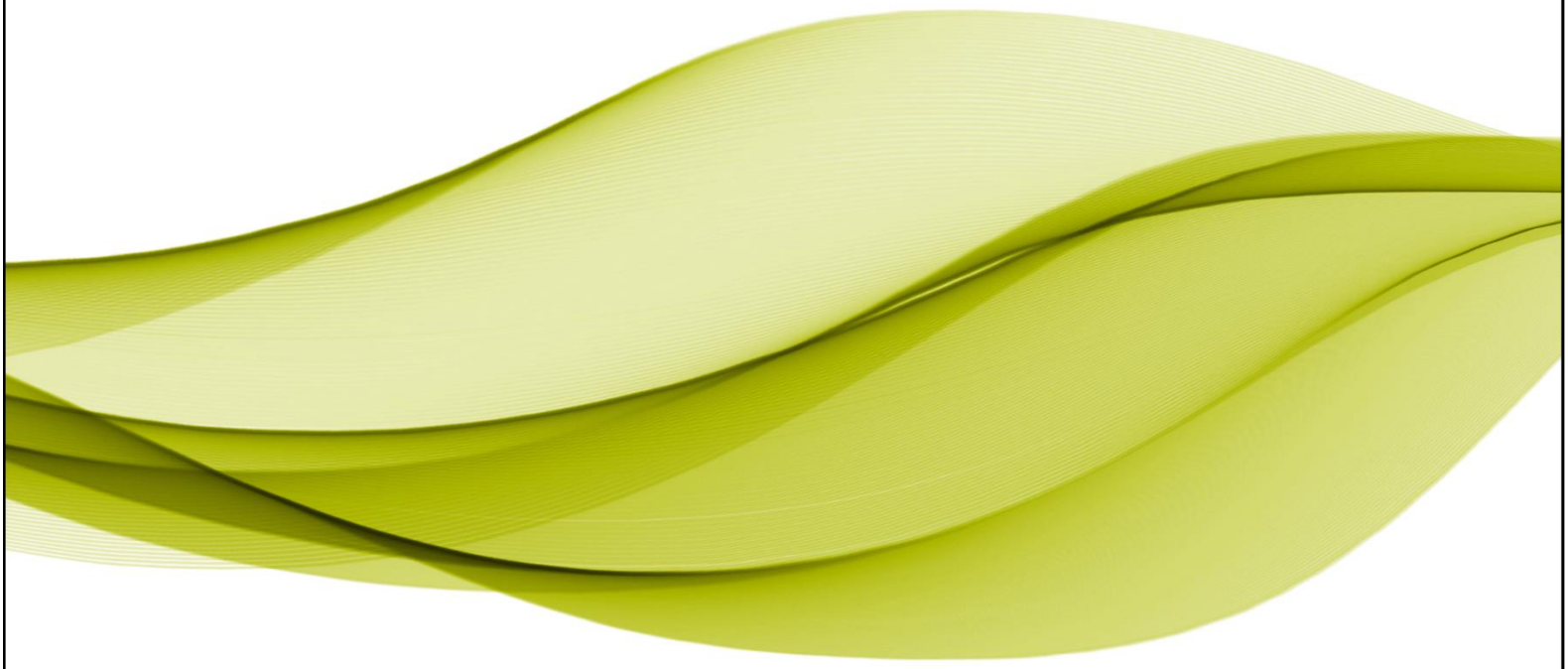

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Undergraduate Student Nurses' Attitude Toward Mental Health Education: A Cross-sectional Analysis

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Erratum

Correction of Author's Affiliation One of the authors requested an affiliation change due the affiliation was published incorrectly. The authors apologize for any inconvenience that it may have caused. Content of correction: 3Department of Nursing Education, College of Nursing, Qassim University, Buraydah 51452, Saudi Arabia → 3Department of Community, Psychiatric and Mental Health Nursing, College of Nursing, Qassim University, Buraidah 51452, Saudi Arabia

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Undergraduate Student Nurses' Attitude Toward Mental Health Education: A Cross-sectional Analysis

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Abstract

Background: Reportedly, there has been a long-standing nursing shortage in Saudi Arabia. This study explored the attitudes of undergraduate student nurses considering them to be a factor contributing to this shortage. This study also investigated the association among gender, hospital exposures, and campus enrollment concerning mental health education.

Methods: Quantitative correlational analysis was used on 124 student nurses in mental health nursing. Using Point Binary, Spearman's rank and one-way ANOVA, significant determinants were correlated to the domains of mental health nursing.

Results: Student nurses have a positive attitude toward mental health education. Gender is significantly related to Preparedness for Mental Health (PMH) (r = 0.193, p = 0.032) and Course Effectiveness (CE) (r = 0.202, p = 0.024). Hospital exposures are significantly correlated to PMH (r = 0.455, p = 0.000), Knowledge on Mental Health (KMH) (r = 0.423, p = 0.000), Negative Stereotypes (NS) (r = 0.514, p = 0.000), CE (r = 0.266, p = 0.003), Anxiety Surrounding Mental Illness (ASMI) (r = 0.586, p = 0.000), and Valuable Contributions (VC) (r = 0.488, p = 0.000). A correlation was noted in campus enrollment between NS (r = 0.267, p = 0.012) and ASMI (r = 0.337, p = 0.001).

Conclusions: Developing a positive attitude increases the acceptance of mental health education. Gender, hospital exposure, and course introduction positively influence students' views in selecting mental health nursing as their specialization.

Keywords: attitude, mental health, nursing

INTRODUCTION

Mental health care is a significant component of global health care. Mental health problems, especially among children, increased before COVID-19 and an upsurge during the pandemic.[1] According to the United Nations, mental health is an essential aspect of humanity that enables us to enjoy our lives to the fullest.[2] Health is related to an individual's emotional, psychological, and social well-being, influencing how one believes, feels, and behaves. Furthermore, it affects how a person handles stress, form relationships with others, and make wise decisions. Finally, mental health is essential in all phases of life.[3]

Mental health nurses are critical healthcare providers who significantly promote and support individuals suffering from mental illnesses in their recovery journey. These nurses typically provide care and support to persons experiencing mental health difficulties. Smith defined mental health nursing as "a subsection of nursing practice that involves the care of patients who have a mental health disorder to aid in their recovery and improve their quality of life." [4] Thus, it is essential to accomplish the goal of mental health nursing through intellectual preparation and training.[4]

In Australia and Ireland, nursing students' perceptions of mental illness and mental health nursing showed differing responses, with a tendency toward more positive attitudes toward mental Health as a theory relative to Finland, Norway, and the Netherlands.[5] A study conducted in the Midwestern U.S. demonstrated that clinical experience in a mental health facility provided a good foundation for nursing practice.[6] However, a few students believed their exposure needed improvement to prepare them to pursue this career.[6] Thus, additional time and content exposure may assist in attracting nurses to opt for mental health nursing as a career.[7]

In a quantitative and quasi-experimental study on the first day of clinical duty, 300 nursing students enrolled in the psychiatric nursing course in Michigan displayed a negative attitude and a moderate sense of knowledge and preparedness when interacting with mentally ill patients.[8] However, on their last day of clinical duty, a significant improvement was recorded in the factors mentioned above.[8] However, the nursing students continued to

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express low interest in mental health nursing as their future career choice.[9]

The health sector in the Kingdom of Saudi Arabia (KSA) is involved in a system-wide transformation concerning the corporatization of hospitals, the expansion of the healthcare system, and improvement in their efficiency, focusing on value-based healthcare.[10] This movement requires a substantial increase in local nurses available to achieve Vision 2030, which aims for healthcare transformation. However, according to Aboshaiqah *et al*., the KSA's nursing workforce is still dependent on expatriates, with a significant shortage of Saudi natives, particularly women.[7] Furthermore, this nursing shortage has been attributed to several variables, including culture, beliefs, a negative perception of the nurses, and their work conditions.[7]

According to the WHO reports, KSA ranks second globally regarding the nurse-patient ratio, after only the United Arab Emirates. However, KSA's nurse-to-patient ratio is still low compared to other countries.[9] Nurses significantly contribute to the healthcare sector in all countries. The demand for more nurses is dramatically rising with the population and the different aging sectors. KSA's population is expected to expand at a 2.5% annual rate by 2030.[11] In this situation, mental illness is most likely to aggravate, as evidenced by the pandemic experience, considering that approximately 34% of Saudis meet the criteria for mental health at some point.[12] According to the 2015 the Global Burden of Disease study, drug-use disorders, depressive disorders, and anxiety disorders are the third, fourth, and sixth leading causes of disability in the KSA.[13] The demand for nursing positions to be filled by this year is 150,000 or (0.15 million) Saudi nurses without any overseas recruitment.[14]

In 2017, the profile of the Saudi nursing force reflected that the majority of them were employed in the fields of medical, surgical, emergency, midwifery, and out-patient departments, with only a tiny percentage practicing in other areas such as the intensive care unit, mental Health, and pediatric care.[14] One major factor contributing to this nursing shortage in mental health settings is the lack of interest, with a negative attitude toward working under these conditions and the lack of technical nursing practices, which is a part of the mental education provided by the universities.[15–17] This observation indicated that some educational challenges such as the curricula and clinical sites significantly contribute to this low percentage of aspirants pursuing mental Health as a career in the country.

The proportion of nurses working in the KSA is within the standards when counting the expatriate nurses. However, it has been reported that there is a substantial deficit of nurses when the natives are used as a baseline, providing a ratio of 2.1 nurses/per 100,000 population in 2018.[18] This shortage was identified due to factors such as the low enrollment levels in nursing courses, mainly due to the poor image of nursing relative to other professions, and workplace-related difficulties, such as shifting jobs.[19] Nursing graduates remain to rank mental health nursing as their lowest preference of career choice and instead appear to be opting for positions within other specialties.[20] On-job training is also limited. As a result, several nurses are deployed in locations where they have been primarily trained and exposed, which is ideal for them to be for their desired assignment.[18]

A study conducted among 315 nursing students in Hail, Saudi Arabia, showed favorable attitudes toward people with mental illness, focusing on their willingness to work, stay, or be close friends with mentally ill patients.[21] However, in another study conducted in Riyadh, Saudi Arabia, after clinical placement, only 13.7% of the nursing students responded to select psychiatric nursing as a career option. This past study focused on students' attitudes and intentions toward mental health nursing.[22] No studies have explained the factors related to these paradoxical results. However, past evidence suggested that pre-nursing factors significantly influence students' likelihood of selecting psychiatric nursing, especially those with a positive attitude. This concern may improve recruitment and alleviate the shortages in the psychiatric nursing field.[14] In addition, after enrollment in the Bachelor of Science in Nursing program, student nurses need counselling and enough information regarding mental health nursing to influence their negative perceptions and stereotypes and provide a better understanding of this particular field of nursing.[19]

Hence, this study aimed to investigate further the factors affecting Saudi nursing students' mental health education attitude to provide the baseline data for improving the course and motivating and inspiring students to pursue mental health nursing as a future career.

METHODS

A quantitative correlational design was adopted in this study to investigate the factors that are perceived to influence mental health education. A purposive sampling method was employed, which included 127 enrolled nursing students at Shaqra University across different campuses. A total of 124 (98%) students completed their responses. Three of them were excluded because they provided incomplete answers or refused to answer some of the items as their personal preference, which the researchers respected. The Psychiatric/Mental Health Clinical Placement Survey Pre-Placement Tool was extracted directly upon request through email from Ms. Brenda Happel.[17] This tool was used to assess nursing students' attitudes toward mental health nursing education and the consumers of mental health services, as well as to evaluate the perceived value and quality of the theoretical

learning and future clinical placement from the student's perspective.

Before beginning their mental health clinical placement, the participants were asked to complete a pre-placement survey using a Google form. It was divided into two portions. Section A consisted of 24 statements designed to examine students' attitudes and experiences. Each sentence was graded on a 7-point Likert scale, with 1 = strongly disagree, 2 = very strongly disagree, 3 = disagree, 4 = neither agree nor disagree, 5 = agree, 6 = fairly strongly agree, and 7 = strongly agree. Section B included three questions to collect demographic information, The respondent's gender, number of hospital experiences, and campus enrollment. The seven subscale scores were calculated using responses to the 24 statements in Section A.

The questionnaire was previously validated and tested at Shaqra University for content. Three experts in the nursing education field served as validators. The team included the Dean of the Nursing Department of the College of Applied Medical Sciences-Quwayiyah campus and two assistant professors of the Dawadmi Campus, both faculty members of the nursing department. It was unanimously approved that all items appeared to measure and were appropriate for the intended study. After content validation, a pre-test was conducted with a minimum of 20 nursing students to assess the instrument's reliability. The reliability test yielded an alpha coefficient of 0.81, as presented in Table 1.

The Institutional Review Board of Shaqra University was approved (release date: 7 February 2022 with Ethical Review Committee reference number ERC_SU_20220005). Data collection was performed between 19 March 2022, and 29 July 2021, by respective lecturers by providing the students with the Google form at the end of their class hours with sufficient time provided to answer the questionnaire.

The responses were electronically collected and analyzed using SPSS v.21. Point-Biserial correlation, Spearman's rank correlation, and one-way ANOVA were employed to compute the correlation of gender, the number of hospital exposures, and the respective domains of mental health nursing education enrolled in, respectively.

TABLE 1. Survey subscale composition and internal consistency estimates

Subscale	Item	Cronbach's alpha
PHMF	1,4,7,10 and 22	0.90
KMI	9, 18, 19, and 23	0.88
NSs	8, 21, and 24	0.77
FC	6 and 12	0.92
CE	14, 15, 16, and 17	0.78
ASMI	3 and 5	0.69
VCs	2, 11, and 20	0.72

Data displayed on the different subscale domains as per item by Cronbach's alpha. PMHF: preparedness for the mental health field; KMI: knowledge of mental illness; NSs: negative stereotypes; FC: future career in mental health nursing; CE: course effectiveness; ASMI: anxiety surrounding mental illness; VCs: valuable contributions.

RESULTS

The sample in the present participants encompassed undergraduate nurses (N = 124) of Shaqra University. The majority of the respondents were female (53.23%). A significant number of respondents (65.32%) had three and more times hospital exposure, several (26.61%) had zero exposure, and some (8.06%) had 1–2 times hospital exposure. Moreover, as shown in Table 2, the respondents were enrolled in the BScN program from three different campuses of Shaqra University, namely Dawadmi Campus (57.3%), Shaqra Campus (31.7%), and Quwayiyah campus (18.7%).

The results showed a mean value of 5.83, indicating a strong agreement toward mental health education which means a generally good attitude. Specifically, undergraduate students showed a positive attitude toward Preparedness for Mental Health (PMH), Knowledge about Mental Health, Negative Stereotypes (NS), Course Effectiveness (CE), Anxiety Surrounding Mental Illness (ASMI), and Valuable Contributions (VC) all having weighted means of 6.10, 6.09, 6.08, 5.50, 5.40, and 6.15, respectively.

However, as shown in Table 3, their attitude toward mental health as their future career had an overall mean of 5.08, which was interpreted as an agreement—a positive attitude—based on the Likert scale.

In Table 4, using the point Biserial formula, gender indicated a significant relationship with PMH; correlation = 0.193, $p = 0.032$) and CE (correlation = 0.202, $p = 0.024$) at 0.05 significance level. Hence, female nursing students showed higher levels of PMH and believed more in its CE than male nursing students.

TABLE 2. Characteristics of the respondents (N = 124)

Variables	N	%
Gender		
Male	58	46.77
Female	66	53.23
Number of hospital experience		
0	33	26.61
1–2	10	8.06
3 and above	81	65.32
Campus enrolled		
Shaqra Campus	37	29.84
Dawadmi Campus	64	51.61
Quwayiyah Campus	23	18.55

TABLE 3. Mental health nursing education survey criteria

Mental Health Nursing Education Survey	Mean	Interpretation
I feel well prepared for my psychiatric/mental health clinical placement.	6.13	Strongly Agree
Psychiatric/mental health nursing makes a positive contribution to people experiencing a mental health problem	6.41	Totally Agree
I am anxious about working with people experiencing a mental health problem	5.72	Strongly Agree
I have a good understanding of the role of a psychiatric/mental health nurse	6.22	Totally Agree
I am uncertain how to act toward someone with a mental illness	4.66	Agree
I will apply for a Graduate Program in psychiatric/mental health nursing	3.98	Neutral
I feel confident in my ability to care for people experiencing a mental health problem	5.77	Strongly Agree
Psychiatric/mental health nursing can assist people with a mental illness in their recovery	6.48	Totally Agree
People with mental illness are unpredictable	6.04	Strongly Agree
Mental illness is not a sign of weakness in a person	6.01	Strongly Agree
I am concerned I may be harmed by a person with a mental illness	6.03	Strongly Agree
The theoretical component of psychiatric/mental health nursing has prepared me well for my clinical placement	6.19	Totally Agree
People with mental illness are more likely to be violent	5.83	Strongly Agree
This clinical placement in psychiatric/mental health nursing will provide valuable experience for my nursing practice	6.33	Totally Agree
I intend to pursue a career in psychiatric/mental health nursing	3.97	Neutral
If I developed a mental illness, I would not tell people unless I had to	5.69	Strongly Agree
My course has prepared me to work as a graduate nurse in a medical-surgical graduate program	6.00	Strongly Agree
Mental illness can affect people from all walks of life	6.41	Totally Agree
My course has prepared me to work as a graduate nurse in a psychiatric/mental health graduate program	5.65	Strongly Agree
I am familiar with the needs of people with mental illness	5.99	Strongly Agree
Someone I know has experienced a mental health problem	5.73	Strongly Agree
When a person develops a mental illness it is not their fault	6.39	Totally Agree
Mental health services provide valuable assistance to people experiencing a mental health problem	6.26	Totally Agree
I will work in a medical-surgical setting for at least a year before considering a career in mental health nursing	6.03	Strongly Agree
Overall Mean	5.83	Strongly Agree

TABLE 4. Correlation analysis of gender, number of hospital exposures, and campus enrolled in relation to the domains of mental health education

Variables	Measurement	Domains						
		PMH	KMH	NS	FC	CE	ASMI	VC
Gender	r	0.193	0.088	0.116	-0.006	0.202	0.029	0.165
	p	0.032*	0.329	0.199	0.925	0.024*	0.752	0.067
Number of hospital exposures	r	0.455	0.423	0.514	0.073	0.266	0.586	0.488
	P	0.000*	0.000*	0.000*	0.418	0.003*	0.000*	0.000*
Campus enrolled	r	0.138	0.175	0.267	0.159	0.119	0.337	0.212
	p	0.313	0.153	0.012*	0.213	0.423	0.001*	0.062

The data are presented as the correlation (r) and as the *p*-value for the level of significance. *significant at 0.05 level.
PMH: Preparedness for Mental Health; KMH: Knowledge about Mental Health; NS: Negative Stereotypes; FC: Future Career; CE: Course Effectiveness; ASMI: Anxiety Surrounding Mental Illness; VC: Valuable Contribution.

Furthermore, using Spearman's rank formula, the number of hospital exposure of student nurses was found to be highly correlated to their PMH (r = 0.455, p = 0.000), their Knowledge of Mental Health (KMH) (r = 0.423, p = 0.000), NS (r = 0.514, p = 0.000), CE (r = 0.266, p = 0.003), their ASMI (r = 0.586, p = 0.000), and its VC (r = 0.488, p = 0.000). Therefore, as respondents' hospital exposure increased, so did their PMH, KMH, NS, CE, ASMI, and VC.

Finally, campus enrollment showed a strong relationship with NS (r = 0.267, p = 0.012) and ASMI (r = 0.337, p = 0.001) at the 0.05 significance level. Thus, the respondents on the Quwayiyah campus tended to have a higher level of the said dimensions (NS and ASMI).

DISCUSSION

The present study findings indicated a high level of optimism in undergraduate nurses' mental health education, perception, and experience while taking the course. The positive attitude of these nurses in terms of PMH was related to their excellent understanding of the role of a mental health nurse, which was intensified by their belief that an individual's mental illness is not their fault. Undergraduate nurses' attitudes are shaped by molding their beliefs and perceptions, typically during their theoretical classes. Classroom learning, theoretical classes, or the deductive portion of learning among undergraduate nurses significantly predicts their performances in practical experiences.[23] Moreover, implementing effective teaching strategies provides a framework for practice-based approaches that can help promote reflective and analytical learning.[24] Hence, the theoretical part of nursing education is the primary learning tool for undergraduate nurses to gain a positive outlook and optimism toward mental health nursing.

Undergraduate student nurses possess fundamental knowledge about mental illness. As reflected in their responses, they agree that mental illness affects different people from all walks of life. Their belief that mental illness can affect anyone regardless of age, gender, geography, income, social status, race, ethnicity, religion/spirituality, sexual orientation, background, or other aspects of cultural identity implies a good indicator that they openly accept and consider mental illness like any other medical condition. This understanding conforms to the characterization of mental illness by the American Psychiatrist Association.[25]

NS signifies negative feelings of nurses toward mental Health, which impacts how they treat mentally ill patients. This behavior affects the healthcare efficacy and can affect patients' avoidance of therapy, as claimed by an authority in Psychology.[23] However, this study revealed that undergraduate nurses deviate from this behavior because the total agreement has the highest computed mean on the item stating that mental health nursing can assist people with a mental illness in their recovery. Nurses play a significant role in assisting individuals in assessing personal health status and assimilating health behaviors in their recovery campaigns using different assessment tools, nursing care plans, and communication techniques.[26]

Notably, undergraduate nurses agree that the theoretical component of psychiatric/mental health nursing has adequately prepared them for clinical placement, as reflected by their high mean score in item 12 of the questionnaire. It only implies that adequate theoretical preparation must be provided before their exposure to any clinical rotation for psychiatric nursing experience.[27] The degree of agreement in this domain suggests that they are interested in joining the working force in the future as mental health nurses. This aspect again indicates the importance of good classroom instruction as the foundation of good practical nursing experiences for students that they would apply in a hospital environment. Furthermore, a strong agreement on the CE domain and the consideration of the VC of mental health nursing reflects that these undergraduate students were satisfied by taking their course regarding the knowledge obtained and the orientation received on this type of nursing practice. In addition, this finding implies that they were well motivated as being taught by their respective professors and lecturers in their theoretical classes. Hence, the influence of classroom teaching during their course provides them with motivation, satisfaction, and a positive perception of the course and the profession.[28]

Based on the results of this study, female undergraduate nurses were found to have a significantly higher level of PMH education and CE, which implies that nursing can still be considered a female-oriented profession. This profession has therefore been deemed more suitable for women because of its nature as an extension of a domestic job portrayed mainly by women. Female undergraduate students learn more independently and possess the self-regulatory learning that justifies the result of this report. This observation is also following the results presented in one of the previous studies,[29] wherein the number of hospital exposure—as a variable of interest—was found to be significantly related to the following domains of mental health education: PMH, KMH, NS, CE, ASMI, and VC. The clinical learning experience serves as the standard in the nursing curriculum toward strengthening all aspects of learning of students enrolled in the nursing course. It was an excellent tool for learning and teaching that could facilitate teaching-learning opportunities to advance the competencies and proficiencies of undergraduate student nurses and provide a suitable venue as they apply learnings from their classroom sessions. Moreover, clinical learning experience, as was realized through hospital exposures, facilitated positive adaptive capabilities of undergraduate student nurses to a new environment and their integration into the healthcare team and system. This experience helped them bridge the gap in their learning needs as their respective clinical instructors mentored them.[30] Moreover, a systematic review reported that clinical teaching is a student-centered learning approach that builds better knowledge and understanding of the concepts along with self-development among students, which brings forth improvement in their learning and competencies.[31]

Finally, the present results revealed that the campus where the students were enrolled significantly affects their negative perceptions and anxiety toward mentally ill patients. It was proven from the data that undergraduate students from the Al-Quwayiyah campus managed their NS and ASMI properly. This condition was influenced by the established environment on their respective campuses. The school environment and the practices therein affect their approach to coping and functioning, further aggravating their negative experiences toward mental health.[32]

Professors and instructors of mental health nursing subjects should provide motivational support to student nurses toward preparation for mental health nursing training. The syllabus and course contents must develop a better structure focusing on enhancing optimism among undergraduate student nurses toward mental health nursing and making it a preferable career option.

This study also recognized its limitations as it was concentrated only in one university, and the total number of respondents affected the generalizability of the results. Some suggestions have been made to include other institutions and colleges in the KSA. Moreover, this study can be considered through other research methods that evoke higher analysis.

CONCLUSIONS

A positive attitude provides better perception, acceptance, and understanding of mental health nursing education, which results in a higher level of student nurses' PMH and KMH and alleviates NS and ASMI. Gender is relative to the preparedness and effectiveness of mental health education. The more hospital exposure an undergraduate student has, the higher his or her positivity in attitude toward mental health nursing. Furthermore, the campuses where they were enrolled were relative to acquiring optimism on mental health education in nursing as influenced by the school structure, curriculum implementation, and environment.

CONFLICT OF INTEREST

The author has no conflict of interest to declare.

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Social Media Addiction Among Nursing Students and Its Related Factors

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Social Media Addiction Among Nursing Students and Its Related Factors

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Abstract

Background: Social media use has become an indispensable part of our lives as a result of technology advancement and is quite high among students.

Methods: This study employed a cross-sectional design. Participants were 289 students from the Faculty of Health Sciences at Artvin Coruh University, Turkey. The Social Media Addiction Scale (SMAS) was used to obtain data. T-test, one-way ANOVA, Pearson's correlation, and Bonferroni analysis were used to analyze the data.

Results: The participants' mean SMAS score was 81.03 ± 34.79, which was moderate. A weak and positive correlation was found between social media addiction and daily social media use. Statistical differences were found between social media addiction and social class, maternal education level, place of residence, income level, and general health status. Further, statistically significant differences were found between access to social media such as Facebook, Twitter, and Skype, and SMAS and subscales ($p < 0.05$).

Conclusions: The nursing students in this study showed moderate levels of social media addiction. Factors such as daily social media use, year of study, maternal education level, place of residence, income level, and general health status are associated with the degree of social media addiction.

Keywords: addiction, internet, nursing, social media

INTRODUCTION

Given the rapid development of Web 2.0 information and communication technologies in recent decades, such internet-based tools have become an indispensable part of our lives. The gradual increase in internet access has likewise expanded its use, especially among young people in their professional and social environments.[1] Internet use primarily takes place through social media.[2] Spending too much time on social media platforms such as Facebook, Twitter, and Instagram is considered social media addiction. Though it is not considered an addiction by the World Health Organization, excessive use of social media has attracted attention and led to further research in this field.[3] Social media involves a variety of internet applications that allow over three billion people to connect by sharing texts, messages, photos, and videos in real time. The popularity of social media networks is widespread in developing countries, especially among the young population.[4] The number of monthly active social media users worldwide is expected to reach 3.43 billion by 2023, which is approximately one third of the world's population.[3]

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According to the January 2021 digital report by the We Are Social platform, which provides up-to-date internet statistics for Turkey and includes mobile and social media statistics, the number of social media users increased by more than 11 percent, with an increase of 6 percent compared to 2020. million. Based on this estimate, the number of social media users in Turkey constitutes 70.8% of its total population.[5] The primary purposes for social media use are keeping up with global events, following the news, watching entertaining videos and content, spending free time, interacting with friends and family, and sharing photos and videos. Most users spend their time on social networks, online news sites, and film and music portals. In addition, with the recent effects of the COVID-19 pandemic, the number of social media users has increased by 13% since 2020.[5] As such, social network usage patterns are a clear indicator of the transition to mobile platforms.

Through smartphones and tablets, mobile web access facilitates the continuous use of mobile-first or mobile-only platforms such as Twitter, Instagram, and Snapchat.[6] With the increase in social media use, technology-related addictions have also increased. Studies have shown that the addictive use of social media reduces productivity, healthy social relationships, and life satisfaction, while excessive use causes anxiety, depression, social envy, weak social relationships, poor job performance, and

decreased quality of life.[7] Additionally, social media reduces social interaction and communication among individuals. These findings have important implications in professions where communication is a key skill, such as nursing.[8] Excessive phone use in nursing students was found to be associated with lower sleep quality, self-esteem, perceived social support, and communication skills, and higher social distress.[9] When technology is not used appropriately, it impacts the daily routines of individuals and reduces their sleep quality, which negatively affects the mental and physical health of students and their academic success.[10] Academic achievement decreased in students from health-related departments (medicine, nursing, etc.) as social media addiction increased.[11] Studies have shown that long-term social media use is positively associated with poor mental health, such as anxiety, depression, and stress, and negatively associated with well-being over time.[12] Social media has also been associated with decreased face-to-face communication. Current nursing students born in this age of technology and spending significant time on social media may be affected by these problems, which may negatively impact their communication skills in their professional lives.[13] It is important to develop nurses' communication skills during their student years. Nurses, who comprise the majority of healthcare professionals, most actively promote and safeguard the health of patients, as they spend the most time with patients. To ensure success in their careers, greater awareness of their social media use and better management of the time spent on such platforms is important. Therefore, this study investigated social media addiction and its influencing factors in students in a nursing program.

METHODS

This study employed a cross-sectional design. Data were collected from first-, second-, third-, and fourth-year students from Department of Nursing, Faculty of Health Sciences, Artvin Coruh University, Turkey between December 1, 2021 and February 1, 2022. A total of 289 nursing students participated in the study. Students who did not volunteer to participate in the study were excluded from the sample. The study sample size was calculated based on the universal formula on OpenEpi. As the population was 419 individuals, the minimum sample size needed was 201 individuals, with a confidence interval of 95% and error margin of 5%. In addition, considering a 50% observation rate, 1% standard deviation, and 99% confidence interval using OpenEpi, a sample calculation program, 258 students were deemed to be an appropriate sample size. Students older than 18 years of age were included. Participants' sociodemographic characteristics were considered the independent variables, while their Social Media Addiction Scale (SMAS) scores formed the dependent variables. Students who provided consent were included in the study. Data were collected by the researchers through in-person surveys. When taking a sampling method, 62% of the samples were reached. The inclusion criteria were age being ≥18 years and being a nursing student. The exclusion criteria were refusal to be involved in the study and incomplete questionnaires. A descriptive information form and the social media addiction scale were used to collect data.

The descriptive information form was developed by the researchers after a literature review. It includes 20 questions regarding the participants' characteristics such as age, education level, monthly income, social media usage time, sleep time, internet usage time, and place of residence.

Social Media Addiction Scale (SMAS) was developed by Şahin (2017) to determine social media addiction levels in secondary education, high school, and university students. Within the framework of validity studies, exploratory and confirmatory analyses were conducted and the SMAS-AF (Social Media Addiction Scale–Adult Form) was found to use a 5-point Likert-type scale. The scale consists of 29 items across four subscales: virtual tolerance, virtual communication, virtual problem, and virtual information. Items 1–5 covered virtual tolerance, 6–14 covered virtual communication, 15–23 covered virtual problem, and 24–29 covered virtual information. The internal consistency coefficient (Cronbach's alpha) was 0.93 for the whole scale, while internal consistency coefficients were between 0.81 and 0.86 for the subscales. The maximum possible score on the scale is 145 and the minimum possible score is 29. Responses ranged from not at all appropriate to very appropriate, with 1 point for not suitable at all and 15 points for very suitable. High scores indicate that individuals perceive themselves as addicted to social media.[14]

The data were analyzed using IBM's SPSS program, version 25 to obtain descriptive statistical methods (number, percentage, min-max values, mean and standard deviation), and normal distribution was tested with skewness and kurtosis. As the data were normally distributed, we performed a parametric t-test and one-way ANOVA. Pearson's correlation coefficient was calculated to understand the relationships between the scales, and a Bonferroni analysis was used to find the difference in multiple comparisons. A 95% confidence interval and $p < 0.05$ error level were considered in evaluating the results.

The study was carried out in accordance with the principles of the Declaration of Helsinki. Students were informed about the study and their consent was obtained. The ethics committee approval for this study was received from the Artvin Coruh University Ethics Committee (No. E-43747944-044-26873, October 21, 2021).

RESULTS

SMAS and subscale scores

The mean score for the SMAS was 81.03 ± 34.79, which was found to be moderate. The mean subscale scores were14.96 ± 6.48 for virtual tolerance, 24.84 ± 11.22 for virtual communication, 23.14 ± 11.89 for virtual problem, and 18.08 ± 71.16 for virtual information. Cronbach's alpha reliability coefficient for the SMAS was 0.98, with virtual tolerance = 0.94; virtual communication = 0.92; virtual problem = 0.96; and virtual information = 0.92. (Table 1).

Correlation results for social media addiction and daily internet use, daily social media use, and the number of social media applications used

Pearson's correlation analysis showed a weak positive correlation between social media addiction and daily social media use (r = 0.200, p = 0.001), a moderate positive correlation between daily internet use and daily social media use (r = 0.416, p = 0.000), a weak positive correlation between daily internet use and the number of social media applications used (r = 0.175, p = 0.003), and a weak positive correlation between daily social media use and the number of social media applications used (Table 2).

Comparison of mean SMAS scores by sociodemographic characteristics

The distribution of the sociodemographic characteristics showed that mean age was 21.25 ± 2.04, with most students aged between 20 and 22 years (69.6%). About 72.7% were female students, a majority were Anatolian high school graduates (42.6%), and 26.3% were in their fourth year. In terms of maternal education level, 38.1% had primary education; for paternal education level, 27.3% were high school graduates and 27.3% had primary education. Nearly 46.7% of the students lived with family, 56.4% had income that was lower than their expenses, and 57.8% had good general health. Daily internet use was 4.45 ± 3.05 hours, while daily social media use was 3.12 ± 1.71 hours. While no differences were found between social media addiction and age, gender, type of high school, or paternal education level (p > 0.05), differences were found for year of study, maternal education level, place of residence, income level, and general health status (p < 0.05). A Bonferroni analysis showed the difference resulted from third-year students, whose mean SMAS scores were higher than all other students. In terms of maternal education level, students whose mothers had secondary education showed higher mean SMAS scores than students whose mothers had primary education. Differences in terms of place of residence was observed in students living alone and whose mean SMAS scores were higher than those of students living with family and other people (with friends, etc.). Students with income lower than their expenses had higher SMAS scores than those with higher incomes. In terms of general health, differences were found in the group with moderate general health, suggesting that students with good and poor health levels had higher SMAS scores than those with moderate health (Table 3).

Comparison of SMAS and subscale mean scores in terms of internet/smartphone use

When the mean SMAS and subscale scores of the students who participated in the study were compared in terms of internet/smartphone use, no statistically significant difference was found between checking the phone during sleep hours or phone use delaying sleep latency and scores on the SMAS and its subscales (p > 0.05). A statistically significant difference was found between checking the phone at night and checking the phone on waking up and the virtual tolerance and virtual communication subscales, as well as between losing sleep due to internet use and SMAS and all subscale scores (p > 0.05). An independent t-test showed that the mean virtual tolerance and virtual communication subscale scores were higher in students who checked their phone at night compared to those who did not. Mean SMAS and all subscale scores for students who lost sleep owing to internet use were higher than those of students who did not lose sleep. In addition, mean virtual tolerance subscale and virtual communication subscale scores for students who checked their phones on waking up were higher compared to those who did not (Table 4).

Comparison of mean SMAS and subscale scores in terms of social media characteristics

When mean SMAS and all subscale scores of the students who participated in the study were compared in terms of social media characteristics, no statistically significant difference was found between social media use, believing that social media is harmful, Instagram, WhatsApp, and other social media applications and SMAS score (p > 0.05). However, a statistically significant difference was found between access to social media such as Facebook, Twitter, and Skype, and SMAS and subscales (p < 0.05). A Bonferroni analysis showed that social media addiction levels of students who used desktop and mobile devices to access social media were higher than those of the students who used only mobile devices.

In terms of social media applications, students who used Facebook often or excessively had higher SMAS scores than students who never or seldom used it, while students who used Twitter and Skype often or exclusively had higher SMAS scores than students who never, seldom, or moderately used them (Table 5).

TABLE 1. Means scores of the Social Media Addiction Scale (SMAS) and subscales used in the study and descriptive statistics

Scale	Number of Items	Items	Min-Max	Mean ± SD	Cronbach's Alpha
SMAS	25	1–29	29–145	81.03 ± 34.79	0.98
Virtual tolerance	5	1–5	5–25	14.96 ± 6.48	0.94
Virtual communication	9	6–14	9–45	24.84 ± 11.22	0.92
Virtual problem	9	15–23	9–45	23.14 ± 11.89	0.96
Virtual information	6	24–29	6–30	18.08 ± 7.16	0.92

TABLE 2. Correlation between social media addiction and daily internet use, daily social media use, and the number of social media applications used

Correlation results of social media addiction	1	2	3	4
Social media addiction	1.000	0.023	0.200*	0.090
Daily internet use		1.000	0.416*	0.175*
Daily social media use			1.000	0.306*
Number of social media applications used				1.000

*$p < 0.01$

TABLE 3. Comparison of mean SMAS scores by sociodemographic characteristics (N = 289)

Characteristics	N (%)	Mean ± SD	*p*	Bonferroni
Age* ** (21.25 ± 2.04)				
17–19	39 (13.5)	87.00 ± 3.06	0.341	
20–22	201 (69.6)	79.29 ± 34.16		-
≥23	49 (17.0)	83.44 ± 33.82		
Gender**				
Female	210 (72.7)	82.87 ± 35.00	0.143	-
Male	79 (27.3)	76.15 ± 33.94		
Type of high school attended***				
Anatolian	123 (42.6)	73.36 ± 35.04	0.118	
Regular	30 (10.4)	76.93 ± 31.96		-
Health	71 (24.6)	87.66 ± 34.28		
Vocational	65 (22.5)	84.53 ± 35.29		
Year of study***				
First	69 (23.9)	80.43 ± 35.95	0.000*	Third > Second Third > Fourth Third > First
Second	72 (24.9)	71.51 ± 26.57		
Third	72 (24.9)	99.26 ± 38.72		
Fourth	76 (26.3)	73.34 ± 30.37		
Maternal education level***				
Illiterate	57 (19.7)	76.94 ± 33.55	0.009*	
Primary education	110 (38.1)	73.61 ± 33.59		
Secondary education	77 (26.6)	88.92 ± 33.50		Primary < Secondary
High school	32 (11.1)	92.03 ± 38.40		
University	13 (4.5)	88.00 ± 35.52		
Paternal education level***				
Illiterate	21 (7.3)	84.09 ± 33.62	0.537	
Primary education	79 (27.3)	76.70 ± 34.67		
Secondary education	73 (25.3)	79.20 ± 35.48		-
High school	79 (27.3)	85.88 ± 35.06		
University	37 (12.8)	81.81 ± 34.09		
Place of residence***				
With family	135 (46.7)	71.86 ± 31.77	0.000*	Other < Alone
Alone	63 (21.8)	103.33 ± 29.97		
Other	91 (31.5)	81.65 ± 36.48		Other < Alone
Income level***				
Income = expense	89 (30.8)	77.77 ± 33.44	0.007*	Income < Expense > Income > Expense
Income > expense	37 (12.8)	67.32 ± 30.50		
Income < expense	163 (56.4)	85.93 ± 35.55		
General health status***				
Good	167 (57.8)	82.80 ± 36.28	0.000*	Good > Moderate Poor > Moderate
Moderate	75 (26.0)	68.94 ± 31.58		
Poor	47 (16.3)	94.06 ± 28.24		

*$p < 0.05$; ** t-test; ***F=one-way ANOVA

TABLE 4. Comparison of mean SMAS and subscale mean scores in terms of internet/smartphone use (N = 289)

Variables	Subscale/Scale	*p*
Checking the phone during sleep hours	Virtual tolerance	0.109
	Virtual communication	0.273
	Virtual problem	0.267
	Virtual information	0.443
	SMAS total	0.234
Checking the Phone at night	Virtual tolerance	0.027*
	Virtual communication	0.029*
	Virtual problem	0.124
	Virtual information	0.323
	SMAS total	0.065
Losing sleep due to internet use	Virtual tolerance	0.012*
	Virtual communication	0.006*
	Virtual problem	0.003*
	Virtual information	0.045*
	SMAS total	0.005*
Checking the phone on waking up	Virtual tolerance	0.027*
	Virtual communication	0.029*
	Virtual problem	0.124
	Virtual information	0.323
	SMAS total	0.065
Phone use delaying sleep latency	Virtual tolerance	0.821
	Virtual communication	0.980
	Virtual problem	0.929
	Virtual information	0.610
	SMAS total	0.919

*$p < 0.05$

TABLE 5. Comparison of Mean SMAS and Subscale Scores in Terms of Social Media Characteristics (N = 289)

Variables	Subscale/Scale	*p*	Bonferroni
Social media use**	Virtual tolerance	0.661	
Yes	Virtual communication	0.403	
No	Virtual problem	0.426	
	Virtual information	0.420	
	SMAS total	0.430	
Believe social media is harmful**	Virtual tolerance	0.352	
Yes	Virtual communication	0.133	
No	Virtual problem	0.362	
	Virtual information	0.528	
	SMAS total	0.272	
Social media access***	Virtual tolerance	0.000*	
Desktop	Virtual communication	0.000*	Desktop and mobile
Desktop and mobile	Virtual problem	0.000*	>
Only mobile	Virtual information	0.000*	Only mobile
	SMAS total	0.000*	
Facebook***	Virtual tolerance	0.000*	
Never or seldom	Virtual communication	0.000*	Often or excessively
Moderate	Virtual problem	0.000*	>
Often or excessively	Virtual information	0.000*	Never or seldom
	SMAS total	0.000*	
Instagram***	Virtual tolerance	0.165	
Never or seldom	Virtual communication	0.067	-
Moderate	Virtual problem	0.059	
Often or excessively	Virtual information	0.327	
	SMAS total	0.088	

TABLE 5. Continued

Variables	Subscale/Scale	*p*	Bonferroni
Twitter* **	Virtual tolerance	0.000*	Often or excessively > Never or seldom; Often or excessively > Moderate
Never or seldom	Virtual communication	0.000*	
Moderate	Virtual problem	0.000*	
Often or excessively	Virtual information	0.000*	
	SMAS total	0.000*	
WhatsApp* **	Virtual tolerance	0.599	-
Never or seldom	Virtual communication	0.374	
Moderate	Virtual problem	0.815	
Often or excessively	Virtual information	0.629	
	SMAS total	0.606	
Skype* **	Virtual tolerance	0.000*	Often or excessively > Never or seldom; Often or excessively > Moderate
Never or seldom	Virtual communication	0.000*	
Moderate	Virtual problem	0.000*	
Often or excessively	Virtual information	0.000*	
	SMAS total	0.000*	
Other (TikTok, blogs, forums)* **	Virtual tolerance	0.166	-
Never or seldom	Virtual communication	0.163	
Moderate	Virtual problem	0.305	
Often or excessively	Virtual information	0.106	
	SMAS total	0.159	

*$p < 0.05$

DISCUSSION

It is important for nurses to develop their communication skills during their student years. Because nurses spend a lot of time with patients, they actively promote and maintain patient health. They are more likely to succeed professionally if they are more skilled in using social media wisely and managing their time. Internet access and use are increasing worldwide, and social media use is also increasing with this ease of access.[6] Studies have found that social media addiction levels increase as time spent on social media increases.[15–17] The mean scores for the SMAS was 81.03 ± 34.79, which was moderate. In a study conducted on university students, social media addiction levels increased with increased internet addiction.[16] Nursing students in particular are at risk of social media addiction since they spend excessive time on the internet and social media.[18]

A moderate and positive correlation was found between daily internet use and daily social media use. Similar to this result, a study conducted with university students showed that social media addiction increased as daily internet use increased.[19] Students who spent five hours or more daily on social media had higher social media addiction levels, and addiction increased as time spent on social media increased.[20] Nurses use social media to communicate with patients and their families, for educational purposes, to foster professional connections, and to educate and inform health professionals and society.[21] Social media is believed to be the preferred way to use the internet as it provides a platform for communication, obtaining information, and entertainment.

No correlation was found between students' gender and social media addiction. Similarly, gender was not associated with risk of social media addiction.[16,22] Since both genders had similar purposes (online communication, chat, shopping etc.) for social media use, gender cannot be considered a factor associated with addiction levels. In our study, third-year students had higher social media addiction levels, which was confirmed in another study.[23] In a study conducted with health sciences students, while social media addiction was high in second-year students, it was low in first-year students.[20] Differences in these results suggest that sociodemographic characteristics correlate with students' social media addiction levels.

In terms of education level, significant correlation was found between maternal education level and social media addiction. In a study conducted with high school students in Spain, students from families with higher education levels were found to have higher addiction levels, similar to the results of our study.[24] A study conducted with female university students showed that problematic internet use decreased as parents' education levels increased and, when parents were university graduates, their children used technology less for entertainment.[25] Family awareness increases with higher education levels and children's options for acquiring knowledge likewise increase. With increased education levels, the need for technology increases and this may result in addiction.

Students who lived alone had higher social media addiction levels, presumably because they tend to be more active in online social networks when alone.[26] Studies conducted with students have shown that those with high levels of loneliness and low levels of social

support are more addicted to social media.[27] One study found that being single, being young, and living in a small town was associated with loneliness, and internet use was higher in individuals who lived alone.[28] While individuals use the internet and social media to communicate, obtain information and have fun, it is thought that individuals living alone prefer social media applications to socialize and relieve stress.

Significant correlation was found between income level and social media addiction. A study conducted with female university students showed that low family socioeconomic status is not only a social problem but also causes addiction to other technologies.[25] Individuals with insufficient and unstable financial sources potentially use the internet to cope with stressful life events, which may lead to increased addiction.[29]

Students with a moderate level of general health showed higher social media addiction. Unlike our study, social media addiction in university students has been found to increase as their depression levels increased.[19] Social media addiction is believed to increase because social media applications are used as sources of information today; individuals seek solutions to health problems and want to discuss these problems with others.

Our study showed that students who checked their phones at night had higher virtual tolerance and virtual communication mean scores than students who did not. In a study conducted with medical faculty students, those with poor sleep had a higher probability of reporting excessive social media use. Sleep patterns were found to deteriorate as time on social media increased.[30] Depending on the purpose for social media, spending too much time on the phone to keep up with events may cause various health problems. Individuals who check their phone to keep up with the latest developments on social media or who feel that they will miss something important otherwise tend to be more addicted.

In our study, students who lost sleep owing to internet use had higher SMAS and subscale scores. In a study conducted on medical faculty students, male students with smartphone addictions who used smartphones before bed reported low sleep quality, avoided social interactions, were uncomfortable when smartphone use was restricted, and allocated more time to online and offline games.[31]

In our study, students who checked their phones as soon as they woke up had higher mean virtual tolerance and virtual communication scores than students who did not. In a study with medical faculty students, 83.9% of students checked their phones for notifications as soon as they woke up.[32] Another study showed that individuals experienced negative psychological and sometimes physiological symptoms when they paused social media use, causing social media addiction and more problematic behaviors in these individuals.[33]

Individuals who used desktop and mobile devices to access social media had higher social media addiction levels than those who used mobile devices exclusively. With the increasing number of touch screen phones, mobile access to social networks has increased. In addition, it has been observed that installing social networking applications on mobile phones increases the time spent on virtual social networks.[34] In a study of individuals with an average age of 14.2, 99.2% used WhatsApp and mobile devices the most to follow social media.[35] Smartphone addiction in nursing/midwifery students has also reportedly increased as the time they spent using social media increased.[36] Social media addiction has become concerning because, in recent decades, users have gained convenient access to such applications from portable devices such as tablets and phones.[25] The portability and ubiquitousness of such devices increases the time spent on social media applications and consequently addiction levels.

In our study, statistically significant differences were found between access to social media such as Facebook, Twitter, and Skype, and SMAS and subscales. A study conducted with university students suggests that with the increasing number of social media accounts, social media addiction will also rise.[3] The greater the number of social media applications individuals use to keep up with events, communicate, or for entertainment and the more time spent using them is believed to increase the level of addiction.

Students who used Facebook have shown higher social media addiction levels. A study of Akdeniz university students showed that social media usage differs across Facebook, Twitter, and Instagram. While students used Twitter to express themselves and socialize, Instagram was used to promote themselves.[37] The purpose for social media use is believed to influence the type of social media used and addiction levels. This study has some limitations. First, participants were limited to nursing students and were approached online and not personally. Second, nursing students from only one university were included. Third, psychological factors associated with social media addiction were not determined. Therefore, future studies should consider different populations and with larger samples.

CONCLUSIONS

The nursing students in this study showed moderate levels of social media addiction. Factors such as daily social media use, year of study, maternal education level, place of residence, income level, and general health status are associated with their social media addiction levels. Students use social media for their information needs, to

learn about new technological developments, and for entertainment during their free time, which is believed to lead to addiction to social media.

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CONFLICT OF INTEREST

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Nurses' Perception of Work-Environment Uncertainty and Readiness for Organizational Change

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Nurses' Perception of Work-Environment Uncertainty and Readiness for Organizational Change

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Abstract

Background: Healthcare organizations have a dynamic work-environment that changes constantly. This study aimed to explore whether there is a relationship between work-environment uncertainty and nurses' readiness to participate in organizational change.

Methods: A cross-sectional study was conducted at two tertiary hospitals. The sample size was 222 nurses. A self-report questionnaire was adopted, translated to Arabic, and used for collecting data; it consists of three scales, personal data sheet, organizational readiness for implementing change scale, and perceived environmental uncertainty in hospitals scale. Descriptive statistics t-test and analysis of variance were used to analyze the data.

Results: The level of agreement with the change efficacy statements with the total mean percentage of nurses' readiness for organizational change (change efficacy) was 67.0%, and it was slightly higher than the commitment statements, in which the total mean percentage of nurses' readiness for organizational change (change commitment) was 64.2%. In addition, one of the work-environment uncertainty dimensions, which is the individual attribute (need for information), positively correlated with the organizational readiness to change.

Conclusions: The organizational readiness to implement organizational change is high. Environmental complexity was highly perceived among nurses as one of the work-environment uncertainty dimensions. An organizational environment considering employee characteristics must be developed to improve their knowledge, skills, and attitude to adapt to change and uncertainty.

Keywords: nurses, organizational change, Saudi Arabia, uncertainty, work-environment

INTRODUCTION

Healthcare organizations go through various challenges. These challenges result in a dynamic work-environment that changes constantly and consequently leads to continuous quality improvement efforts while keeping costs contained. This is an international concern to which Saudi Arabia is not exempted. The Saudi healthcare system, in an active initiative of the national transformational plan (2020) and as part of the Saudi Arabia Vision 2030, is targeting the strategic plans of all sectors to place the Kingdom of Saudi Arabia in the leading position.[1] Moreover, an exclusive aspect of healthcare services in Saudi Arabia is that millions of pilgrims visit Makkah annually, and the Ministry of Health (MOH) provides all necessary preventive and curative health services for visitors. The total number of Makkah pilgrims was approximately 2.5 million in 2018, in which approximately 74.48% of them are foreign visitors. To this end, the MOH has established 25 hospitals, 8 of which are seasonal. In addition, it has 154 health centers, of which 112 were seasonal. In total, there are 4,998 hospital beds with a rate of one bed per 505 pilgrims. The total amount of personnel is 30,003 (excluding visiting health manpower). Physicians, nurses, and allied health personnel constituted 74.95% of the assigned personnel.[2] This justifies the efforts of the MOH toward improving healthcare services throughout the Kingdom, and the Makkah region is not exempted to an innovative transformation in the healthcare system.

During reforms, planned and unplanned changes are expected in the dynamic healthcare settings of hospitals; as a result, uncertainty is expected to occur.[3] Such expectation has been proved in the literature and confirmed according to the environmental uncertainty theory, in which the complexity in the work-environment and rate of change interaction led to environmental uncertainty.[4] Moreover, developing and managing communication networks will have a significant role in reducing uncertain conditions in the changing environment.[5] Work-environment uncertainty not only affects the organization's development but also individuals' health, wellbeing, and satisfaction with the

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organization. Moreover, stressful situations such as lack of job control from rapidly changing environments in the workplace result in an unhealthy work-environment, which can cause up to 125,000 employee deaths annually and costs organizations up to $130 billion in excess annual costs.[6] Organizational readiness is a critical prerequisite for the implementation of changes. Thus, the individual and organizational capacity for change along with understanding its importance must be assessed. This is the essence of planned change, which is a conscious decision to increase individual and organizational capability.[7]

Related literature review revealed a research gap with respect to whether the level of organizational uncertainty affects employees' readiness to be active participants in deploying changes planned in their organization. In healthcare-related literature, no studies have explored the relationship between environmental uncertainty and nurses' readiness for organizational change. Understanding nurses' perceptions regarding uncertainty in the hospital environment and connecting them to their level of readiness for change in the organization will help us understand the organization's behavior on both micro and macro levels. Thus, strategies for reducing the uncertainty level can be recommended to help people become more certain about accepting the changes and be active participants in the reform efforts for organizational development.

This study aimed to explore whether there is a relationship between work-environment uncertainty and nurses' readiness to participate in organizational change. This aim was achieved by identifying nurses' perception of work-environment uncertainty in the selected study setting, whether a significant difference exists between the selected characteristics of participants and their perceptions of work-environment uncertainty, the extent of nurse's readiness for organizational change, whether a significant difference exists between the selected characteristics of participants and their level of readiness for organizational change, and the relationship between perceptions of work-environment uncertainty and nurses' readiness for organizational change.

METHODS

A cross-sectional descriptive correlational design was used in this study. The study was conducted in two hospitals in the Makkah region. The nonprobability proportional quota sampling technique was used to determine the participants. The sample comprised two main groups. The first group included all first-line nurse managers (head and charge nurses, clinical educator, and quality nurses) who had been working in their current setting and position for not less than 1 year in the nursing administration office (administrative; N = 47). The second group comprised staff nurses working in direct contact with patients (bedside; N = 477). The total number was 524 in the two hospitals, and the quota set depended on predetermined settings (Table 1).

TABLE 1. Sample characteristics

	King Faisal Hospital	King Abdelaziz Hospital	Total
Administration	11	9	20
ICU	29	26	55
ER	32	36	68
MW	35	44	79
Total	107	115	222

For this group, staff nurses working in any of the selected settings (ICU, ER, MW, and nursing administration office, nurses have enough opportunity to be exposed to, and involved in, changes in their work-environment), working in their current setting of not less than 1 year, available at the time of data collection, and willing to participate in the study were included. From the accessible population (N = 524), the sample size was calculated using Raosoft. The margin of error was 5%, at a confidence level of 95%, and the result was 222. Since the participants were not included randomly (convenient instead), the sample was further increased by 10% to account for contingencies such as nonresponse and/or potential dropouts, bringing the final sample size to 244 nurses.

This study used three questionnaires which were a researcher-made personal data sheet, the Organizational Readiness for Implementing Change (ORIC) scale, and Perceived environmental uncertainty in hospitals (PEU-H) scale. A researcher-made personal data sheet included information about the participants such as age, sex, years of experience, position, and educational background. The ORIC scale used was developed by Shea *et al*. (2014) and geared toward assessing the extent to which nurses are ready for organizational change. The questionnaire contains 12 items corresponding to two main domains: change commitment (5 statements) and change efficacy (7 statements).[8] The responses to the questionnaires were assessed on a 5-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). The questionnaire was previously tested for its reliability of scales (α = 0.91 [change commitment] and 0.89 [change efficacy]).[8] The psychometric evaluation or the PEU-H scale was performed to measure nurses' perceptions of uncertainty in the hospital environment.[5] The PEU-H is a 14-item scale that includes two main subscales, namely, environmental attributes and individual attributes. [9]

Environmental attributes were represented by three domains: (a) environmental dynamism or change rate, which refers to "the frequency and magnitude of turbulence in the relevant environment"; (b) environmental complexity, which refers to "the number and diversity of factors that must be considered in decision making"; and (c) environmental dominance, which

describes the environmental dominance of individual actions as "being closely related to the locus of control."

Individual uncertainty refers to the individual's perception that critical information about the environment is unavailable, which results in the inability to accurately predict changes.[9] Individual attributes were represented by the need for information, i.e., "Both content and amount of information affect the perception of uncertainty." Each item was assessed using a 5-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). The validity of the scale is supported by both content experts and acceptable internal consistency reliability (Cronbach's alpha = 0.83).[9] For the negatively worded statements within each scale, the scoring was inverted to enable the processing of the data loaded for statistical analysis.

The questionnaire was translated into Arabic. First, the questionnaire was translated from the original language (English) to the target language (Arabic). Then, it was back-translated from the target language (Arabic) into the original language (English) by another translator who was unaware of the original form of the questionnaire.

The official permission (IRB Number: H-02-K-076-0319-107, 24.04.2019) to distribute the questionnaire was obtained from both hospitals, and the researchers approached the available sample to identify the eligible participants for the present study, and the researchers started to contact nurses who met the inclusion criteria. Then, the researchers distributed the questionnaire to all nurses who met the inclusion criteria and agreed to participate in the study. The estimated time for questionnaire completion was approximately 15 min. Questionnaires were collected from participants in all units. Data were collected in 6 weeks.

Internal validity was measured for both ORIC and PEU-H scales using the Pearson correlation test, where a *p*-value of <0.05 was considered to indicate a correlation between the overall scale and its items; therefore, items measured what they were intended to measure. All items related to ORIC and PEU-H scales were valid and could measure what they intended to measure, since they correlated with the overall scale score and P-values were less than 0.05. The researcher estimated the reliability of both questionnaires; ORIC and PEU-H were tested with Cronbach's α, interitem correlation, and item–total correlation of 0.903.

A pilot study was conducted on 26 nurses to ensure the clarity and applicability of the study measures. No modifications were needed to test the feasibility and applicability of the study tools. Participants of the pilot study were excluded from the actual study.

For data collection, official permission to use the questionnaire was obtained from the authors of the PEU-H scale and ORIC scale. Participants were assured that no personal information would be revealed. They could choose to withdraw from the study at any time without consequences, and confidentiality of the participants' identities was maintained throughout data collection.

A set of descriptive (mean and standard deviation) and inferential statistical tests were used to determine the significant differences and/or associations between and among study variables and groups. Moreover, ANOVA and t-test were used to determine the significant differences between groups. The Pearson correlation coefficient (r) was used to determine the relationship between variables measured on ratio or interval scales. Various methods can be employed to measure correlation and express the relationship between two or more variables. The standard Pearson correlation coefficient (r) measures the extent to which two variables are related. It quantifies the relationship between two variables.[10]

RESULTS

This study aimed to explore whether a relationship exists between work-environment uncertainty and nurses' readiness to participate in organizational change. Of the 244 questionnaire sheets distributed, 237 were returned and seven were not returned, 15 were excluded for being incomplete or having invalid data; thus, 222 were used in the statistical analysis. The response rate was 97.1%.

The vast majority (93.2%) of the study participants were female bedside nurses (90.5%). Moreover, 48.6% of the study participants were 20–30 years old, and 45.9% were 30–40 years old. Moreover, the majority (78.4%) of the study participants had a bachelor's degree and attended neither a change-related workshop (71.2%) nor an innovative program (83.3%). In addition, 34.2% of the study participants had 6–9 years of work experience, and 27.5% had 3–6 years of work experience.

The total mean percentage of environmental dynamism as a dimension of environmental uncertainty was 72.4%. The study participants frequently perceived environmental dynamism as a dimension of environmental uncertainty. In this context, 64.4% of the participants agreed with "have no control over the types of patients in my patient care," and 62.2% agreed that if their patients did not have such complex problems, they could do a better job.

The total mean percentage of environmental complexity as an environmental attribute was 80.0%. Most of the study participants very frequently perceived environmental complexity as a dimension of environmental uncertainty. This was clear in the statements by the nurses who agreed that "if they had

more information about their patient's current condition" they could do a better job, with a positive percentage of 77.5%. Moreover, 73.8% of them positively agreed that they "must take a lot of information into consideration when they plan care for their patients."

The total mean percentage of environmental dominance as an environmental attribute was 70.2%. The study participants frequently perceived environmental dominance as a dimension of environmental uncertainty. Moreover, 67.5% of the nurses agreed that they "have to talk to several health care practitioners (such as physicians, social workers, dieticians, etc.) before they can make decisions about patient care," and 43.2% agreed that "frequent discharges from the unit make it difficult for them to do a good job."

The total mean percentage of environmental dominance as an environmental attribute was 70.2%. The study participants very frequently perceived the need for information as an individual attribute in the work-environment uncertainty: 73.4% of the nurses agreed that "if I got feedback about the patient care decisions I make, I could do a better job," and 73.8% agreed that "if I got timely feedback on unit management decisions (e.g., assignments and staffing) I make, I could do a better job."

The total mean of work-environment uncertainty was 3.77, with a positive percentage of 64.4%. Most of the study participants, with a positive percentage of 71.3%, very frequently perceived environmental complexity, with a mean of 4.0, as a dimension of environmental uncertainty and the most perceived environmental attribute. In addition, the individual attribute of the need for information, with a positive percentage of 69.2%, was very frequently perceived with a mean of 3.84.

Nurses' readiness for organizational change commitment. The total mean percentage of nurses' readiness for organizational change (change commitment) was 64.2%. In addition, 48.6% of the nurses agreed that "people who work here will do whatever it takes to implement this change," and 50.9% agreed that "people who work here feel confident that the organization can support people as they adjust to this change."

Nurses' readiness for implementing change. The total mean percentage of nurses' readiness for organizational change (change efficacy) was 67.0%. Moreover, 51.8% of the nurses agreed that "people who work here want to implement this change," and 52.3% agreed that "people who work here are determined to implement this change." The total mean percentage of nurses' readiness for implementing change was 65.8.

The total mean of organizational readiness for implementing change was 3.29, with a positive percentage of 50.0%. Most study participants, with a positive percentage of 51.8%, very frequently perceived change efficacy. with a mean of 3.35. In addition, change commitment, with a positive percentage of 48.0%, was very highly perceived with a mean of 3.21.

As shown in Table 2, a significant difference was found between the selected characteristics of the participants and ORIC. Table 2 shows that education, working units, job title, and participation in innovation program were significant factors associated with ORIC. Nurses with a master's level of education were more likely to be ready for implementing change compared with nurses with a diploma or bachelor's degree, as indicated by the mean of the total ORIC. Nurses working in emergency department and medical wards had higher levels of readiness for

TABLE 2. Significant difference between the selected characteristics of the participants and organizational readiness for implementing change (ORIC)

Variables	Mean ± SD	*p*
Age (years)		
20 > 30	40.6 ± 12.7	
30 > 40	42.3 ± 11.9	
40 > 50	38.5 ± 14.8	
≥50	36.0 ± 0.01	
Analysis of variance (f-test) (f-value 0.5699)		
Sex		
Female	39.8 ± 13.5	0.683
Male	38.3 ± 15.6	
t-test for independent samples (t-value −0.409)		
Education		
Diploma	34.7 ± 15.3	0.034*
Bachelor	40.2 ± 13.3	
Master	44.6 ± 9.8	
Analysis of variance (f-test) (f-value 3.43) **p* significant at 0.05		
Years of experience		
1 > 3	39.8 ± 15.5	0.737
3 > 6	38.0 ± 15.3	
6 > 9	40.4 ± 12.1	
+ 9	40.4 ± 12.7	
Analysis of variance (f-test) (f-value.422)		
Working unit		
ICU	39.8 ± 13.3	0.048*
Emergency department	40.3 ± 13.3	
Medical ward	40.3 ± 13.0	
Others	27.2 ± 19.7	
Analysis of variance (f-test) (f-value 2.701) **p* significant at 0.05		
Job title		
Nursing admin	45.5 ± 11.6	0.038*
Bedside nurse	39.0 ± 13.7	
t-test for independent samples (t-value 2.09) **p* significant at 0.05		
Join an innovative program		
No	40.7 ± 14.0	0.002**
Yes	34.4 ± 10.4	
t-test for independent samples (t-value 3.11) ***p* significant at 0.01		
Attend change-related workshop		
No	40.0 ± 12.9	0.594
Yes	38.8 ± 15.4	
t-test for independent samples (t-value 0.534)		

implementing change. In addition, administrative nurses were more likely to be ready for implementing change compared with bedside nurses, as shown by the means of ORIC and ensured by the *p*-value of the t-test for independent variables.

As shown in Table 3, a significant difference was found between the selected characteristics of the participants and perceived environmental uncertainty (PEU). The table shows that educational level was significantly associated with PEU. The higher the educational level of nurses, the lower the PEU, as indicated by the means of PEU. Administrative nurses had PEU slightly less frequently than bedside nurses.

Table 4 summarizes the results of the correlation analysis of the study variables. ORIC significantly and positively correlated with ORIC-CC, ORIC-CE, and PEU-IN. In addition, ORIC-CC significantly and positively correlated with PEU-IN. ORIC-CE negatively correlated with PEU-EDO and positively correlated with PEU-IN. PEU positively correlated with the subcomponents of PEU.

TABLE 3. Significant difference between the selected characteristics of the participants and perceived environmental uncertainty (PEU)

Variables	Mean ± SD	*p*
Age (years)		
20 > 30	52.5 ± 10.8	0.553
30 > 40	53.5 ± 12.1	
40 > 50	54.3 ± 11.2	
≥50	43.0 ± 0.01	
Analysis of variance (f-test) (f-value 0.594)		
Sex		
Female	52.8 ± 11.2	0.448
Male	55.1 ± 13.7	
t-test for independent samples (t-value 0.760)		
Education		
Diploma	54.4 ± 10.1	0.001**
Bachelor	49.7 ± 15.5	
Master	43.9 ± 9.8	
Analysis of variance (f-test) (f-value 6.968) ***p* significant at 0.01		
Years of experience		
1 > 3	53.5 ± 12.4	0.727
3 > 6	52.0 ± 13.9	
6 > 9	54.0 ± 9.0	
+ 9	52.3 ± 10.6	
Analysis of variance (f-test) (f-value.436)		
Working unit		
ICU	53.0 ± 12.1	0.195
Emergency department	54.9 ± 10.3	
Medical ward	51.0 ± 11.5	
Others	54.1 ± 12.5	
Analysis of variance (f-test) (f-value 1.650)		
Job title		
Nursing admin	52.8 ± 11.4	0.393
Bedside nurse	55.0 ± 10.9	
t-test for independent samples (t-value.856)		
Join an innovative program		
No	53.4 ± 11.3	0.267
Yes	51.1 ± 11.6	
t-test for independent samples (t- value 1.126)		
Attend change-related workshop		
No	52.3 ± 12.0	0.191
Yes	54.5 ± 9.5	
t-test for independent samples (t-value 1.312)		

DISCUSSION

Regarding nurses' perceptions of work-environment uncertainty, this study investigated environmental dynamism as an environmental attribute. The result of the study reflects that most study participants agreed that they have no control over the types of patients in their care, and more than half agreed that if their patients did not have such complex problems, they could do a better job. In this study, two-thirds of nurses frequently perceived environmental dynamism in their work-environment. Environmental dynamism or change rate had a high percentage of agreements. This has been normal for the health sector for the past decade. Healthcare changes strategies, systems, and reforms to provide equitable, effective, and efficient care. These changes are applied to all business, clinical, and operation models.[11] Likewise, when a human service organization manager was asked about the reason for the need to acquire business, finance, and management skills, the answer was the continual change in their environment.[12] Transformational leadership behavior is better where environmental dynamism is high. This gives us the insight that strategic leadership decisions are based on the work-environment situation. Another study stated that in a more dynamic environment, transformational leadership behavior by CEOs was more beneficial to the pursuit of organizational innovation.[13]

In addition, the present study shows environmental complexity as an environmental attribute. The results of this study reflect that most nurses agree that if they had more information about their patient's current condition, they could do a better job, as most of them have to consider large data when they plan care for their patients. In this study, all nurses frequently perceived environmental complexity in their work-environment. This is consistent with a finding that was confirmed in the present study, i.e., nurses agreed that environmental complexity had the highest percentage among environmental attributes. Multiple issues came with complexity. Conceptual ambiguity is a type of uncertainty that emerges from complexity, and ambiguity is a strong predictor of turnover intention among new graduate nurses[14] and, as examined, will affect their performance.[15] As presented previously, two-thirds of the participants agreed that if their patients did not have such complex problems, they could do a better job.

TABLE 4. Correlation between work-environment uncertainty and nurses' readiness to implement organizational change

	ORIC	ORIC-CC	ORIC-CE	PEU	PEU-EDY	PEU-ECO	PEU-EDO	PEU-IN
ORIC	1.000							
ORIC-CC	0.919**	1.000						
ORIC-CE	0.866**	0.763**	1.000					
PEU	0.041	0.065	0.024	1.000				
PEU-EDY	−0.122	−0.092	−0.140	0.515**	1.000			
PEU-ECO	0.148	0.132	0.155	0.582**	0.537**	1.000		
PEU-EDO	−0.157	−0.107	−0.187*	0.563**	0.040	0.184*	1.000	
PEU-IN	0.186*	0.203*	0.169*	0.623**	0.379**	0.425**	0.373**	1.000

*Significant at 5% **Significant at 1% Pearson's correlation coefficient (r)
ORIC: Organizational Readiness for Implementing Change; CC: Change Commitment; CE: Change Efficacy; PEU: Perceived Environmental Uncertainty; EDY: Environmental Dynamism; ECO: Environmental Complexity; EDO: Environmental Dominance

Furthermore, regarding the individual attribute of the need for information, more than half of the nurses said that if they got feedback about the patient care decisions, they think they could do a better job. In addition, if they got timely feedback on unit management decisions (e.g., assignments and staffing) they made, they could do a better job. Most of the analyzed nurses frequently perceived the need for information as an individual attribute in their work-environment. Because of the diversity of factors that nurses must consider regarding patient care decisions from their managers and other practitioners, feedback is an important part of nurses' performance. The results of this study matched those of a study analyzing the relationship between hospital competition and probability of medical arguments, which, according to the social control theory, revealed that feedback has a great influence on hospital staff decisions.[16] In addition, for undergraduates to effectively accomplish their educational objectives, they need informative feedback that is timely and descriptive.[17]

In this study, two-thirds of the nurses perceived that people who work in both hospitals will do whatever it takes to implement this change, along with the perception that people who work in the organization feel confident that the organization can support people as they adjust to this change. Moreover, more than half of the nurses agreed that people who work in the organization are committed to implementing the change. In addition, more than half of the nurses studied agreed that people who work in the organization feel positive toward the change efficacy of implementing the change. Change efficacy scored slightly higher than change commitment. The results of the study were incompatible with those of a study conducted at a Danish Obstetrics and Gynecology Department assessing the organizational readiness of all employees for implementing a large-scale change. The results show high commitment and lower efficacy.[18] In another study in hospitals across Switzerland, with a sample of 1,833 registered nurses, change commitment was rated slightly higher than change efficacy.

Study results showed a significant difference in the mean level of nurse's perceptions of work-environment uncertainty and education and a significant difference in the mean level of nurses' readiness for organizational change and education, working unit, and job title. The results of this study contradict those of other studies, which did not find significant relationships between any of the demographics and other characteristics and readiness for change.[18] Along with the significant correlation between education and work-environment uncertainty in the present study, a study found through a focus group interview with a participant that in the context of uncertainty in the organization, the more training and education an employee had, the more they could manage work-environment uncertainty.[19] This was also observed in the present study, as bedside nurses had more work-environment uncertainty than administrative nurses. From the researcher's perspective, this may be due to information sharing and involvement in decision making between frontline staff and nurses' managers. Thus, an uncertainty in a work-environment, especially manager uncertainty, will negatively affect information sharing with frontline nurses. In addition, the readiness level to implement organizational change was higher in nurses in administrative positions because managers were all directly involved in and accountable for the change implementation in the organization; thus, they may have had a better understanding of the change's purpose and had access to the resources available.[18] The results of this present study show a strong correlation between the nurses' readiness for implementing organizational change and their components of change commitment and change efficacy and between one another. In addition, a correlation was noted between nurses' perceptions of work-environment uncertainty and components of environmental dynamism, complexity, and dominance.

Even with a complex unpredictable environment and a shortage of information, nurses present with an acceptable readiness to implement organizational change. Correspondingly, a positive and interesting

readiness to implement organizational change among nurses has multiple explanations. First, Saudi Arabia is an eastern country that predominantly has a collectivist national culture according to Hofstede, where people have social tightness and feel that they are a part of a group and tend to look after each other. It makes sense to have a high level of readiness when it comes to implementing organizational change since it reflects both organizational members' shared resolve to execute a change (change commitment) and belief in their group's ability to do so (change efficacy). Second, most of the researched samples are generation Y (millennials), who from their characteristics are optimistic about the future and their ability to overcome challenges and have strong social relationships. They are early adopters of any innovation in the organization.[20] Finally, when an organization is going through a large-scale change, its employees gained the perception that change is required. Staff perceived the change as something that "has to" be done but left them with some uncertainties about what "to do" and "how to" do it.[18] Likewise, the Hawthorne effect or, as Paradis and Sutkin start referring to it, "participant reactivity" is defined as "participants' active engagement with the research and its aims, a process that leads to behavioral adaptation that aligns with perceived social norms."[21] It is important to realize that the organizational work-environment under many changes is presented as follows: going into "transition phase"; complex; fast and uncertain; the organizational change is socialized; and the demands to adjust to these changes are a social responsibility.

The need to have a high organizational readiness to implement organizational change is important in the age of agile organizations and competitiveness. The results of this study could be used by healthcare organization leaders to encourage employees of the organizations' ability to implement changes, in particular their collective capability to implement a change in the healthcare sector. In addition, strategies must be set to reduce work-environment uncertainty and elevate the organizational readiness to implement change, followed by continued tracking of the change projects to ensure sustainability. Moreover, the hospital administration must develop an information system. This is to transmit information in a timely systemic manner to and from all organization management levels in times of uncertainty and before a change initiative to keep all staff involved. In addition, nurses from the frontline must be included in the change initiative project as a whole and in making decisions on their unit.

The study did not demonstrate the association between PEU-H and ORIC. However, to determine a relation, a study can be replicated with other variables such as information sharing or information quality as predictors for change readiness or environment uncertainty. The generalizability of the findings is limited by the focus on one setting and one category of participant (i.e., nurses) and results may change from one setting and/or participant category to another. Regarding participant selection, not all those studied were actively involved in developing specific changes in workshops or as participants in working groups. During data collection, the researcher helped the head nurses distribute the survey sheet to their staff; this action may interfere with participant voluntary response, since it may affect their response. Further research can be applied to study both work-environment uncertainty and ORIC among healthcare providers, which will provide a wider picture of organizational environment conditions involving every employee.

CONCLUSIONS

The study findings revealed that the ORIC is high. Moreover, environmental complexity was frequently perceived among nurses as one of the work-environment uncertainty dimensions. The organizational environment must be investigated with consideration of employee characteristics to promote their knowledge, skills, and aptitude toward adapting to change and uncertainty. Supportive efforts between hospital management, nursing directors, and decision-makers are needed to investigate the organizational environment conditions with consideration of employee characteristics and promotion of their knowledge, skills, and attitude to adapting to change and uncertainty in a dynamic complex health service environment. Organizations must undertake training sessions representing the concepts of change management and how to be a change agent to all hospital staff, including nurses. In addition to information management, the important aspect of communication is how/when/where information is disseminated.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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Unmet Need for Family Planning in Indonesia and Its Associated Factors

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Unmet Need for Family Planning in Indonesia and Its Associated Factors

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Abstract

Background: The unmet need for family planning in Indonesia has been stagnant since the early 2000s in the 10%–12% range with substantial socioeconomic and geographic disparities. This study sought to better understand the factors underlying the nonuse of contraceptives among women with an apparent need for family planning so that evidence-based corrective actions can be taken.

Methods: Three sources of quantitative data were used in the study—the 2017 Indonesia Demographic Health Survey, the 2018 Village Potential Survey, and the National Population and Family Planning Board service statistics. Further insights were obtained from online focus group discussions and in-depth interviews with participants in 12 districts/cities in seven provinces.

Results: The analyses indicated that health concerns, service delivery-related factors, and opposition to family planning all contribute to the unmet need for family planning in Indonesia. Importantly, the salience of these factors varied significantly across different subgroups of women and geographic areas.

Conclusions: Successful efforts to reduce the unmet need for family planning are complex in that they must contend with the interplay between local sociocultural contexts, individual beliefs/aspirations/preferences, and the supply environment of family planning services. Differentiated interventions for different population subgroups and geographic areas will be needed.

Keywords: family planning, Indonesia, unmet need

INTRODUCTION

Since its introduction more than 50 years ago,[1] the unmet need for family planning has been among the more widely used metrics for monitoring the performance of family planning (FP) programs. The unmet need for family planning is defined as the percentage of women of reproductive age who do not want to become pregnant but are not using contraception.[2] The unmet need for family planning can be further divided into two components: (1) unmet need for limiting, defined as the proportion of women of reproductive age who do not want any more children but are not using a contraceptive method, and (2) unmet need for spacing, which consists of women of reproductive age who would like to postpone their next pregnancy by at least two years but are not using any method of family planning. Unmet need can also be defined in terms of the use of modern vs. all contraceptive methods, the latter of which includes traditional methods (i.e., the de facto unmet need for modern methods).

Although there has been some recent criticism of the unmet need metric because it does not capture consumer satisfaction with the methods they are using, which raises questions as to the extent to which need is being satisfied,[3,4] unmet need remains an important metric for national family planning for several reasons. One reason is that the failure of a national family planning program to facilitate the satisfaction of the reproductive aspirations of both women and couples is viewed as a failure to implement rights-based criteria for family planning.[5–8] Rights-based family planning is endorsed as an underlying principle by most countries of the world, including Indonesia.

Beyond issues related to reproductive rights, global evidence shows that family planning is among the most cost-effective public health (as well as overall development) interventions available to countries, with the potential to reduce both maternal and child mortality.[9] A study by Ahmed *et al*. quantified the magnitude of potential gains of reductions in the unmet need for family planning in a multicountry study. The

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authors estimated that if the proportion of satisfied demand for family planning were to reach 100%, unwanted pregnancies would be reduced by 70%, maternal deaths by 25%, and neonatal deaths by 18%.[10]

Reducing the unmet need for family planning is challenging due to the myriad and complex nature of factors that contribute to unmet needs. A study conducted in 52 countries[11] reported that the most common reasons for the unmet need for family planning among women of reproductive age fell into four categories: (1) concerns about side effects and health risks (26%), (2) no or infrequent sexual intercourse (24%), (3) opposition to contraceptive use (23%), and (4) postpartum amenorrhea/breastfeeding after having a baby (20%). A sizable number of individual–country studies have identified a wide variety of correlates of the unmet need for family planning, most of which were variations on the four basic categories of underlying reasons noted above, but also entailed life cycle and setting-specific contextual factors.[12–32]

Further reducing the unmet need for family planning in Indonesia is important for both human rights and maternal/neonatal health reasons. Regarding human rights, a recent study[33] documented significant gaps between the Indonesian government's rights-based principles and actual implementation of family planning programs, especially concerning informed choice and the wide socioeconomic and geographic disparities in demand and the unmet need for family planning. Regarding maternal health, Indonesia continues to struggle with high levels of maternal mortality, with a maternal mortality ratio of 305 per 100,000 live births in 2015,[34] far above the global Sustainable Development Goals (SDGs) 2030 target of 70 per 100,000 live births and the National Development Strategic Plan (*RPJMN*) 2020–2024 target of 183 per 100,000 live births.[35] As described above, in a multicountry study, there is potential to avert maternal mortality if unmet needs are reduced. The importance of family planning for maternal mortality reduction in Indonesia was demonstrated in a recent study that estimated that every percentage point increase in the contraceptive prevalence rate (CPR) was associated with maternal mortality ratios that were lower by 7.0 deaths per 100,000 live births.[36] This is achieved through the reduction of unwanted and high-risk pregnancies, which may lead to maternal deaths.

Contraceptive prevalence in Indonesia has risen steadily over the years, with the CPR reaching 63.6% in 2017.[37] However, while there was a slight decrease in the unmet need for family planning between 2012 and 2017 from 11.4% to 10.5%, the unmet need for family planning has been stuck in the 10%–12% range since the turn of the century.[37]

In the present study, we combine detailed reanalyses of existing data with new qualitative data to better understand the underlying factors that have led to stagnant levels of unmet need for family planning in Indonesia. The focus of the analyses is toward identifying evidence-based corrective actions that might be taken to move the needle on unmet needs and maternal mortality in Indonesia.

METHODS

This study has ethics clearance from Atmajaya University. The number is 00291/III/LPPM-PM.10.05/09/2021. A mixed-methods approach was adopted for the study. The study used a concurrent triangulation design of mixed methods as both quantitative and qualitative data were collected and analyzed simultaneously. This is done to reach a better understanding and enrich the findings on the unmet need for family planning in Indonesia, although it also requires more resources and careful analysis to conduct. Quantitative and qualitative data and the methods used to analyze them are described in separate sections below.

Quantitative data

Three sources of quantitative data were analyzed in the study: the 2017 Indonesia Demographic Health Survey (IDHS), the 2018 Village Potential Survey (PODES), and National Population and Family Planning Board (BKKBN) service statistics. The IDHS sample consisted of 35,681 currently married women aged 15–49 years. The IDHS 2017 data were used to measure the unmet need for family planning and potential correlates thereof: sociodemographic and economic characteristics, husband–family factors related to family planning, and women's living environment characteristics. The PODES data were used to measure community-level characteristics related to health infrastructure for family planning services. The BKKBN service statistics were used to measure the volume of community-level family planning activities.

Data processing and analyses were undertaken using Microsoft Excel and Stata ver. 16 licensed to Knowledge Hub for Reproductive Health Indonesia. Logistic regression was used to undertake multivariate analysis.

A substantial portion of the quantitative analyses focused on 2017 IDHS data on reasons for nonuse of contraception among female IDHS respondents who wanted to limit or delay future pregnancies but were not using a contraceptive method at the time of the survey. The reasons stated were grouped into useful analytic categories, ranked in terms of importance, and compared between different population subgroups (e.g., women classified by age, education, and household wealth).

Variables used in the analysis were age, education (none, primary, secondary), working status, wealth index

(poorest, poorer, middle, richer, richest), residence (urban, rural) and region (Western, Central, Eastern Indonesia). Other variables used were parity, birth interval, husband's approval of contraceptive use, husband's ideal number of children, FP discussion with family/relation, source of FP information, distance to health facility, method knowledge, exposure to mass media (radio, tv, newspapers), physician density (number of physicians per 1,000 population), midwife density (number of midwives per 1,000 population), FP field officer density (number of FP field officers per 1,000 population), and the unmet need for FP.

Qualitative data

Qualitative data collection was undertaken via online focus group discussions (FGDs) and in-depth interviews (IDIs). Five (5) informant groups were : a) Group 1: Married women of reproductive age (WRA) with unmet needs (attended by 24 women); b) Group 2: Family planning (FP) program managers 1–Representatives of district and provincial health offices (attended by 20 persons); c)Group 3: FP program managers 2–Representatives of district FP officers, province FP officers, and BKKBN province (attended by 24 persons); d) Group 4: Health providers from hospitals and primary health centers (attended by 20 persons); e) Group 5: FP field officers and cadres (attended by 23 persons).

IDIs were conducted by phone with male partners of women with unmet needs who participated in the FGDs. The information obtained via the FGDs and IDIs with individual female and male respondents consisted of (1) Knowledge about FP and (2) Reasons for not using contraceptives. Information from program managers, health providers, and FP field officers/cadres consisted of (1) FP program planning and implementation, (2) Constraints/challenges of program implementation, and (3) Lessons learned concerning the unmet need for FP.

Qualitative data collection was undertaken in 7 provinces and 12 districts/cities across the Western, Central, and Eastern regions of Indonesia which were selected based on high percentages of unmet needs and low CPR according to BKKBN service statistics. Before data collection, coordination with the Ministry of Health (MoH) and the BKKBN was performed to select informants based on the stated criteria and develop the questions and data-collection methods that aligned with the quantitative methods and research questions. All FGD and IDI activities were recorded, transcribed, and subjected to thematic content analyses.

RESULTS

Quantitative findings

Table 1 presents the distribution of married WRA included in the IDHS 2017 sample by background characteristics. Over half of the women were in the group of 35–49-year-olds and had a complete primary education. The majority of women were working. Respondents were more or less equally distributed by the level of household wealth. Slightly more respondents lived in rural than urban areas, and most (82.4%) lived in Western Indonesia, reflecting the wider population distribution of the country.

Table 2 presents the results of a multivariable logistic regression analysis of correlates of the unmet need for FP. As may be observed, only two of the six sociodemographic factors included in the analyses emerged as statistically significant—parity and birth interval length. Women of parity four or higher and those whose last completed birth interval was less than 24 months were significantly more likely to have an unmet need for FP. The fact that no significant differences emerge in terms of the socioeconomic variables is a credit to the national FP program regarding its ability to provide services to women and families at all socioeconomic levels.

Unmet needs were strongly influenced by the husband's views on contraception and family engagement in FP discussions. Married WRA whose husbands approved of contraception were 5.5 times less likely to have an unmet need than those with a husband who disapproved. Women who discussed FP with their families had 46% lower adjusted odds of having unmet needs. Husband–wife differences in the ideal number of children were unrelated to unmet needs.

Regarding program factors, the provision of FP information by health workers had the greatest influence. Compared to women who never received FP information, women who received the information from health workers had 32% lower odds of having unmet needs (AOR = 0.68, 0.60–0.78). Women who perceived that the distance to a health facility was a big problem were 20% (AOR = 1.20, 1.03–1.39) more likely to have unmet needs than women who did not perceive the physical distance to a health facility to be an issue. No significant association of unmet needs with exposure to mass media was observed.

Among local FP supply environment factors, only the number of midwives per 1,000 population had a significant association with unmet needs. However, a high population density of midwives is associated with somewhat lower odds of unmet needs, as might be expected (AOR = 1.20, 1.05–1.38).

Table 3 provides a summary of the reasons given by 2017 IDHS who indicated a desire to space out or limit future births for not using contraception at the time of the survey. The data displayed employed the categories used in the IDHS survey to collect the data, and the respective reasons are displayed separately for women

with demand for spacing out and limiting future births. Four reasons were given by 10% of respondents or more—lack of access (19.7%), fear of side effects (18.8%). infrequent sex (18.1), and postpartum amenorrhea (11.3%). As may be observed, the relative importance of several reasons varied depending on women's desire to space out births vs. limiting future births.

Table 4 shows the reason given by groups of women for not using contraceptives, based on socioeconomic factors. The group division consisted of Group 1, namely, a group of women who did not use contraceptives due to opposition to their use; Group 2's nonuse was due to health concerns; Group 3's nonuse was due to service delivery issues; Group 4's nonuse was due to postpartum amenorrhea; and Group 5's nonuse was due to infrequent sex.

Noncontraceptive use for women who had a demand or need for FP for reasons of "opposition to use" (Group 1) seems to be more common among women with lower education and in low-income households. Nonuse due to"health concerns" (Group 2) on the other hand, tends to be higher in urban areas, among women with higher education and residing in the wealthiest households. Similar to Group 1, nonuse due to "service delivery issues" (Group 3) was also seen to be higher among women with lower education and in low-income households, but only slightly so. Women with lower levels of education were less likely to cite having postpartum amenorrhea (Group 4) as the reason for nonuse of contraception, while no clear pattern of socioeconomic differences emerged from the data in Table 5 concerning nonuse of contraception due to infrequent sex (Group 5).

Although differences by urban–rural residence are relatively muted (see Table 4), differentials by province are rather more pronounced (Table 5). Women who do not use contraception due to "opposition to use" (Group 1) tend to reside in selected provinces mostly in Eastern Indonesia, such as Papua (at27.2%, the highest), Maluku (12.1%), and East Nusa Tenggara (11.8%). There might be cultural belief factors behind this high number. In Group 2, due to "health concerns," the number of nonuse women tends to be very high in Western Indonesia, such as 35.2% in Jakarta and 34.9% in Lampung, and very low in certain provinces in Eastern Indonesia, such as 13.7% in Papua. Noncontraceptive use due to "service delivery issues" (Group 3) tends to be higher in certain provinces, especially in Central Indonesia, such as North Kalimantan (36.6%), and in Eastern Indonesia such as Maluku (45.3%, the highest). Nonuse of contraception due to postpartum amenorrhea (Group 4) tends to be the highest on the island of Sumatra and lowest in Eastern Indonesia. Nonuse due to infrequent sex, on the other hand, tends to be less frequent in Sumatra and Eastern Indonesia and more frequent in Java and selected provinces in Central Indonesia.

TABLE 1. Respondent characteristics (N = 35,681)

Variable	Married women of reproductive age (%)
Age	
15–19	2.0
20–34	43.2
35–49	54.8
Education	
No education/incomplete primary	10.9
Complete primary/incomplete secondary	50.8
Complete secondary/higher	38.3
Working status	
Not working	38.4
Working	61.6
Wealth index	
Poorest	17.7
Poorer	19.9
Middle	20.7
Richer	21.2
Richest	20.5
Residence	
Urban	48.4
Rural	51.6
Region	
Western Indonesia	82.3
Central Indonesia	13.6
Eastern Indonesia	4.1

TABLE 2. Logistic regression analysis of correlates of unmet needs for family planning

Variable	Unmet Need	
	Adjusted Odds Ratio (AOR)	95% CI
Age		
15–19[Ref]	1.00	
20–34	1.46	0.08–27.6
35–49	2.14	0.11–40.4
Education		
No education/incomplete primary[Ref]	1.00	
Complete primary/incomplete secondary	0.98	0.84–1.14
Complete secondary/higher	0.98	0.82–1.16
Working status		
Not working[Ref]	1.00	
Working	0.92	0.84–1.01
Wealth index		
Poorest[Ref]	1.00	
Poorer	1.07	0.92–1.26
Middle	1.10	0.94–1.30
Richer	1.15	0.97–1.37
Richest	1.21	0.99–1.46

*$p < 0.05$

TABLE 2. Continued

Variable	Unmet Need	
	Adjusted Odds Ratio (AOR)	95% CI
Parity		
<4[Ref]	1.00	
4 or more	1.38*	1.23–1.55
Birth interval		
≥24 months[Ref]	1.00	
<24 months	1.29*	1.10–1.52
Residence		
Urban[Ref]	1.00	
Rural	0.90	0.81–1.00
Region		
West Indonesia[Ref]	1.00	
Central Indonesia	1.28*	1.06–1.53
East Indonesia	1.71*	1.40–2.29
Husband's approval of contraceptive use		
Approves[Ref]	1.00	
Disapproves	5.50*	4.55–6.57
Husband's ideal number of children		
Wants the same[Ref]	1.00	
Wants more	0.92	0.82–1.04
Wants fewer	1.02	0.82–1.26
FP discussion with family/relation		
Yes[Ref]	1.00	
No	1.54*	1.40–1.70
Source of FP information		
Never obtain FP info[Ref]	1.00	
From health workers	0.68*	0.60–0.78
From the FP field officers	1.14	0.84–1.53
From health workers and FP field officers	0.98	0.80–1.21
Distance to health facility		
Not a big problem[Ref]	1.00	
Big problem	1.20*	1.03–1.39
Methods knowledge		
Know ≥7 methods[Ref]	1.00	
Know <7 methods	1.09	0.98–1.21
Exposure to mass media (radio, tv, newspapers)		
Accesses 1–3[Ref]	1.00	
Accesses to none	1.09	0.82–1.45
Physician density		
≥1.3 per 1,000 pop[Ref]	1.00	
<1.3 per 1,000 pop	1.03	0.90–1.73
Midwife density		
≥2.5 per 1,000 pop[Ref]	1.00	
<2.5 per 1,000 pop	1.20*	1.05–1.38
FP field officer density		
≥1.2 per 1,000 pop[Ref]	1.00	
<1.2 per 1,000 pop	0.94	0.81–1.09

*p <0.05

Qualitative findings

Reasons for not using contraceptive methods

Based on the results of FGDs and IDIs, all groups of informants stated that the main reason for not using contraception was the fear of side effects, especially with the use of short-term contraceptive methods such as pills and injectables. Most admitted that they had headaches and felt weak while taking the pills, and the side effects of using injectables were weight gain and irregular menstruation. It also made the husbands disapprove of using contraception for the fear of side effects and disliking it if their wives gain weight. Some men also said they did not know much about other contraceptives, mostly long-term methods such as the Intrauterine Device (IUD) and implants, therefore, they were doubtful about their safety. In addition, as with the quantitative findings, many couples of reproductive age did not use contraception because one of them works outside town/island or far away which leads to infrequent sex.

"My reason is like this, when my fourth child was already 1 year old, I used pill then after 2 years I felt like unwell, felt a headache every day, lazy, then I tried to not use it for several months and actually I feel okay 4 years now, still well and safe. Due to the side effect that made me weak. I had used pill but always had complaints. So, I tried after my fourth child using pill but still like that. I have not tried implant." DA, female, 42 years old, Mahakam Ulu

"…My husband does not support using contraceptive because afraid I will gain weight." NJ, female, 22 years old, South Sorong

"I am afraid with chemical ingredients in pill. If it consumed every day, it may have side effect that affect kidneys or others, right. I do not use condom because, I have told by my friend too, but I am just afraid to use it. To use other contraceptives like injection, I am also afraid. If we use it, afraid it will have side effects…" N, male, 38 years old, Samarinda

Information was obtained from health workers, FP field workers, and cadres; in some cases, women were reluctant to use contraception because they already felt old (even though they were still of reproductive age) so they thought it was impossible or very unlikely that they would get pregnant again. Another reason is related to family beliefs such as patriarchy or traditional beliefs that prohibit contraceptive use. For example, in the South Nias District, there is a tradition that sons are the successors of the family so women are expected to keep having pregnancies until they gave birth to a son. Even though women want to limit having children, usually their husbands and family (such as in-laws) will oppose her use of contraception.

"About unmet need, usually they are not using contraceptive anymore because they already feel at old age, but if we look at our target data of couple in 15-49 years old, they actually are still at the age of 43 or 42" IB, Puskesmas health worker, South Sorong

Other reasons for noncontraceptive use that were stated by FP program managers were the lack of knowledge and difficulty in accessing health services. The access difficulty mostly happened in outer islands or mountain areas, which are far from health facilities and require large costs for transportation. This is consistent with quantitative findings, which also report that the lack of method knowledge and problems in accessing health facilities mean higher odds of unmet need.

TABLE 3. Reasons for not using contraception among women with an unmet need for spacing and limiting

Reason given	Demand for spacing (%)	Demand for limiting (%)	Total (N = 3,802) (%)
Fertility-related reason			
Not having sex	1.9	1.1	1.3
Infrequent sex	18.7	17.8	18.1
Postpartum amenorrhea	21.5	7.2	11.3
Breastfeeding	7.3	1.6	3.2
Fatalism	0.9	2.2	1.8
Opposition to use			
Respondents opposed	1.3	2.6	2.2
Husband/partner opposed	4.2	2.4	2.9
Others opposed	0.2	0.2	0.2
Religious prohibition	0.3	0.5	0.5
Lack of knowledge			
Knows no method	0.9	0.4	0.5
Knows no source	0.2	0.1	0.1
Method-related reason			
Lack of access/too far	21.3	19.1	19.7
Too costly	1.0	0.4	0.5
Preferred methods not available	1.2	2.6	2.2
No method was available	0.3	0.2	0.2
Fear of side effects	10.6	22.2	18.8
Inconvenient to use	0.0	0.1	0.1
Interferes with the body's processes	5.4	6.1	5.9
Weight gain/loss	3.6	2.5	2.8

TABLE 4. Group of nonuse contraceptive women based on socioeconomic factors (N = 3,802)

	Group 1 (%)	Group 2 (%)	Group 3 (%)	Group 4 (%)	Group 5 (%)
Type of residence					
Urban	6.0	29.2	22.4	7.8	14.8
Rural	4.9	23.0	22.4	10.1	15.8
Education					
No education	15.5	18.1	27.4	2.9	6.7
Primary	5.2	26.8	21.1	4.5	16.2
JHS	4.1	27.3	21.8	9.0	18.1
SHS	5.0	23.9	24.1	13.9	14.8
Academy	11.1	21.3	20.7	18.9	10.2
University	5.3	31.2	23.2	14.8	11.1
Wealth index					
Poorest	7.4	21.4	25.2	9.5	13.1
Poorer	5.1	23.3	22.2	9.4	17.3
Middle	4.9	25.8	23.0	8.2	16.9
Richer	5.1	27.6	22.2	8.8	14.8
Richest	4.7	31.5	19.8	8.9	14.5

TABLE 5. Group of nonuse contraceptive women based on provincial differences

Province	Group 1 (%)	Group 2 (%)	Group 3 (%)	Group 4 (%)	Group 5 (%)
Aceh	4.8	27.8	21.0	13.4	5.0
North Sumatra	3.7	22.9	29.3	14.2	6.1
West Sumatra	4.5	21.9	35.9	16.1	10.2
Riau	5.9	24.8	30.9	12.2	12.0
Jambi	5.8	29.9	13.5	21.2	9.8
South Sumatra	1.1	23.5	15.5	9.8	11.9
Bengkulu	7.6	31.1	15.0	18.3	7.1
Lampung	6.7	34.9	27.3	7.6	11.3
Bangka Belitung	1.7	32.2	40.4	16.5	18.6
Riau Islands	10.0	23.4	23.3	5.4	15.2
Jakarta	6.9	35.2	28.7	5.8	12.1
West Java	4.7	32.7	17.9	6.3	14.4
Central Java	6.3	25.4	14.9	7.7	21.1
Yogyakarta	0.0	15.8	11.9	9.9	30.0
East Java	2.0	20.9	19.6	10.2	24.1
Banten	6.4	34.5	16.1	6.7	6.6
Bali	7.3	19.0	24.7	8.7	17.3
West Nusa Tenggara	2.8	22.0	31.3	13.0	15.9
East Nusa Tenggara	11.8	28.0	28.1	6.6	13.8
West Kalimantan	2.1	26.7	10.6	8.7	15.2
Central Kalimantan	0.0	22.1	26.5	13.9	18.3
South Kalimantan	4.0	16.3	25.9	9.9	25.9
East Kalimantan	6.1	26.3	33.3	13.8	17.9
North Kalimantan	5.2	37.5	36.6	14.7	14.0
North Sulawesi	0.0	25.1	26.1	5.9	25.7
Central Sulawesi	8.4	26.5	32.7	3.3	12.5
South Sulawesi	4.0	11.5	33.9	8.3	14.5
Southeast Sulawesi	4.8	13.7	28.5	15.0	16.2
Gorontalo	9.6	16.0	31.7	2.9	9.4
West Sulawesi	4.7	17.1	33.4	9.7	17.3
Maluku	12.1	19.3	45.3	5.7	9.2
North Maluku	4.6	21.0	19.6	7.3	8.9
West Papua	4.4	23.3	29.4	6.0	13.6
Papua	27.2	13.7	23.9	9.2	11.3

Another factor for not using contraceptives is the lack of support from the local government. One mentioned case was not supporting the National Family Planning Board (BKKBN) program "two children are enough" because there is suspicion that this program would gradually eliminate certain local ethnicities.

Obstacles or challenges of the FP program

Most of the informants mentioned the lack of service provider competency as a constraint to the FP program. Many service providers claimed they need to update their knowledge of FP services, but it had been a long time since the last training was received. Some also stated that they had not received any FP training or certification so they could not provide further services, such as the insertion or removal of the IUDs.

"... There are some obstacles that had been informed also about certification. That is one of the obstacles for the midwife, many midwives have competency (to do the services), but do not have certification. So that they cannot do services" GE, OPDKB Kupang

Another obstacle to the FP program is the availability of contraceptives, stock scarcity, or expiry experienced in some areas. It affected the delivery of contraceptive services and could lead to the low achievement of FP program targets. Many informants from the Central and Eastern regions of Indonesia mentioned these problems. Distribution delays or stock shortages have occurred from a few weeks to six months. Some claimed that it could be made worse due to the COVID-19 pandemic. In addition, the FP program constraints occur due to the

lack of access, which makes it difficult to reach out to the community and hinders the distribution of logistics.

"Stock of contraceptive was run out in the past 6 months, or maybe because our condition in Wakatobi is quite difficult or maybe because of the pandemic…" AH, Wakatobi health officer

Several program managers also mentioned the unsynchronized recording and reporting of FP data between the MoH and the BKKBN as a program obstacle. They pointed out the negative effects of the lack of synchronization on program planning and monitoring.

DISCUSSION

The factors underlying the unmet need for FP in Indonesia are both several and complex. In a broad perspective like those observed in other countries, the key underlying factors vary across different population subgroups and geographic areas, ruling out simple one-size-fits-all solutions.

One theme concerning factors underlying unmet needs identified in the analyses concerns opposition to their use by husbands and family members. The results of this and a parallel study of male involvement in FP in Indonesia[38] show that support from husbands/partners and discussions about contraceptive use with family members have a positive impact on female contraceptive use. Comparable findings have been reported in studies in other countries.[19,24,29,30] Overall, male opposition to FP in Indonesia is low (4.3% as per the 2017 IDHS) but is more common in Eastern Indonesia, especially in Papua. The engagement of political and religious leaders and other public opinion influencers will, thus, be essential in addressing this issue. Promotional campaigns targeted at males, and more specifically to males of low socioeconomic status, to increase support for FP will be needed. Program efforts should be directed to increasing not only male approval of FP, but also active male involvement as FP clients, partners, or agents of change, each of which can make contributions to reducing the unmet need for FP.[39]

A second major theme emerging from the analyses was health concerns, most notably the fear of side effects. Commonly cited effects included headache and irregular menstruation when using short-term methods. Health concerns were more commonly cited in Western Indonesia and by women of higher socioeconomic status, who may have greater knowledge of the risks and side effects of using contraceptives. The role of health concerns in elevating the unmet need for FP in Indonesia is likely related to inadequate counseling of women concerning side effects and how they can be managed. This interpretation is supported by Indonesia's low global ranking on the FP2020 Method Information Index, an indicator of the quality of FP counseling.[40] Indonesia's total Method Information Index (MII) score in 2017 was 28.7, less than half of that of the ASEAN peer countries Philippines (59.8) and Cambodia (67.4). Among the three components of the MII score, performance on the components pertaining to informing clients about the side effects of alternative contraceptive methods and what can be done about the side effects has been the weakest by far. Concern over side effects is likely also at least partially responsible for the sizable increase in the use of traditional methods among more highly educated, urban women observed between 2012 and 2017.[41] These results indicate the need for improved communication/education and counseling concerning health issues related to different contraceptive methods delivered in ways that are the most suitable for different subgroups of women and local geographic contexts.

A third theme concerned service delivery issues, which were cited more frequently in Eastern Indonesia. Among the issues cited were contraceptive stock shortages in difficult-to-reach areas and a lack of service provider training and certification related to long-acting methods (implants, IUDs, and sterilization). As health service delivery (including FP) in Indonesia is decentralized, local governments have the primary responsibility for addressing service delivery barriers and bottlenecks. However, the central-level government plays a key role in commodity procurement and training. Regarding stock shortages, a real-time logistics information system (LMIS) would go a long way toward minimizing service disruptions due to inadequate supplies of contraceptives. Ensuring that provinces and districts include commodity distribution costs in their annual budgets would also help minimize the "last-mile" distribution disruptions that are often the cause of stock shortages. In areas where physical access to FP services is challenging, mobile and/or online services might be expanded. Regarding training, more up-to-date information on staff training needs is needed if the MoH and the BKKBN are going to be able to provide effective support to cities and districts. In this regard, the MoH is in the process of developing a learning management system for the transformed primary healthcare system and national public laboratory network. A comparable LMIS will also be needed at the BKKBN.

For a substantial number of women with an apparent need for FP, the reason given for the nonuse of contraception was postpartum amenorrhea. Such an explanation was given more frequently by women with higher levels of education, likely reflecting their better understanding of the protective effects of postpartum amenorrhea and exclusive breastfeeding. The danger here is that postpartum women wait too long to begin/resume contraceptive use after having a child. Indeed, an earlier study found that while the unmet need for FP among postpartum women in Indonesia was

relatively low compared with other low- and middle-income countries, Indonesian women tended to initiate contraceptive use relatively late, considering the limited duration of exclusive breastfeeding practiced by most Indonesian women.[42]

In considering strategies to reduce the unmet need for FP, it should be borne in mind that Indonesian women have, historically, shown a preference for nongovernment service providers, with such providers having a 60%–70% market share since the early 2000s. Greater collaboration with nongovernment providers will, thus, be needed to reduce the unmet need for FP significantly. The BKKBN would be prudent to adopt a total market approach as it targets efforts to reduce unmet needs geographically. Such collaboration might, for example, take the form of the BKKBN focusing on government resources more heavily in areas that are currently underserved by nongovernment providers. At the same time, nongovernment providers such as religious organizations and civil society organizations can help fill gaps where ensuring the provision of government FP services has proved challenging. On the all-important matter of client information/counseling and informed choice, given the market share of nongovernment providers, Indonesia will find it challenging indeed to significantly improve performance on informed choice unless it can productively engage nongovernment providers to improve the quality of information and counseling services.

As was noted earlier, recent global literature has focused on the limitations of the conventional definition of unmet need for FP in that it does not consider women's satisfaction with the methods they are currently using.[3,4] The argument is that women who are not satisfied with the method they are using are more likely to discontinue use and thus should not be viewed as having met their needs. A recent study in Kenya estimated that the level of unmet need (11.5%) would be increased by 25%–70% depending upon the definition of consumer dissatisfaction applied in the definition of unmet need.[3] This matter merits deliberation in Indonesia. One way to pursue this would be by including relevant questions in the next IDHS to support the empirical analysis of the implications of the use of more rigorous definitions of the unmet need for FP in the future.

Finally, although the focus of the present study was on the unmet need for FP, the fact that the demand for FP is quite low in some parts of Indonesia should not be overlooked. For example, according to the 2017 IDHS, demand for FP was only 64% in West Papua and 54% in Papua against a national figure of 75%. In such areas, unmet need tells only part of the story. Efforts to generate demand in Eastern Indonesian needs to continue and be made more effective in parallel with reducing the unmet need for FP. To do this, effective communication strategies and local stakeholder involvement are crucial.

A coordinated MoH–BKKBN initiative is recommended to systematically address the factors underlying stubbornly high levels of unmet needs for FP. As business-as-usual practices and intervention strategies have not moved the needle on unmet needs significantly for the past 20 years, new approaches are needed. This will entail (1) developing communication strategies and messaging (including FP counseling) that address effectively such factors as concerns over side effects, opposition to FP, limited male participation in FP, and limited demand for FP (in some areas), in ways that resonate with important population subgroups and community leaders as well as in different geographical areas, and (2) adopting on a wider scale service delivery approaches that overcome barriers to physical access to services. Each locality must be viewed as a separate market and interventions should be developed and implemented that best address local factors underlying the unmet need. More meaningful engagement by nongovernment service providers would also be prudent and is recommended. Given their sizable market share, such providers can be of considerable assistance to the national FP program in strengthening FP counseling and informed choice as well as providing service delivery options in many locations and filling the gaps in the geographic coverage of public sector services.

CONCLUSIONS

Successful efforts to reduce the unmet need for FP are complex in that they must simultaneously contend with the interplay between local sociocultural contexts, individual beliefs, aspirations, and preferences, and the supply environment for FP at both the national and local levels. The fact that the relevance of these factors varies across different population subgroups and geographic areas means that there is no simple, one-size-fits-all solution to reducing the unmet need for FP in Indonesia. Differentiated interventions for different population subgroups and geographic areas will be needed if progress is to be made.

CONFLICT OF INTEREST

None declared.

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Factors Associated with the Use of Traditional Health Services in Indonesia: A Secondary Analysis of the Indonesian Basic Health Research

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Factors Associated with the Use of Traditional Health Services in Indonesia: A Secondary Analysis of the Indonesian Basic Health Research

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Abstract

Background: Traditional health services in Indonesia have been used increasingly over the past few years because patients nowadays are more proactive in seeking various alternative modes of self-care. This study aimed to analyze factors associated with the use of traditional health services in Indonesia.

Methods: This quantitative study used a cross-sectional research design. The research data were secondary data from the 2018 Indonesian Basic Health Research. The research samples were 163,259 respondents aged >10 years and the statistical test for data analysis was multiple logistic regression.

Results: The percentage of respondents who used traditional health services was 73.8%. The bivariate results in this study indicate that age, gender, employment status, educational level, residence, marital status, and access to health facilities had a significant relationship with the use of traditional health services.

Conclusions: The use of traditional health services was influenced by age, gender, residence, marital status, and distance. The Indonesian government needs to consider these factors when extending the use of traditional health services.

Keywords: Indonesia, risk factors, traditional health services

INTRODUCTION

The number of traditional and complementary medicine (TCM) users is increasing. Traditional medicine or non-conventional medicine in various countries is often referred to alternatively as complementary medicine. The increased use of TCM sees East Asian countries being well-known for the highest number of traditional medicine users.[1] In addition, a significant increase in the use of traditional medicine was reported by several countries such as the United States (42%), Australia (48%), France (49%), Canada (70%), and developing countries such as China (40%), Chile (71%), Colombia (40%), and African countries (up to 80%).[2] The World Health Organization (WHO) strongly emphasizes the importance of establishing the prevalence and determining factors in the use of TCM. The WHO's Traditional Medicine Strategy 2014–2023 aims to support countries that use TCM for health care. Health care that is patient-centered and promotes the safe and effective use of traditional medicine must be supported by regulating, researching and integrating TCM products, practitioners, and practices in the health system.[3]

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In addition to obstacles to the development of traditional medicine products, the 2018 Indonesian Basic Health Research (RISKESDAS) reported the proportion of utilization of traditional health services in Indonesia is still uneven in every province, where the province of South Kalimantan (54.1%) is the province with the most utilization of traditional health services while the province of West Sulawesi is the province with the least utilization of traditional health services (8.5%).[4] Because traditional medicine may not meet current safety, efficacy, and quality of health treatment standards, the Indonesian Ministry of Health issued the Regulation of the Indonesian Food and Drug Authority No. 14 of 2021 on the certification of good manufacturing practices for traditional medicine.

Several previous studies have reported the use of traditional medicine. Research conducted by Pearson *et al.* states that traditional medicine is used widely by patients with chronic diseases in Cambodia.[5] Nearly half of the Cambodian population has used herbal medicine in the last 12 months.[5] A study in Ethiopia reported the use both conventional physicians and traditional medicine. The use of traditional medicine in Ethiopia has been shown to have increased by 80% for socio-cultural reasons, especially including religious and cultural beliefs, as well as the relatively cheaper cost.[6] Recently, interest in complementary and alternative medicine (CAM) has been increasing in Korea and around the world. In Western countries, CAM incorporates traditional medicine from

Eastern countries, such as Korea and China, to complement and compensate for the limitations of conventional medicine.[7] Moreover, social and environmental factors become health determinants of behavioral, biological, and health service factors. A study in Enugu reported that social and economic factors were found to be associated with the patronage.[8]

Research in Indonesia has frequently explored the use of traditional health services in hospitals and healthcare centers. However, the data have not broadly described the factors that affect the use of these traditional health services. The current study, therefore, addressed the factors associated with the use of traditional medicine by using secondary data from Indonesian Basic Health Research. Information on the use of traditional medicine in Indonesia is important for the government to improve policy-making for TCM production and distribution. This study analyzed factors associated with the use of traditional health services in Indonesia.

METHODS

This study used secondary data from the 2018 Indonesian basic health research and a cross-sectional research design. RISKESDAS is a community-based national health survey whose indicators can describe issues from a national level up to district/city levels.[3] Data collection is conducted every five years because that is considered the right interval to assess the development of public health status, risk factors, and health development measures. RISKESDAS survey cohort comprises respondents across 34 provinces of Indonesia.

The samples consisted of 163,260 respondents aged >10 years selected based on inclusion and exclusion criteria. The inclusion criterion of the respondents was being able to answer the questionnaire about the use of traditional health services in Indonesia; the exclusion criterion was missing data. This study used traditional health service use as a dependent variable. It refers to the respondents who took advantage of the traditional health services in the past year either by use of herbal potions, skilled therapy (traditional massage, hypnotherapy and energy transfer), or practice (by themself or a traditional health service provider). The answers to the questions on the use of traditional health services were simply yes or no. For the independent variables, the research included age, gender, level of education, occupational status, marital status, residence, the type of traditional health service accessed, assistance from a traditional health worker, and time spent at a health facility. Age was grouped into productive ages (15–64 years) and unproductive (> 65 years). Gender was divided into women and men. The level of education was classified as primary education (not finishing elementary school), secondary education (junior and senior high school), and higher education (graduating from college). Occupational status was divided into not working and working. Marital status was divided into single (unmarried) and married or divorced. Residence was divided into urban and rural areas. The types of traditional health services were grouped into herbal and skilled therapy. The skilled treatment divided into traditional massage, hypnotherapy and energy transfer. Questions related to assistance from traditional health workers had yes and no options. Time spent at health facilities was the average time spent at health facilities (hospitals, primary healthcare centers, or doctor clinics).

The current study used univariate, bivariate, and multivariate data analyses. Variables were first summarized in descriptive statistics. Then, bivariate analysis was performed using the chi-square test to derive the relationship between independent and dependent variables. The analysis used for categorical variables (age, gender, marital status, level of education, occupational status, residence, and travel time to health facility) used a 95% confidence interval and a degree of significance (α) of 0.05.

For the multivariate analysis, a multiple logistic regression model was performed. Variables whose p-values were more than 0.05 were excluded from the multivariate model. Variables with p-values of more than 0.05 were excluded from the one-unit model starting with the variable with the largest value. Our final model was employed to adjust the determinants of the use of traditional health services. This study passed an ethics review from the Center for Ethical Studies of the Faculty of Public Health, Sriwijaya University with the approval letter No. 030/UN9. FKM/2021.

RESULTS

The characteristics of the respondents and the use of traditional health services in Indonesia are presented in Table 1. The results show that 73.8% of respondents used traditional health services, and 56% used skilled therapy. Most of the respondents were in the age group of > 65 years (93.8%) and females (53.2%). A low educational level was found to be dominant (48.5%). The majority of the respondents worked (62.5%) and were married (70.6%). More than half of the respondents lived in rural areas (57.7%). Respondents who used traditional health services mostly visited traditional health workers (98.8%). Respondents mostly took <30 minutes to travel to health facilities (99.8%).

Table 2 shows the bivariate analysis results using a chi-square test. Gender, age, educational level, employment status, region, marital status, assistance from traditional health workers, and time to travel to health facilities had a significant relationship with the use of traditional health services ($p < 0.05$). The multiple logistic regression model shown in Table 3 shows that gender, age, residence, marital status, and travel time to health facilities have a significant association with the use of the health service and the most

associated variable is gender. Male respondents were 1.11 times more likely to use health traditional health services than female respondents.

TABLE 1. Characteristics of respondents (N = 163,259)

Variable	N	%
Use of traditional health services		
Yes	120,479	73.8
No	42,789	26.2
Age (years)		
15–64	10,066	6.2
> 65	153,193	93.8
Gender		
Male	76,406	46.8
Female	86,853	53.2
Level of education		
Primary education	79,214	48.5
Secondary education	72,208	44.2
College	11,836	7.3
Occupational status		
Not working	61,292	37.5
Working	101,967	62.5
Marital status		
Single	47,944	29.4
Married	115,315	70.6
Residence		
Rural	94,266	57.7
Urban	68,993	42.3
Use of traditional health workers		
Yes	161,308	98.8
No	1,951	1.2
Types of traditional health services		
Herbal	71,892	44.0
Skilled therapy	91,367	56.0
Travel time to a health facility		
> 30 minutes	320	0.2
< 30 minutes	162,939	99.8

DISCUSSION

This study aimed to analyze factors associated with the use of traditional health services in Indonesia. The results show that 73.8% of all respondents had used traditional health services. Residence have associated with the use of traditional health services. In this case, respondents who live in rural had a 1.1 times higher likelihood of using traditional health services than respondents in urban. Gender have associated with the use of traditional health services. In this case, male respondents had a 1.11 times higher likelihood of using traditional health services than female respondents. Previous study reported that proportion of men prefer to use traditional higher than women.[9] Another study found that male respondents used many types of traditional health services such as acupuncture.[10] The findings are supported by previous research that found that the use of CAM in women is somewhat lower than was found in recent studies in Europe, the US, and Australia. In conclusion, men have a higher probability of using traditional health services.[11] Hence, treatment safety must be a priority in traditional health services. Some variables are considered predictors of the use of TCM/CAM at the individual level. These include gender, educational level, monthly income, perceived health, experience with Western medical care, and the cost, effect, and satisfaction with treatment.[12]

Another factor associated with the use of traditional health services is age.[13] This study revealed that respondents aged 15–64 years were 0.961 times less likely to use traditional health services. Older age groups were found to use traditional health services more because they believe that traditional health services will improve physical endurance.[13] Younger age and higher income are often associated with the use of CAM in women but it is not significant.[14] A study mentioned that processed herbs were used most widely by the older age group because they believe that herbs derived from medicinal plants are effective in addressing health problems. Cultural beliefs may affect some groups' perceptions of traditional health services.[10]

The current study showed that unmarried respondents were 0.939 times less likely to use traditional health services than married people. There is a significant relationship between marital status and the use of traditional health services.[15] Previous research stated that married women had a 2.56 times greater propensity to use herbal medicine than unmarried women. Previous study found that 82% of married couples used CAM or herbal remedies to overcome fertility problems and given this trend, healthcare providers need to provide counseling to patients.[16]

Our findings also showed that rural areas had a higher likelihood of using traditional services than urban areas. It is contrary with previous study in In Indonesia that residence in urban area was associated with practitioner.[13] The use of traditional Korean medicine is more common among people in urban residential areas compared to rural areas, because urban areas provide easier access to medicines.[7] Previous research in Ghana and India shows that lower socioeconomic status, unemployment, residence in rural areas, and low health status lead people to use traditional healers who provide cheaper treatment.[17] The use of traditional health services in urban and rural areas still poses some constraints. Providing complementary traditional health facilities where people can access acupuncture, acupressure, and herbal products is one of the ways to improve accessibility. Traditional health workers should be given the education so that they can provide accurate and examined information and practices of traditional health treatments.[18]

TABLE 2. Association between the independent variables and the use of traditional health services

Variable	Yes		No		*p*	OR (95% CI)
	N	%	N	%		
Age						
15–64 years	7,159	71.0	2,907	28.0	< 0.001	0.961 (0.945-0.978)
> 65 years	113,311	74.0	39,881	26.0		
Gender						
Male	57,172	74.0	19,233	25.0	< 0.001	1.027 (1.019-1.035)
Female	63,297	72.0	23,556	27.0		
Educational level						
Primary education	57,863	73.0	21,351	27.0	< 0.001	0.909 (0.845-0.977)
Secondary education	53,742	74.0	18,455	25.0	< 0.001	0.976 (0.911-1.045)
College	88,644	74.0	2,799	25.0		
Occupational status						
Not working	44,641	72.8	16,650	27.2	< 0.001	0.979 (0.970-0.988)
Working	75,829	74.4	26,138	25.6		
Marital status						
Single	34,850	72.7	13,093	27.3	< 0.001	0.979 (0.970-0.988)
Married	85,620	74.2	29,695	25.8		
Residence						
Rural	70,288	74.6	23,977	25.4	< 0.001	1.025 (1.010-1.041)
Urban	50,181	72.7	18,812	27.3		
Travel time to a health facility						
> 30 minutes	194	60.8	125	39.2	< 0.001	0.823 (0.737-0.919)
< 30 minutes	120,275	73.8	42,663	26.2		

TABLE 3. Multiple logistic regression model

Variable	*p*	OR (95% CI)
Age		
15–64 years	0.001	0.904 (0.845-0.967)
> 65 years[Ref]		
Gender		
Male	0.001	1.111 (1.077-1.146)
Female[Ref]		
Marital status		
Single	0.001	0.939 (0.903-0.976)
Married or divorced[Ref]		
Residence		
Rural	0.001	1.105 (1.043-1.171)
Urban[Ref]		
Travel time to a health facility		
> 30 minutes	0.001	0.559 (0.422-0.741)
< 30 minutes[Ref]		

Travel time to health facilities is also known to be a factor associated with the use of traditional health services. The participating respondents who reached health facilities in > 30 minutes had 0.559 times fewer chances of using traditional health services than those spending < 30 minutes. Another research mentioned that there is a significant relationship between the distance to a health facility and the frequency of visiting traditional health services.[19,20] Health facilities close to home were usually used widely by most respondents. A shorter distance to the treatment area allows a much higher probability of people choosing treatment there because of easy access and low cost. Difficulties accessing healthcare systems are mostly found in rural areas. Therefore, the National Center for Complementary and Alternative Medicine recommends that healthcare providers combine conventional health services and traditional medicine or CAM for an overall better quality of health service.[21]

In terms of limitations, secondary data in this study were not enough to give a general conclusion on associated factors of traditional medicine use. The analysis was not aimed at finding the causes and effects of the factors since this study was a cross-sectional study. It only covered limited variables such as age, gender, educational level, employment status, marital status, residence, and access to health facilities. Several variables (economic status and socio-cultural reasons, especially including religious and cultural beliefs) were not included in this study due to limited data.

We found that the use of traditional health services was influenced by age, gender, residence, marital status, and distance. This study implies that these factors should be considered for expanding the use of traditional medicine and that the government should promote traditional medicine. Future studies should explore other variables associated with traditional medicine use such as the role

of economic status and socio-cultural reasons, especially religious and cultural beliefs.

CONCLUSIONS

Most respondents in this study used traditional health services. Age, gender, residence, marital status, and distance to health facilities were associated with the use of traditional health services. The Indonesian government needs to consider these factors when expanding the use of traditional health services.

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CONFLICT OF INTEREST

The authors stated that there are no conflicts of interest in this article.

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Determination of Individuals' Attitudes Toward COVID-19 Vaccines and Health Fatalism: A Cross-sectional Study from Turkey

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Determination of Individuals' Attitudes Toward COVID-19 Vaccines and Health Fatalism: A Cross-sectional Study from Turkey

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Abstract

Background: Vaccines have positive effects on the course of epidemics. This study was conducted to determine individuals' attitudes toward coronavirus disease-2019 (COVID-19) vaccines, their health fatalism, and factors affecting these.

Methods: This cross-sectional study included 944 participants living in Turkey, who were included in the study by snowball sampling, one of the nonprobability random sampling methods. Participant information form, attitudes toward the COVID-19 vaccine scale, and religious health fatalism scale were used to collect the study data. Independent sample t-test, one-way analysis of variance and Pearson correlation analysis were used in the data analysis.

Results: Participants had mean positive attitudes toward COVID-19 vaccine score of 3.63 ± 1.14, mean negative attitudes toward COVID-19 vaccine score of 3.44 ± 0.91, and mean health fatalism score of 45.75 ± 17.43. Negative and significant correlations were found between participants' mean health fatalism score and their mean positive attitudes score (r = −0.213) and their mean negative attitude score (r = −0.362) (p < 0.001).

Conclusions: Individuals were found to have high positive and low negative attitudes toward COVID-19 vaccines and moderate levels of health fatalism. Individuals with high health fatalism had low positive and high negative attitudes toward COVID-19 vaccines.

Keywords: attitude, COVID-19 vaccines, health fatalism

INTRODUCTION

Epidemics are diseases that occur with an increase in cases in a specific area or community, which spread to a large population and affect society if uncontrolled.[1] COVID-19, which started in Wuhan City, China, in 2019, has spread rapidly worldwide.[2] The COVID-19 pandemic has caused many deaths since its onset and has unprecedented effects on national health systems and the global economy.[3] The rapid transmission and asymptomatic spread of COVID-19 affects human health negatively; therefore, the search and discovery of an effective and safe vaccine have become an urgent global need.[4] Considering the contagious nature of COVID-19, the only sustainable long-term solution is to develop robust vaccine protocols.[5]

A vaccine is an antigenic material that provides the development of adaptive immunity by stimulating the immune system against a pathogen, and it can prevent or reduce mortality and morbidity caused by many infections.[6]

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The World Health Organization stated that vaccines prevent 3.5–5 million deaths from infectious diseases annually.[7] Realizing the inevitability of the spread of the epidemic has greatly accelerated the development of vaccines that can provide primary protection against symptomatic infection, severe clinical presentation, and death.[8] COVID-19 vaccines protect against the current severe symptoms of the disease and are an important tool to reduce virus spread and infection rate.[9] A meta-analysis found that in fully vaccinated populations, the efficacy of the vaccine was 89.1% for severe COVID-19, 97.2% for COVID-19-related hospitalizations, 97.4% for admission to the intensive care unit, and 99% against death.[10] In a similar study, higher vaccine coverage was reported to be associated with lower COVID-19 mortality and incidence rates.[11]

Access to vaccines and acceptance by the vaccinated population are shown as critical components of successful vaccination.[12] Acceptance of vaccination is an outcome behavior that is potentially influenced by various factors and results from a complex decision-making process.[13] Attitudes affect behaviors, and the attitudes of individuals toward vaccination vary widely, which includes supporting, accepting, hesitating, resisting, rejecting, or opposing.[14,15] Even in established vaccination systems, the

reluctance for vaccination is a major barrier to the vaccination of the population.[16] A study conducted in North-Eastern Ethiopia showed that negative attitudes and perceptions about COVID-19 vaccination are important factors to reject vaccination.[17]

Fatalism expresses the belief that everything that happens in life is predetermined, it is not possible to go beyond this predetermination, destiny is governed by an invisible power that will not change whatever a person does, and a person is powerless in the face of inevitable life events.[18] More than 90% of the Turkish population is Muslim, and fatalism is frequently seen in society because the widespread religious belief supports fatalism.[19,20] One of the six pillars of faith in Islam is the belief in fate. In terms of health, fatalism negatively affects various health behaviors and behavioral health determinants.[21] A study of patients with hypertension showed that patients with high fatalistic tendencies had low adherence to treatment.[22] In one study, lower cancer fatalism correlated with higher stool occult blood test intake.[23] Women who thought that cervical cancer occurred because of were three times less likely to have a Pap test than women who did not.[24] Studies have also shown an inverse relationship between fatalistic beliefs and preventive behaviors toward COVID-19.[25,26]

Understanding the factors that shape the attitudes of society toward vaccines will enable planning for evidence-based interventions to increase vaccine intake globally.[27] Studies have evaluated the attitudes of Turkish society toward COVID-19 vaccines [28–30]; however, no studies have evaluated attitudes toward COVID-19 vaccines within the context of health fatalism.

This study was conducted to determine individuals' attitudes toward COVID-19 vaccines, their health fatalism, and the factors affecting these.

METHODS

Ethical approval

Permission was taken from the Ministry of Health Scientific Research Platform. The study was approved by the Artvin Çoruh University Ethics Committee (Date: 04.01.2022, No. E-18457941-050.99-34667). Before the study, the participants were given online information about the purpose of the study. Online consent was obtained from the participants before the study. Permission to use the scales (attitudes toward the COVID-19 vaccine scale and religious health fatalism scale) was taken from the original authors. The study was conducted in line with the Declaration of Helsinki.

Study population and sample

This study was conducted as a cross-sectional study. The study population consisted of individuals aged ≥18 living in Turkey. The study sample was determined with the snowball sampling method, one of the nonprobability sampling methods. This method has cost and time advantages but includes non-random selection procedures.[31] The data were collected between January 5 and February 16, 2022. A total of 947 participants filled in the survey; however, since three were filled in by participants aged <18 years, they were excluded from the analysis, and the study was completed with 944 participants.

In the post-hoc power analysis based on the positive attitude score and health fatalism score, the power of the study was 0.99 at a 95% confidence interval and alpha of 0.05.

Inclusion criteria

Individuals aged ≥18 years who did not have reading and comprehension problems and who volunteered to participate in the study were included.

Data collection tools

The participant information form, attitudes toward the COVID-19 vaccine scale, and religious health fatalism scale were used to collect the study data.

Participant information form: The form, which was prepared by the researchers in line with the literature,[29,32,33] included 15 questions on the sociodemographic characteristics of the participants and their attitudes (COVID-19 vaccines will end the pandemic, recommending COVID-19 vaccines to others, etc.) and perceptions (fear of being infected with COVID-19, having been infected with COVID-19, etc.) toward COVID-19 vaccines and COVID-19.

Attitudes toward the COVID-19 vaccine scale: The scale was developed by Geniş *et al.* to measure attitudes toward COVID-19 vaccines.[34] The scale is a 5-point Likert-type scale (1, strongly disagree; 5, strongly agree) that consists of nine questions. The scale includes two subscales, namely, positive attitudes (1–4 questions) and negative attitudes (5–9 questions). Higher scores in the positive attitude subscale show increased positive attitudes toward COVID-19 vaccines, whereas higher scores in the negative attitude subscale show decreased negative attitudes toward COVID-19 vaccines. The Cronbach alpha value of the scale was 0.96 for the positive subscale, whereas it was 0.78 for the negative subscale and 0.80 in the overall scale.[34] In our study, the Cronbach alpha values were 0.92, 0.82, and 0.89 for the positive subscale, negative subscale, and overall scale.

Religious health fatalism scale: This scale, which was developed by Franklin *et al*. to determine a pattern between health fatalism and preventive health behaviors, consists of 17 items in a 5-point Likert-type scale (1, strongly disagree; 2, disagree; 3, neutral; 4, agree; 5, strongly agree).[35] The validity and reliability study of the scale was conducted by Bobov and Çapık in our country.[36] The scale is scored

between 17 and 85, and higher scores show increased health fatalism. The Cronbach alpha coefficient of the scale was.91, whereas it was 0.96 in the present study.

Data collection

Study data were collected online through surveys prepared with Google Forms. The prepared survey form was sent to participants online (WhatsApp), and they were asked to fill in the form and share it with people around them. Respondents were prevented from re-entering the survey.

Data analysis

IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA) was used in data analyses. Data were considered significant at 95% confidence interval and $p < 0.05$ level. Data were presented as percentage, mean, and standard deviation. Skewness and kurtosis analyses were used in determining the normality distribution of the data. An independent t-test was used to compare normally distributed data with mean positive attitude, negative attitude, and health fatalism scores, whereas one-way analysis of variance and post-hoc tests were used in more than two normally distributed variables. The correlation between participants' age, attitudes toward COVID-19 vaccines, and health fatalism was evaluated by the Pearson correlation analysis.

RESULTS

The mean age of the participants was 36.25 ± 13.13 (min, 18; max, 75) years, 67.1% were female, 49.5% were living in the city center, 40.8% had an income equal to expense, 52.8% were university graduates, and 23.2% had a chronic disease (Table 1).

Moreover, 91.8% had information about COVID-19 vaccines, and 29.6% of these participants obtained information from healthcare professionals, 91% had COVID-19 vaccination, 81.6% recommended COVID-19 vaccines to others, and 30.2% believed that COVID-19 vaccines will bring the pandemic to an end (Table 1).

In addition, 34.3% of the participants had COVID-19, 66.8% had fears of being infected, and 61% of those who feared the infection had a moderate level of fear and 76.4% followed policies on wearing masks and maintaining a social distance (Table 1).

The participants had mean positive attitude score toward COVID-19 vaccines of 3.63 ± 1.14, mean negative attitude score toward COVID-19 vaccines of 3.44 ± 0.91, and mean health fatalism score of 45.75 ± 17.43.

Significant difference was found between participants' place of residence and their mean positive attitude, negative attitude, and health fatalism scores ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively). The least significant difference (LSD) post-hoc analysis showed that participants who lived in town/village had lower positive and negative attitude scores and higher health fatalism scores than participants who lived in the city center and town (Table 2).

TABLE 1. Characteristics of the participants (N = 944)

Participants' characteristics	N	%
Gender		
Male	311	32.9
Female	633	67.1
Place of residence		
City	467	49.5
District	375	39.7
Town/village	102	10.8
Income status		
Income>expense	176	18.6
Income=expense	385	40.8
Income<expense	383	40.6
Level of education		
Literate	52	5.5
Primary	121	12.8
Middle	64	6.8
High	209	22.1
University	498	52.8
Chronic disease		
Yes	219	23.2
No	725	76.8
Information about COVID-19 vaccine		
Yes	867	91.8
No	77	8.2
Source of information (N = 867)		
Newspaper, Magazine, Book	21	2.4
Internet	285	32.9
Radio, TV	241	27.8
People around	63	7.3
Healthcare professional	257	29.6
Having COVID-19 vaccine		
Yes	859	91.0
No	85	9.0
Recommending COVID-19 vaccine to others		
Yes	770	81.6
No	174	18.4
COVID-19 vaccine will end the pandemic		
Yes	285	30.2
Undecided	398	42.2
No	261	27.6
Having been infected with COVID-19		
Yes	324	34.3
No	620	65.7
Fear of being infected with COVID-19		
Yes	631	66.8
No	313	33.2
Severity of the fear (N = 631)		
Mild	147	23.3
Moderate	385	61.0
Severe	99	15.7
Following the rules of mask and social distance		
Yes	721	76.4
Sometimes	181	19.2
No	42	4.4

TABLE 2. Comparison of participants' characteristics and their attitudes toward COVID-19 vaccines and health fatalism (N = 944)

Participants' characteristics	Positive attitude towards vaccine score		Negative attitude towards vaccine score		Health fatalism score	
	Mean ± SD	*p*	Mean ± SD	*p*	Mean ± SD	*p*
Gender						
Male	3.59 ± 1.25	0.489	3.42 ± 1.01	0.705	46.42 ± 18.88	0.305
Female	3.64 ± 1.08		3.45 ± 0.85		45.32 ± 16.67	
Place of residence						
City	3.69 ± 1.16	**0.000**	3.45 ± 0.92	**0.000**	41.90 ± 16.89	**0.000**
District	3.69 ± 1.07		3.52 ± 0.86		48.77 ± 17.02	
Town/village	3.10 ± 1.17		3.07 ± 0.95		52.27 ± 17.36	
Income status						
Income>expense	3.95 ± 1.11	**0.000**	3.69 ± 0.97	**0.000**	41.93 ± 16.79	**0.000**
Income=expense	3.76 ± 1.05		3.55 ± 0.85		44.92 ± 16.46	
Income<expense	3.34 ± 1.18		3.22 ± 0.89		48.33 ± 18.28	
Level of education						
Literate	3.10 ± 1.10	**0.000**	3.10 ± 0.89	**0.000**	57.19 ± 16.89	**0.000**
Primary	3.36 ± 1.16		3.28 ± 0.96		56.49 ± 16.28	
Middle	3.63 ± 1.07		3.35 ± 0.94		51.15 ± 15.34	
High	3.60 ± 1.08		3.38 ± 0.88		46.66 ± 16.06	
University	3.75 ± 1.15		3.55 ± 0.89		40.74 ± 16.52	
Chronic disease						
Yes	3.73 ± 1.08	0.131	3.41 ± 0.91	0.629	45.96 ± 17.92	0.836
No	3.59 ± 1.16		3.45 ± 0.91		45.68 ± 17.29	
Information about COVID-19 vaccine						
Yes	3.71 ± 1.10	**0.000**	3.49 ± 0.89	**0.000**	44.77 ± 17.15	**0.000**
No	2.72 ± 1.20		2.83 ± 0.92		56.29 ± 16.83	
Source of information (N = 867)						
Newspaper, Magazine, Book	3.86 ± 1.36	**0.000**	3.64 ± 1.07	**0.009**	40.38 ± 20.08	**0.000**
Internet	3.55 ± 1.19		3.37 ± 0.92		43.78 ± 18.17	
Radio, TV	3.77 ± 0.97		3.55 ± 0.77		48.04 ± 15.11	
People around	3.39 ± 1.09		3.35 ± 0.95		52.82 ± 19.35	
Healthcare professional	3.90 ± 1.05		3.62 ± 0.90		41.22 ± 15.85	
Having COVID-19 vaccine						
Yes	3.76 ± 1.05	**0.000**	3.52 ± 0.87	**0.000**	45.11 ± 17.33	**0.000**
No	2.22 ± 1.11		2.64 ± 0.86		52.18 ± 17.22	
Recommending COVID-19 vaccine to others						
Yes	3.95 ± 0.91	**0.000**	3.64 ± 0.81	**0.000**	44.48 ± 17.10	**0.000**
No	2.20 ± 0.98		2.57 ± 0.78		51.37 ± 17.79	
COVID-19 vaccine will end the pandemic						
Yes	4.31 ± 0.87	**0.000**	4.05 ± 0.82	**0.009**	40.89 ± 17.51	**0.000**
Undecided	3.70 ± 0.85		3.41 ± 0.72		46.47 ± 15.78	
No	2.75 ± 1.23		2.82 ± 0.83		49.69 ± 18.49	
Having been infected with COVID-19						
Yes	3.47 ± 1.16	**0.002**	3.38 ± 0.89	0.156	47.32 ± 18.14	**0.045**
No	3.71 ± 1.12		3.47 ± 0.91		44.93 ± 17.00	
Fear of being infected with COVID-19						
Yes	3.78 ± 1.04	**0.000**	3.58 ± 0.83	**0.000**	44.47 ± 17.05	**0.001**
No	3.31 ± 1.27		3.16 ± 1.00		48.34 ± 17.92	
Severity of the fear (N = 631)						
Mild	3.62 ± 1.23	0.067	3.56 ± 0.88	0.529	45.31 ± 18.82	0.482
Moderate	3.82 ± 0.95		3.57 ± 0.80		44.58 ± 16.28	
Severe	3.90 ± 1.02		3.67 ± 0.84		42.68 ± 17.35	
Following the rules of mask and social distance						
Yes	3.82 ± 1.05	**0.000**	3.57 ± 0.87	**0.000**	44.09 ± 16.91	**0.000**
Sometimes	3.22 ± 1.13		3.14 ± 0.90		49.46 ± 17.72	
No	2.10 ± 1.10		2.49 ± 0.77		58.30 ± 17.70	

TABLE 3. Relationship between participants' age, attitudes toward COVID-19 vaccine score, and health fatalism score (N = 944)

Variable	Mean ± SD	Positive attitude towards vaccine score	Negative attitude towards vaccine score	Health fatalism score
Age (min:18, max: 75)	36.25 ± 13.13	r = -0.025 p = 0.435	r = -0.014 p = 0.677	r = 0.125 **p = 0.000**
Positive attitude towards the vaccine score (min:1, max: 5)	3.63 ± 1.14			r = -0.213 **p = 0.000**
Negative attitude towards the vaccine score (min:1, max: 5)	3.44 ± 0.91			r = -0.362 **p = 0.000**
Health Fatalism score (min:17, max: 85)	45.75 ± 17.43			

A significant difference was found between participants' income status and their mean positive attitude, negative attitude, and health fatalism scores ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively). Dunnett's C post-hoc analysis showed that participants who had lower income than expense had lower positive attitude and negative attitude scores and higher health fatalism scores than participants who had equal income and expense and those who had income higher than expense.

A significant difference was determined that between participants' level of education and their mean positive attitude, negative attitude, and health fatalism scores ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively). Tukey's post-hoc analysis showed that participants who were literate and primary education graduates had lower positive attitude and negative attitude scores and higher health fatalism scores than participants who were university graduates.

Participants who did not have information about COVID-19 vaccines had significantly low mean positive attitude and negative attitude scores and significantly high mean health fatalism scores ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively). A significant difference was found between participants' source of information about COVID-19 vaccines and their mean positive attitude, negative attitude, and health fatalism scores ($p < 0.001$, $p < 0.01$, and $p < 0.001$, respectively). Dunnett's C post-hoc analysis discovered that participants who obtained information from individuals around them and the Internet had lower mean positive attitude scores, those who obtained information from the Internet had lower mean negative attitude scores than participants who obtained information from healthcare professionals, and participants who obtained information from the radio, television, and individuals around them had higher mean health fatalism scores.

Participants who did not have COVID-19 vaccination and those who did not recommend COVID-19 vaccines to others had significantly low mean positive attitude and negative attitude scores and significantly high mean health fatalism scores ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively).

Significant difference was found between the participants' "COVID-19 vaccines will put an end to the pandemic" expression and their mean positive attitude, negative attitude, and health fatalism scores ($p < 0.001$, $p < 0.01$, and $p < 0.001$, respectively). Dunnett's C post-hoc analysis determined that participants who believed that vaccines will not put an end to the pandemic when compared with undecided participants and undecided participants when compared with participants who believed that the pandemic will put an end to the pandemic had lower positive attitude and negative attitude scores and higher health fatalism scores.

Participants who had COVID-19 had significantly low mean positive attitude scores and significantly high mean health fatalism scores ($p < 0.01$ and $p < 0.05$, respectively), and participants who did not have fears of getting infected with COVID-19 had significantly low mean positive attitude and negative attitude scores and significantly high mean health fatalism scores ($p < 0.001$, $p < 0.001$, and $p < 0.01$, respectively).

A significant difference was found between the participants' state of following policies of wearing masks and social distancing and their mean positive attitude, negative attitude, and health fatalism scores ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively). LSD post-hoc analysis determined that participants who did not follow policies of wearing masks and social distancing when compared with those who sometimes did, and participants who sometimes followed these policies compared with those who followed such policies had lower positive and negative attitude scores and higher health fatalism scores (Table 2).

A positive and significant correlation was found between participants' mean age and their mean health fatalism score ($r = 0.125$; $p < 0.001$). A negative and significant correlation was found between participants' mean health fatalism score and their mean positive attitude score ($r = -0.213$; $p < 0.001$) and their mean negative attitude score ($r = -0.362$; $p < 0.001$) (Table 3).

DISCUSSION

In this study, the participants had high levels of positive attitudes and low levels of negative attitudes toward COVID-19 vaccines and moderate levels of health fatalism. Individuals with high levels of health fatalism had lower positive attitudes and higher negative attitudes toward COVID-19 vaccines. Healthcare professionals in Turkey had high levels of positive attitudes and low levels of negative attitudes toward COVID-19 vaccines.[28] In a different study conducted in Turkey, levels of negative attitudes toward COVID-19 vaccines were lower than those of positive attitudes.[29] Most citizens in Saudi Arabia and South Korea have been found to have positive attitudes toward COVID-19 vaccines.[16,37] Positive attitudes toward COVID-19 vaccines appear to be promising in decreasing the global COVID-19 burden. Women aged 15 and 49 years in Iğdır had moderate levels of fatalistic tendency.[38] Individuals in east Turkey had high levels of health fatalism.[36] Women in east Turkey were found to have low levels of breast cancer fatalism.[39] A study reported that belief in fatalism increased the possibility of women from Kentucky not to complete HPV vaccine series successfully.[40] Hispanic women with high fatalism similarly had less trust in flu vaccine.[41] Vaccine is important in protecting health, and considering that fatalism negatively affects health behaviors and behavioral health determinants, the results obtained were expected.

Individuals who lived in town/village had low positive attitudes and high negative attitudes toward COVID-19 vaccines and high health fatalism. A study in Bangladesh found that individuals living in rural areas were less likely to accept COVID-19 vaccines than individuals living in cities.[42] In Pakistan, rural people were found to be and refuse to be vaccinated, whereas rural people in Arkansas were more likely to have lower confidence in vaccines than urban residents.[43,44] Women living in rural areas in Mexico were more likely to have Pap smear tests than women living in cities, and they were more likely to believe that the disease was caused by bad luck or fate.[24] Individuals living in rural areas probably have less access to health services, and they have less information about COVID-19 vaccines; thus, they easily attribute their health problems to fate. Negative attitudes and high health fatalism can result from this situation.

Individuals who had lower income than expense had low positive attitudes and high negative attitudes toward COVID-19 vaccines and high health fatalism. Individuals with low annual income in Pakistan expressed a strong distrust toward COVID-19 vaccines.[43] Individuals living in low-income households in England were more likely to reject COVID-19 vaccines.[45] In Italy, the perceived economic difficulty was associated with increased rates of vaccination hesitation.[46] Parents with high income had higher willingness to have their children vaccinated for COVID-19 than parents with low income.[47] Individuals with lower income than expense in east Turkey had higher health fatalism.[36] In different studies examining prostate cancer fatalism in men and breast cancer fatalism in women, income status did not affect fatalism.[39,48] Individuals with low income probably experience difficulties in receiving health services because of their poor economic status; therefore, they may attribute their health problems to fatalism because of limited health access.

Individuals who were literate and those who had primary education had low positive attitudes and high negative attitudes toward COVID-19 vaccines and had high health fatalism. In a cross-sectional study conducted in Turkey, participants who are undergraduates and had higher levels of education were more likely to have a positive perception toward COVID-19 vaccines.[30] In Italy, parents with low levels of education rejected vaccination.[46] Similarly, studies have shown that individuals with high levels of education had positive beliefs about vaccination[49] and were more willing to be vaccinated.[47,50] Individuals with a low education level probably have less information about the benefits and importance of vaccination and they are less conscious, which may result in a negative attitude. Individuals with low education levels are more fatalistic.[36,39] A study reported that some of the correlation between lower education level and higher health fatalism was attributed to difficulties in their experiences of searching for health information on cancer; therefore, developing interventions that help individuals experience more positive information-seeking experiences may decrease the probability of individuals with lower levels of education to have fatalistic beliefs.[51] In our study, older individuals were found to have higher health fatalism. Similar to the results of our study, as age increased, individuals in east Turkey had increased health fatalism, women in Iğdır had increased fatalistic tendencies, and in a study conducted in four cities in Turkey, men had increased fatalism for prostate cancer.[36,38,48]

In our study, individuals who were not well informed about COVID-19 vaccines had low positive attitudes and high negative attitudes toward COVID-19 vaccines and had high health fatalism. Individuals who obtained information about vaccines from individuals around them and Internet had lower positive attitudes, those who obtained information from the Internet had high levels of negative attitudes, and those who obtained information from radio, TV, and individuals around them had high health fatalism. A study reported that individuals who had sufficient information about vaccine safety and efficiency had more positive attitudes toward COVID-19 vaccines.[52] A study conducted on medical students in India reported that a good awareness about COVID-19 vaccines decreased hesitations about vaccination.[53] Individuals who do not have sufficient information about COVID-19 vaccines probably do not have information about the

disease process and ways to protect them from the disease. They show a fatalistic approach because they do not think that they can interfere with the disease process. Individuals who stated that they would have COVID-19 vaccination did not trust social media sites such as Facebook, Twitter, and Instagram.[54] Individuals in Saudi Arabia who obtained information about COVID-19 from official accounts of the Ministry of Health had higher desires to get vaccinated than individuals who obtained information from other sources such as social media.[55] Incorrect information about coronavirus circulating in social media and other sources can make individuals more fatalistic.[56] Thus, individuals should be informed of correct sources about COVID-19 vaccines. Healthcare professionals are the key point in this regard.

Individuals who did not have COVID-19 vaccination and who did not recommend COVID-19 vaccination to others had low positive attitudes and high negative attitudes toward COVID-19 vaccines and had high health fatalism. Healthcare professionals who were vaccinated showed more positive attitudes toward COVID-19 vaccines.[28] Fatalistic Hispanic women trusted flu vaccine less, and fatalistic women from Kentucky were less likely to complete the HPV vaccine series successfully.[40,41] Parents who recommended COVID-19 vaccination to others were more willing to allow their children to get vaccinated against COVID-19 than parents who did not make such recommendations to others.[47] Healthcare professionals who recommended COVID-19 vaccines to others were more willing to have COVID-19 vaccination.[32] Attitudes affect behaviors.[15] Negative attitudes have negative reflections on behaviors of getting vaccinated. There is a certain predetermination in fatalism belief, and no matter what one does, this would not change.[18] Individuals may have avoided vaccination because they thought that they will not get rid of the disease even if they were vaccinated. Health fatalism should be decreased to increase vaccination.

Individuals who believed that COVID-19 vaccination will not end the pandemic had low positive attitudes and high negative attitudes toward COVID-19 vaccines and had high health fatalism. The only long-term sustainable solution for COVID-19 is to develop robust vaccination protocols.[5] In Holland, the strongest determinant of the intention to get vaccinated was the belief that the COVID-19 crisis will end only if a large number of individuals are vaccinated.[57] Healthcare professionals who believed that vaccines can end the pandemic were more willing to get vaccinated.[32] Moreover, 44.1% of the healthcare professionals in northeast Ethiopia stated that decreasing the incidence of COVID-19 without vaccines is not possible.[17] In fatalism, everything is predetermined,[18] and fatalistic individuals believe that the end of the pandemic is predetermined. Therefore, they may be thinking that vaccines will not end the pandemic.

Individuals who had COVID-19 had low positive attitudes toward COVID-19 vaccination and had high health fatalism. Those who did not fear contracting COVID-19 had low positive attitudes and high negative attitudes toward COVID-19 vaccines and had high health fatalism. In Saudi Arabia, individuals who did not have COVID-19 previously were more likely to accept COVID-19 vaccination.[55] In another study, individuals who had high fears of contracting COVID-19 were more likely to show positive attitudes toward vaccines.[29] In Arkansas, individuals who were not afraid of or a bit afraid of COVID-19 were more likely to hesitate COVID-19 vaccination than individuals who were afraid of COVID-19.[44] Individuals who had COVID-19 probably thought that they have antibodies and therefore may have lower attitudes toward vaccines. A study conducted in different cities in Turkey showed that fatalistic attitudes decreased fear of COVID-19.[58] A fatalistic life attitudes helps individuals accept the disease process better and therefore experience less fear and anxiety.[59] Individuals who do not fear COVID-19 probably think that they will be infected no matter what and therefore not scared.

Individuals who did not follow the policies on wearing masks and social distancing had low positive attitudes and high negative attitudes toward COVID-19 vaccines and had high health fatalism. Measures such as hand washing, wearing mask, and social distancing contribute to the slowing of the pandemic.[60] In parallel with our study, individuals who did not plan to get vaccinated in Canada were less likely to wear face masks and apply physical distancing.[61] Individuals who wore masks and paid attention to social distancing tended to have vaccination.[62] Following the policies of social distancing and wearing mask has positive effects on the pandemic, just like vaccines. Individuals with high negative attitudes toward vaccines do not obey mask-wearing and social-distancing rules. Inverse proportion was found between fatalistic beliefs and COVID-19-related preventive behaviors.[25] Fatalistic individuals were less willing to obey social distancing rules.[26] Fatalistic individuals may think that they cannot escape the disease, which could affect their approaches to vaccines and personal protective measures.

The results of this first study, in which the attitudes toward COVID-19 vaccines in Turkey were evaluated in the context of health fatalism, are important, and we suggest repeating the study with different samples.

The use of the snowball sampling model, which is one of the improbable random sampling methods, is an important study limitation. Thus, participants may not have been randomly included in the sampling because the data collection process could not be controlled. In addition, the study only enrolled 944 participants; therefore, the results cannot be generalized to the whole Turkish society.

CONCLUSIONS

In our study, individuals had high levels of positive attitudes and low levels of negative attitudes toward COVID-19 vaccines and moderate levels of health fatalism. Individuals with high levels of health fatalism had lower positive attitudes and higher negative attitudes toward COVID-19 vaccines. Therefore, healthcare professionals should inform the society about COVID-19 vaccines, benefits of vaccines, and their effects on the pandemic.

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CONFLICT OF INTEREST

The authors declare no potential conflicts of interests with respect to the authorship and/or publication of this article.

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Understanding the Experiences Lived by Nurses Caring for Patients with COVID-19: A Hermeneutic Approach

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Abstract

Background: Nursing is highlighted among professions that value caring and is perceived as the profession's heart and soul because of its critical role in providing and delivering high-quality patient care, especially during this coronavirus disease 2019 (COVID-19) pandemic. However, little is understood about the experiences of the frontline workers in caring for persons diagnosed with COVID-19. This study aimed to explore the experiences of nurses in caring for persons diagnosed with COVID-19 inspired by the four lived worlds of van Manen.

Methods: The hermeneutic phenomenology was used in nine nurses working in hospitals of Hail region. This study employed a one-to-one interview approach using the Zoom platform, conducted between June and July 2020.

Results: Nine nurses articulated their experiences in caring for patients with COVID-19. Six themes emerged within the four lifeworld such as the feeling of vulnerability to COVID-19, time of uncertainties, price of being a hero, social stigma, holistic care, and sense of belongingness.

Conclusions: The feeling of vulnerability to COVID-19 infection, time of uncertainties, price of being a hero, social stigma, and sense of belongingness have been understood in the context of lifeworld existential of van Manen. Issues are articulated directly from those who experienced them. Still, revisiting the existing intervention strategies of the government and institution, including regulating negative emotions, reducing related issues, and improving quality of life, is important.

Keywords: COVID-19, emotions, hermeneutics, pandemics, quality of life

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a contagious and seemingly undefeated adversary that placed nurses as frontliners being highly vulnerable to infection. Recent studies have focused on risk management[1] and preparedness among healthcare workers during the COVID-19 pandemic.[2] However, little is understood about the experiences of these frontliners in caring for patients with COVID-19. In nursing, caring is considered fundamental, as it is perceived as the profession's heart and soul. Because of its critical role in providing and delivering high-quality patient care, nursing is highlighted among professions that value caring. Writers dating as far back as Florence Nightingale have expressed compassion as a notion inextricably linked to nursing work. Despite the numerous studies attempting to clarify what caring is,[3] the idea remains unclear and vaguely understood.[4] Caring is an emotion rather than a science that requires specific knowledge and skills.[5] These are some reasons why several authors believe that caring is at the heart of nursing practice.[6] Accordingly, caring is understood as a multifaceted notion that may be characterized in various ways, depending on circumstances and points of view. Despite not being exclusive to nursing, caring is largely acknowledged as one of the profession's theoretical foundations.[7] In such a context, caring for patients with COVID-19 brought many ambivalent feelings to nurses. This is true for those who have cared for patients with COVID-19, yet nurses' experiences in caring for these patients are not well-understood. Although the pandemic has increased the workload for nurses and created unpredictability, nurses still offered an effort to every patient with the same level of care that they had before the pandemic. The prioritization of nursing care was affected most likely as a result of the need for more basic care owing to the patient's high dependency and the development of new technical skills.

Nurses make up a large portion of the healthcare workforce during the COVID-19 pandemic and have been involved in diagnosing, treating, and caring for patients for weeks despite insufficient resources.[8] Consequently, psychological discomfort such as depression and anxiety has been widely reported among medical personnel working on the front lines of the COVID-19 outbreak.[9] Accordingly, the growing number of patients with COVID-19, increased workload, restricted availability of personal protective equipment, positive cases, and death stories in the media spread quickly. Furthermore, the lack of

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appropriate treatment medications and assistance may add to healthcare workers' mental health problems.[10]

Important components of nursing care are expected to be universal; however, nurses' experiences are likely to differ throughout areas and countries because of major differences in the effects of the pandemic.[11] When caring for patients with COVID-19, nurses have demonstrated extraordinary resilience and adaptation, despite resource restrictions and mental and physical health hazards. Conversely, nurses require adequate support from their peers, supervisors, policymakers, and local community to properly prepare for and handle pandemic situations.[12]

To the best of the researchers' knowledge, no study has used a hermeneutic approach to examine the experiences of nurses when providing care for patients with COVID-19. To understand this, van Manen provides the four lifeworld existentials of lived body, lived time, lived space, and lived human interactions as starting points for contemplation on the world of lived experiences[13] of these nurses. According to van Manen,[13] the lived body is a term used to describe the bodily presence in our daily lives, as well as all experiences expressed, hidden, and shared through the lived bodies. One can think of time as an experience when referring to the existential of lived time. The lived time relates to the ways in which one experience the world on a temporal level and is made up of a subjective sense of time as opposed to the more objective or factual time. Time restrictions, liberties, and demands can affect how one feels, and vice versa. The existential lived space can be understood as the felt space, or the individual perception of the places people can find themselves in. Moreover, the lived space investigates how the environment can influence feeling and how emotions can alter how an individual see a certain environment. Finally, existential lived human interactions refer to the relationships that form and/or uphold with people in the lifeworld.[13] In other words, the interactions and conversations with other people occur in the shared and created places and interactions with them.

This study aimed to explore the experiences of nurses in caring for patients with COVID-19 inspired by the lifeworld existentials of van Manen. While lived experiences of nurses caring for patients with COVID-19 were explored through different approaches, this study focused on the description and interpretation of the core elements of the lived experience and understanding of the practical significance of this experience. To explore the materials without imposing planned or predefined themes, van Manen's lifeworld existentials provided a coding structure. As a result, the existentials gave four areas through which the phenomenon under inquiry could start to be understood and investigated rather than imposed preset categories on the facts of what was judged significant to this lived experience. This was deemed crucial in maintaining methodological congruence and remaining loyal to the exploratory and inductive nature of qualitative investigation.

These existentials give the researchers the opportunity to enter the lived experience of others and better understand the nature and importance of everyday experience. Therefore, phenomenological probing, thinking, and writing processes are productive phenomenological research categories for spatiality, corporeality, temporality, and relationality. Moreover, these existentials are a cogent and rigorous approach to analyze the relational, practical, and ethical aspects of everyday pedagogy that are challenging to reach through conventional research methods.

METHODS

Ethical approval

The Institutional Review Board of the University of Hail gave its clearance to conduct the study (H-2020-0214). The participants were informed of the importance and goal of the study, as well as other factors and their right to withdraw at any moment throughout the interview session. Participants' rights, anonymity, and confidentiality were always protected. The researchers emailed the informed consent form for the participants to sign. The signed informed consent was sent back to the researchers before the scheduled interview.

Study design

This study employed a hermeneutic phenomenology to explore the experiences of nurses in caring for patients with COVID-19 inspired by the four lifeworld existentials of van Manen.[13] These lifeworld existentials guided the researchers in identifying significant statements and unraveling emerging concepts, thematic categories, and essential themes for every lifeworld. In this study, the research team had identified commonalities and shared structures in nurses' experiences of caring for patients with COVID-19 through the use of the lifeworlds, which made the more abstract elements of the participants' discussions more concrete.

Participants/sampling

The study participants were nine nurses (one male and eight female nurses) who have cared for patients with COVID-19 (Table 1). These nurses were recruited by snowball and purposive sampling, following the inclusion criteria: (a) had a direct contact and continuous care to patients with COVID-19, (b) had no signs and symptoms of psychological burden as a result of the experience in caring for patients with COVID-19 (for practical, ethical, and scientific considerations), (c) had cared for at least two patients with COVID-19, and (d) participated voluntarily.

Setting

This study was conducted in COVID centers of the Hail region, Kingdom of Saudi Arabia, particularly in the

intensive care units of King Khalid Hospital and King Salman Specialist Hospital. These hospitals were earlier identified by the Ministry of Health as COVID-19 centers of the region.

TABLE 1. Demographic characteristics of the participants

Code Name	Age	Sex	Nationality
Participant A	27	Female	Indian
Participant B	25	Female	Filipino
Participant E	28	Female	Filipino
Participant F	25	Female	Saudi
Participant H	31	Male	Saudi
Participant K	32	Female	Filipino
Participant M	28	Female	Indian
Participant R	24	Female	Filipino
Participant S	26	Female	Saudi

Data collection

Data collection commenced after clearance from ethics review board and hospital directors of each participating hospital. A personalized letter was sent to 15 prospect nurses, inviting them to participate in the study. The letter indicated that no incentives will be given to the participants for joining the interviews. Of the candidates, nine replied, expressing availability to participate. The researchers and participants agreed on the date, time, and mode of interview, which was conducted through Zoom meeting software, with the understanding that only the researcher and participant would be present in the meeting room. The one-on-one interview lasted 60–70 min and was recorded with the permission of the participants as discussed in the written informed consent and reiterated before the meeting.

The researchers used field notes. They used unstructured interview and/or interactive dialog for data collection. Sample questions included, "Can you describe to me your experience in caring for patients with COVID-19?" Sample probing questions included, "Can you further explain or clarify what you mean by that? Can you give an example?" Given the repetitive nature of data, researchers must determine the point at which saturation was observed. In this study, data saturation was reached on the seventh participant. However, two others were included to ensure data saturation. No repeated interviews were conducted. This study was conducted between June and July 2020.

The four researchers (two women and two men) were professors of the College of Nursing, held a doctor of philosophy in nursing degree, and were well trained in the interview process. The researchers' reasons and interest in this research topic are propelled by their purpose of reaching a better understanding of the experiences of nurses caring for patients with COVID-19 so that tailored support can be given on time.

Narrative reflection

Participants' stories provide a lens through which to view the evolving perspectives in caring for patients with COVID-19. We had to be careful as a researcher to distinguish between lived experiences and described experiences and prevent getting the wrong idea of causality. Although the stories may vary, participants' identities stay the same; depending on how they respond to new problems, this fundamental identity may help or hinder them. Participants' challenge may enlarge, improve, or affect them in ways that may not be visible to others but may be included into their story. Comparing some of the story examples was possible, which helped us understand how participants are affected by caring for patients with COVID-19. The researchers believed that while each narrative offered a complete picture of an idea. The stories may have been affected by our function as interviewers because we sought out details or elaborations. We encountered participants who were synthesizing their history, present, and future. The participants presented themselves in a specific way while sharing their stories, revealing or hiding aspects of themselves.

Measures to ensure rigor

In this study, researchers performed member-checking to achieve credibility. Participants were asked to read the verbatim transcripts of their respective interviews and provided feedback on the content. A detailed description of their experiences in caring for patients with COVID-19 was used to establish transferability. An inquiry audit or external audit was used to ensure dependability. The purpose was to evaluate the accuracy and evaluate whether the data support the findings, interpretations, and conclusions. Finally, to ensure rigor, a phenomenological study should have confirmability, which is obtained using audit trials to provide rationale and describe the thought processes behind the data collection, data analysis, and interpretation.

Data analysis

The researchers employed thematic analysis using NVIVO software (QSR International Pty Ltd., Burlington, MA, USA). The data analysis began immediately after the completion of the first transcriptions. Each researcher worked independently on the initial data analysis procedures, following predetermined steps. First, the researchers read the transcriptions and field notes for each interview numerous times to ensure a clear understanding. Then, phrases and expressions that described the experiences lived by nurses caring for patients with COVID-19 were chosen. Finally, meanings related to the experiences of the participants were generated. The researchers collaborated in group and organized the themes, and any discrepancies were resolved by re-evaluating the transcriptions and field notes until an agreement was reached. Subsequently, transcriptions were compared and analyzed for phrases that reflected similar theme descriptions. Then, themes were revised and described in greater depth. Statements

from participants who reflected each topic were chosen and rewritten. To this end, van Manen's four lived worlds were divided into key themes: lived body, lived time, lived space, and lived relations.[13] All nine participants were requested to examine the findings (themes and descriptions) to ensure that the findings matched the information they had provided. The validation process revealed no discrepancies with the information given.

RESULTS

The essential themes of lived body, time, space, and relations were used to describe the experiences of nurses caring for patients with COVID-19. Results showed that five themes and one subtheme have emerged.

Theme 1. Feeling vulnerable to COVID-19

The participants discussed and described their bodies as vulnerable to coronavirus, and this includes everything they experience and feel as they care for patients with COVID-19. During their discussion and description, the theme "Feeling vulnerable to COVID-19" emerged. This theme pertains to the participants' emotional reaction accompanied by a level of uncertainty and entails a readiness to bear the psychological risk associated with the crisis.

When asked about their experiences in treating patients with COVID-19, nurses explained that patients were vulnerable to the infection. They felt that they are at a high risk, which affects them psychologically, emotionally, and physically. Most participants stated that caring for patients with COVID-19 were overwhelmed, making them afraid, cautious, threatened, hopeless, and exhausted. For example, one of the participants stated, "Our only concern is not to transmit anything to our family. That is why I had to isolate myself and was staying alone in the flat." (T)

> Another reported:
> "I am afraid that my body might contract the virus, especially when I am already tired. I think maybe they will have to reduce the off-duty time; instead of 12 hours, they would reduce it to 11 hours, or 10 hours just to help us. We cannot refuse the number of patients coming for treatment, especially because the service here is free." (M)

For some participants, the disease was very contagious as well as deadly, and they felt mentally exhausted because some of them appeared to experience COVID-like manifestations such as low-grade fever, severe headache, and cough. They felt that they are infected with the virus, fearing the unknown and feeling fatigued. The participants also feel physically exhausted when they had a tiring duty and experienced everyday fatigue. Moreover, their emotional state in taking care of patients with COVID-19 affects their emotions, as they will be isolated from their family as mandated by the hospital.

Theme 2. Time of uncertainties

As participants have been exposed to people who have the coronavirus for a longer period and are more likely to contract the disease, the theme "time of uncertainties" has evolved, suggesting that the participants' future is uncertain. The participants expressed their fear concerning such uncertainties regarding the time they might be infected. They thought that they might be the next patient and would not have the chance to live their lives fully (lived time). The participants expressed:

> "I mean, I am here every day, and I think that by tomorrow I will be infected. Hence, you cease to plan for tomorrow. You live a wired life because you know anyway; any time you may be infected and gone." (E)

Moreover, the participants consistently exercised the right procedure to maintain a contagion-free workplace and, thus, expected to reduce the chances of being exposed to COVID-19. However, they question whether they will survive their duties given the uncertain situations. Participants continue to express anguish and anticipation of infection and continually think that long exposure to patients with COVID-19 will render them more susceptible to it. Two participants stated:

> "Occasionally, you always think that maybe one day you will be infected, but I have no choice. I need to stay here and care for the patients because this is the profession I chose, and I pledged to serve the patients." (K)

> "My family had lots of worries and doubts when they found that I am caring an infected individual, but I believe that there are no certainties in this situation. I just assured them that I do all precautionary measures so that I will not be infected." (M)

Theme 3. The price of being a hero

The price of being a hero and "social stigma" have emerged, representing the lived space. The theme "price of being a hero" refers to how participants feel despite their heroic actions; caring for patients with COVID-19 has made them feel distanced from their families, friends, and colleagues. Caring for patients with COVID-19 leads to becoming predisposed to spreading the virus, as the participants are likely to contract the disease.

> "Other colleagues who were assigned to the ER were hesitant to talk to me like we talked about previously. Most of my friends were assigned to the ER. (…) When they came to the COVID isolation ward, they would just put the papers in a box and would not face us. They would go back and leave right away. (…) Feeling bad." (A)

Similarly, one participant mentioned:

> "You met nurses on the way, and they would not even want to look in your direction or to meet you, or they would simply turn away and take another direction so that you would not recognize them. They would not

> even allow you to greet them or spend some time discussing anything with them." (L)

Being known as working in a COVID-19 unit creates fear that often clouds the understanding of colleagues and others. The fear of contracting the disease and not knowing how the disease is spread affect the perception of lived space. A participant stated: "They distanced themselves from us. Now I believe that caring for patients with COVID-19 shows how the nurse may experience a sense of separation." (R)

Subtheme 1. Social stigma

The theme of social stigma refers to the prejudice of another person (e.g., colleagues and friends) toward the participants concerning a possible infection with the disease. Such prejudice has made the participants become distant from their colleagues, family, and friends, thereby acknowledging the limited space of the participants. That is, participants' space (lived space) could not be shared with colleagues and others because of the fear of being infected with the disease and the unpredictability that surrounds the condition, enhancing vulnerability to the life-threatening malady. As a participant stated:

> "You met nurses on the way, and they would not even want to look in your direction, or they do not want to meet you, or they simply turned away and took another direction so that you do not recognize them. They would not even allow you to greet them or spend some time discussing anything with them."

The interpersonal environment that the participants experience as they discuss their care experiences of patients with COVID-19 depends on their relationships with other people. Participants understand and feel their interactions with others in this lived relationship. The "sense of belongingness" and "holistic care" were found to be two recurring themes in this lifeworld.

Theme 4. Sense of belongingness

The sense of belongingness (or passionate service) pertains to understanding participants' experiences and recognizing that despite their struggles, humanity exists. This is without regard for his or her self amid the fear of contracting the virus. The participants still committed themselves to caring for others, especially those with COVID-19. The participants conveyed that they gave their selves to be with the patients who had contracted the virus. Their wholehearted service for others delineated a conscious giving of self in a planned relationship (lived relationship). In this situation, the participants deliberately dedicated themselves to caring for and being with the patients in uncertain conditions. The participants described their relationships with others as empathetic, inspiring them to be fearless and trusting. A participant mentioned:

> "Caring for patients with COVID-19 needed a wholehearted service. One must be empathetic because I can only imagine myself getting the disease and feeling bad about it. Many questions were going on in my mind. I asked, "Who will care for these sick patients if we don't?" I sympathized with them, giving me courage. Even though the nurses were accused of being COVID-19 nurses or dirty nurses, they had the empathy to continue their care for patients in COVID-19 isolation wards." (R)

In addition, other participants shared their points of view, stating that:

> "(…) if there is no teamwork, no one will survive in this pandemic. You cannot survive alone (H)," and that "(…) we will not be effective if we will not work as a team (…) Be mindful of our communication with our colleagues. How we need each other in duty." (B)

One also stated that "(…) when you work with other colleagues, the thinking is less, and the work becomes easier as we help us in providing patient care (…). It is also psychologically healthy to have a colleague with you." (H)

The participants recognize the sense of belongingness as a responsibility of professional nurses, realizing that patients with COVID-19 have the same rights to be cared for like anyone else. Additionally, the participants reported that they had to devote themselves to working hard in COVID-19 isolation wards.

Theme 5. Holistic care

Holistic care is a shared awareness of how nurses care for their patients with physical, psychological, emotional, and spiritual qualities. This is the provision of care and their relationship to patients based on a mutual understanding with the nurse to care for their physical, psychological, emotional, and spiritual dimensions (lived relation). Two participants refer to this by saying that "you can provide better service to the patients as you help each other, focusing on the whole aspect of the person" (H) and that "we provide comfort to our patients by praying with them and reassuring them that we are with them all the way." (F)

Staying overtime in the isolation ward brought them closer together. They valued each other's presence. The participants prayed with their patients. They continued to provide comfort, committed to caring, and give patients hope and reassurance despite the social distancing, wearing of full personal protective equipment, and handwashing. They also provided psychological support and extended financial help to non-Saudi patients. They trusted in the divine power to heal their patients and empower patients to care for themselves. Despite the uncertainties and different behaviors such as uncooperativeness and complaint, they still appreciated the value of the care that they provided to their patients. Indeed, they were very happy and felt that to discharge a

patient becoming negative for COVID-19 was very self-rewarding. Participants were cheering up each other for their present situation. A participant stated:

> "It was very rewarding to us when we discharged patients in good condition. In fact, we cheered them up in support of their courage to beat the deadly COVID-19. This is because we do everything using humanism and holism as a guide to treating the patients." (S)

DISCUSSION

This study aimed to understand the experiences of nurses in caring for patients with COVID-19 using the lifeworld existentials of van Manen to gain deeper insights into the experiences of the participants as they battle with the coronavirus. Indeed, the discovery of new variants of the original coronavirus infection exposes healthcare providers to a new risk. Nurses feel vulnerable to the coronavirus infection in this context for being exposed to the disease. In this study, the feeling of vulnerability is just one of the challenges faced by these frontliners. Earlier studies have reported that many healthcare workers mimic COVID-19 symptoms, which makes them psychologically distressed. For example, similar concerns regarding contagion exposure and personal and family health have been highlighted among those caring for patients during H1N1 outbreaks.[14] In this context, people's ability to deal with their emotions may be improved by cultivating adaptive views toward stress,[15] helping alleviate negative physical symptoms, and improving physiological functioning. Findings such as the ones presented in this study emphasize the need to provide psychological support and prepare healthcare workers during the COVID-19 outbreak.

Participants accepted the situation while remaining fearful and concealed their anguish around patients during time of uncertainties. They triumphed in stabilizing their fears with the fulfillment obtained from caring for patients. Similar experiences have been eminent in other studies on nursing experiences during an upsurge of a disease.[16] In Henan, China, nursing staff described the negative (e.g., fear and anxiety) and positive (e.g., confidence and happiness) emotions in COVID-19 isolation wards during their first week of exposure. However, after this period, 70% of the nurses had positive reactions.[17] Such a result shows that these frontliners must receive continuous support from the institution and social assistance be made available to circumvent psychological disturbances, which could have a long-term negative effect on their mental health.

The price of being a hero has echoed among the participants as a result of their frustration for feeling excluded, despite being called the unsung heroes. These nurses put their lives on the line to save others and play a critical role in stopping the virus from spreading, yet they have not received fair treatment in return. As expressed by the participants, their colleagues have rejected them, which made them feel their space tightening, which adds up to their psychological burden and harms their moral code. Previous study examined how actions that breach an individual's moral code or a sense of betrayal by others might cause the so-called moral damage.[18] Moral damage has been recognized as a potentially major risk for healthcare professionals during the COVID-19 outbreak. Moreover, healthcare workers have shared experiences where they felt deceived by their colleagues and society, and this could be a risk factor for additional mental health issues, which can be dangerous during a pandemic.[19] A greater understanding of this concern among frontliners could aid in the development of personalized interventions that effectively support the psychological health of these frontline workers.

Social stigma, being a subtheme in this study, marks the experiences of the frontlines on how colleagues and other individuals treat them for caring for patients with COVID-19. Accounts of nurses' caregiving experiences during earlier outbreaks of contagious illness are covered with references to societal stigma and its detrimental psychological effects.[16] Indeed, nurses who cared for patients with COVID-19 have experienced stigma,[20] which may hinder the efforts of healthcare workers and health authorities to prevent COVID-19.[21] In addition, most frontliners have had similar experiences. For example, nurses were not allowed to enter their rented housing, were not provided a house to rent, were not allowed to use public transportation having to rely on bicycles, and were attacked while on duty.[22] The public's fear of being infected with COVID-19 is to blame for the disease's stigma.[23] Such stigma is characterized by misconceptions and negative attitudes against nurses and may impair the workforce and self-respect of healthcare personnel who provide support, treatment, and care to patients with COVID-19, potentially jeopardizing the prevention of COVID-19 outbreaks.[24]

Amidst the fear of contracting the virus, the study participants are still committed to caring for patients and thereby promoting the sense of belongingness to humanity. Participants' caregiving experiences were also structured by their relations with patients and other members of the healthcare team. Most observations indicate that the sense of professional obligation is rooted in social and religious principles. Accordingly, nurses have formed a spiritual pledge to treat patients with COVID-19. Earlier studies have also reported that relationships with patients and other members of the healthcare team have shaped caregivers' caring experiences.[16,25–27] Connecting socially with patients and advocating for their needs can give frontliners a sense of belongingness and add significance to their work. In this context, the study participants have demonstrated their professional responsibilities and ethical commitment to patient-

centered care. Moreover, participants reported that the pandemic made them recognize the value of professional solidarity and that they valued and supported one another more socially and psychologically because of the pandemic.[28] Thus, in this study, nurses showed the need for self-reflection as it helps them become more aware of nursing and caring, as well as the inner ethical principles in caring. This demonstrates that nurses will be able to get a better grasp of caring in their nursing practice.

In this study, the frontliners believed that holistic care must be delivered. Holistic care is the delivery of care to patients based on a mutual understanding between the patient and the nurse to address physical, psychological, emotional, and spiritual needs. The mental health, recovery rate, and satisfaction of patients with COVID-19 may all be influenced by holistic care.[29] Such care may be amplified at a low cost and benefit patients in both government and private health institutions. Indeed, this holistic care has also been echoed in India where nurses said they lacked a holistic COVID-19 approach to care. Owing to time constraints, the nurses claim that empathy and compassion-focused care, as well as listening to patients with COVID-19, are missing. Furthermore, there is no consensus in caring for and understanding patients.[30] Nurses' experiences in caring for patients with COVID-19 may be comparable with those in other settings, but administrative actions required may differ.

The used of van Manen lifeworlds as framework in this study stresses the peculiarities of the method. This method provides potential explanation for the phenomenon being studied. Therefore, a theoretical model, like the idea of the lifeworld existentials, provides a prism through which to investigate personal experience. In context, the use of this method provided us a way to start defining the different interrelated components that make up a specific lived experience.

This study contributes to the understanding of the experiences of frontline nurses during the surge of the COVID-19 pandemic and shows that nurse managers should focus on protecting nurses' well-being. By doing so, nurses can provide better and safer care performance and quality care that is expected of them.

This study has limitations that need further exploration in future studies. For example, the years of experience of these nurses were not a part of the inclusion criteria, and it might have implications concerning their experience in handling COVID-19. Moreover, the interview was conducted through a Zoom meeting where some of the visual cues were not fully observed.

CONCLUSIONS

The feeling of vulnerability to COVID-19, living in times of uncertainties, price of being a hero, social stigma, and sense of belongingness have been understood in the context of lifeworld existentials of van Manen. The issues are articulated directly from those who experienced them. A need to revisit existing intervention strategies of the government and institution to include regulating negative emotions, reducing related issues, and improving quality of life are of paramount importance. In this contribution, the potential and unique value of the approach for pedagogical inquiry are demonstrated, together with certain methodological ideas and fundamental research practice tasks. Knowing nurses' experiences in caring for patients with COVID will eventually provide valuable information for future nursing care, not only those who were diagnosed with COVID but also those under similar life-threatening experiences.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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Protective Effect of Betulinic Acid Administration on Kidney Damage in Acetaminophen-Induced Nephrotoxicity Model

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Protective Effect of Betulinic Acid Administration on Kidney Damage in Acetaminophen-Induced Nephrotoxicity Model

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Abstract

Background: Acetaminophen (APAP) is the most widely used analgesic drug worldwide, but it may induce renal toxicity. Betulinic acid (BA) ameliorates the oxidative stress and inflammatory response to renal damage. The present study aimed to investigate the potential protective effects of BA treatment through an experimental kidney damage rat model administered with APAP.

Methods: Sprague–Dawley male rats were randomly divided into four groups: control, BA (25 mg/kg for 15 days), APAP (1 g/kg), and APAP + BA groups. BA was administered via oral gavage at a dose of 25 mg/kg for 15 days. APAP was dissolved in hot saline and administered on the last day to produce nephrotoxicity via a single oral gavage at a dose of 1 g/kg. Kidney tissue samples were analyzed for human cartilage glycoprotein 39 (YKL-40), kidney injury molecule 1 (KIM-1), interleukin 18 (IL-18), superoxide dismutase (SOD), and malondialdehyde (MDA). Data were subjected to one-way analysis of variance and the Wilcoxon rank-sum test

Results: Renal tissue YKL-40, KIM-1, IL-18, and MDA levels in the APAP group were significantly higher than those in the control group ($p < 0.05$). The BA treatment completely restored renal KIM-1, YKL-40, and MDA levels and partially restored renal IL-18 and SOD levels in the rats subjected to renal damage induction ($p < 0.05$). The intertubular regions of rats administered with APAP had degeneration, necrosis, and infiltration of inflammatory cells and were immunopositive for IL-1 beta and 8-hydroxy-2'-deoxyguanosine.

Conclusions: BA can be used in the prevention and replacement treatment of nephrotoxicity due to its inhibitory properties in multiple pathways and powerful antioxidant effects.

Keywords: acetaminophen, betulinic acid, interleukin 18, kidney injury molecule 1, malondialdehyde, superoxide dismutase

INTRODUCTION

Acetaminophen (APAP) is one of the most widely used analgesic drug worldwide despite its capability to induce renal toxicity at overdose. Metabolites from APAP–glutathione and APAP–cysteine conjugates have been implicated in renal toxicity.[1] APAP transforms into the harmful p-aminophenol metabolite, which is a nephrotoxin in the kidney that initiates tissue damages, specifically tubular and cortical necrosis.[2] In addition to APAP-induced oxidative stress and renal damages,[3] the activation of inflammatory and oxidative mediators contributes to nephrotoxicity.[4]

The principal response to kidney injury is the development of inflammation and oxidative stress, which can lead to renal fibrosis. Biomarkers associated with renal inflammation and repair may be helpful in distinguishing patients at risk of kidney damage from those who are likely to recover.[5] Biomarkers are frequently examined to diversify risk prediction, in addition to the usual clinical variables, and to explore potential pathological mechanisms that may be targets for future intervention. Human cartilage glycoprotein 39 (YKL-40), a member of "mammalian chitinase–like proteins," is secreted by macrophages, neutrophils, chondrocytes, endothelial cells, vascular smooth muscle cells, and cancer cells and also known as chitinase-3-like protein 1. It is a novel biomarker for acute and chronic inflammation. A high serum YKL-40 concentration indicates poor prognosis in a wide range of diseases and clinical conditions.[6,7]

The kidney can effectively recover from an ischemic or toxic insult that results in cell death as the tubular epithelium can proliferate and replace lost cells. The balance between injury and repair is the key determinant of the fate of the injured kidney. Potent factors induced by injury facilitate adaptive repair.[8] Kidney injury molecule 1 (KIM-1), a transmembrane glycoprotein, is upregulated more than any other protein in the proximal tubule of the kidney with various forms of injury. KIM-1 is a phosphatidylserine receptor that mediates phagocytosis of apoptotic bodies and oxidized lipids. The chronic

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expression of KIM-1 results in progressive kidney fibrosis and chronic kidney failure, which are possibly related to its phagocytic function to take up noxious compounds, such as oxidized lipids.[9,10]

The role of inflammation in nephrotoxicity has been increasingly appreciated with the involvement of leukocytes, adhesion molecules, chemokines, and cytokines. Interleukins (ILs) are important mediators of the immune reaction in the innate immune system response and adaptive immunity. IL-18 is a proinflammatory cytokine involved in the pathogenesis of acute kidney damage.[11,12]

Betulinic acid (BA) is mainly isolated from plant sources, such as birch, eucalyptus, and plane trees.[13] It's potent physiological and pharmacological activities are related to anti–diabetic, antitumor, anti-inflammatory, and antibacterial effects. BA can help protect cells against oxidative damage by reducing the oxidative stress caused by free radicals. These antioxidant effects can potentially mitigate the negative effects associated with aging, inflammation, and certain diseases. BA exerts a strong anti-inflammatory effect by inhibiting inflammation. BA can also reduce the excessive response of the immune system and regulate the production of inflammatory cytokines.[14,15] The present study was conducted to determine whether BA has protective effects on experimentally induced kidney damage using a rat model administered with APAP.

METHODS

Animals and experimental design

Ethics committee approval of the study was obtained from Atatürk University Local Ethics Committee for Animal Experiments. Male Sprague–Dawley rats (N = 32, 200–250 g, and 6–8 weeks old) from the Experimental Animal Laboratory of Atatürk University were housed in special rooms with an ambient temperature of 22°C ± 2°C and humidity of 50%–60% under a photoperiod of 12:12 h light:dark conditions. The animals were given tap water and standard diet *ad libitum*. The rats were randomly divided into four groups (n = 8 per group): (1) control, (2) BA, (3) APAP, and (4) APAP + BA groups. BA (Sigma Chemical Co., St. Louis, MO) was administered via oral gavage at a dose of 25 mg/kg for 15 days.[16] APAP (Sigma Chemical Co., St. Louis, MO) was dissolved in hot saline and administered on the last day to induce nephrotoxicity via a single oral gavage at a dose of 1 g/kg.[17] APAP was administered 24 h after the last BA treatment.

After APAP injection for 24 h, the rats intraperitoneally administered with ketamine (80 mg/kg; Ketalar®, 50 mg/ml, Eczacibasi, Istanbul, Turkey) and xylazine (10 mg/kg; Rompun®, 2%, Bayer, Istanbul, Turkey) were sacrificed, and blood and kidney tissues were harvested for analyses. Blood samples were centrifuged at 3000 rpm for 15 min to separate the sera. Serum samples were analyzed for blood urea nitrogen (BUN), creatinine, alanine amino transferase (ALT), and alkaline phosphatase (ALP). Kidney tissues were stored in a −80°C freezer for the analyses of KIM-1, YKL-40, IL-18, superoxide dismutase (SOD), and malondialdehyde (MDA).

Biochemical examination

Serum BUN, creatinine, ALT, and ALP were analyzed using an autoanalyzer (RX Monaco; Randox Laboratories Ltd., County Antrim, UK). The method of Sun *et al*.[18] was used to determine the SOD activity (U/mg protein) in kidney tissue samples; the method is based on the utilization of the xanthine oxidase system as a superoxide generator and inhibition of nitroblue tetrazolium reduction. Renal MDA levels (nmol/mg protein) were determined by the method of Esterbauer and Cheeseman[19] based on the measurement of the absorbance of the pink complex that formed in the presence of thiobarbituric acid at a wavelength of 532 nm.

Renal KIM-1, YKL-40, and IL-18 levels (pg/mg) were measured by enzyme-linked immunoassay (ELISA; ELK Biotechnology Co., Ltd, Wuhan East Lake Hi–Tech Development Zone, Hubei, China), in accordance with the manufacturer's instructions. In the ELISA method, an antigen immobilized on a solid surface was complexed with an antibody linked to an enzyme. Detection is accomplished by assessing the conjugated enzyme activity via incubation with a substrate to produce a measurable product at 450 nm.

Histopathological examination

The kidney tissue samples were fixed in 10% buffered formalin and routinely processed for histological examination by embedding in paraffin wax. The tissue sections were cut at 4 µm thickness and stained by hematoxylin–eosin (HxE) for observation under a light microscope (Olympus Bx51 with a DP72 camera system, Olympus Corp., Tokyo, Japan).[20]

Each specimen was examined in 10 randomly selected areas of an X40 objective. The scores for hyperemia, degeneration, necrosis, and inflammatory cells were derived semi-quantitatively using light microscopy on the preparations from each rat and reported as follows: Grade 0 = –(negative); Grade 1 = +1 (mild); Grade 2 = +2 (moderate); Grade 3 = +3 (severe); Grade 4 = +4 (most severe).[21]

Immunohistochemical examination

All the tissue samples were cut into 4 µm sections and processed for immunohistochemical examination by a standard avidin–biotin–peroxidase method described by the manufacturer. Rabbit polyclonal antibodies that react with rat IL-1β antibody (Catalog No. ab9722, Santa Cruz Biotechnology, Dallas, US) and 8-hydroxy-2'-deoxyguanosine

(8-OHdG) (sc–66036, Santa Cruz Biotechnology, Dallas, US) at the dilution of 1:200 were used for 60 min. A secondary antibody was used following the manufacturer's protocol (exposed mouse and rabbit-specific HRP/DAB detection IHC Kit, Abcam Cat. No. ab80436; Abcam, Cambridge, UK). After three washes with 0.1% Tween 20 in phosphate-buffered saline, the sections were incubated with 3,3-diaminobenzidine (Dako Cytomation, Santa Clara, CA) and counterstained with Mayer's hematoxylin (Dako Cytomation).

Statistical analysis

The data were analyzed using a commercial software (Statistical Analysis of the System (SAS), Version 9.0, SAS Institute Inc., Cary, NC). Biochemical parameters (continuous data) were subjected to one-way analysis of variance using the GLM procedure. The group mean differences were elucidated by the least-significant difference option. Histopathological and immunohistochemical parameters (discrete data) were subjected to the Wilcoxon rank-sum test using the NPAR1WAY Procedure (SAS). Values at $p \leq 0.05$ were considered significant.

RESULTS

Kidney injury markers

The APAP administration group caused 4.1-, 2.7-, 3.3-, and 2.5-fold increases in concentrations of BUN, creatinine, ALT, and ALP, respectively, compared with the control group ($p < 0.05$, Table 1). Except for that of ALP, the BA treatment reduced BUN, creatinine, and ALT concentrations in the APAP group to the levels of the control group.

TABLE 1. Effect of BA treatment on serum biochemistry profile of rats exposed to APAP-induced nephrotoxicity*

Groups[2]	Parameters[1]			
	BUN (mg/dL)	Creatinin (mg/dL)	ALT (U/L)	ALP (U/L)
Control	14.7 ± 1.1[b]	0.80 ± 0.08[b]	34 ± 3.0[b]	65 ± 5.0[c]
APAP	60.7 ± 7.6[a]	2.13 ± 0.39[a]	111 ± 13.0[a]	165 ± 12.0[a]
BA	15.1 ± 1.0[b]	1.07 ± 0.10[b]	33 ± 3.0[b]	64 ± 6.0[c]
APAP+BA	25.3 ± 2.3[b]	1.13 ± 0.14[b]	39 ± 3.0[b]	101 ± 5.0[b]

*Data are the least square means ± standard error (SE). Different superscripts within columns differ ($p < 0.05$).
[1]BUN = blood urea nitrogen; ALT = alanine aminotransferase; ALP = alkaline phosphatase.
[2]BA was administered via oral gavage at a dose of 25 mg/kg for 15 days (Nader and Baraka 2012). The APAP, after its dissolution in hot saline, was administered on the last day to produce nephrotoxicity via a single oral gavage at a dose of 1 g/kg (Dokumacioglu *et al.* 2017).

TABLE 2. Effect of BA treatment on renal KIM-1, YKL-40, IL-18, SOD, and MDA levels in rats exposed to APAP-induced nephrotoxicity*

Groups[2]	Parameters[1]				
	KIM-1 pg/mg	YKL-40 ng/mg	IL-18 pg/mg	SOD U/mg protein	MDA nmol/mg protein
Control	348 ± 41.0[b]	27.9 ± 3.2[b]	221 ± 31.0[c]	250 ± 47.0[a]	24.6 ± 2.5[b]
APAP	755 ± 63.0[a]	63.4 ± 8.5[a]	724 ± 47.0[a]	90 ± 14.0[c]	49.3 ± 4.3[a]
BA	354 ± 24.0[b]	28.7 ± 2.5[b]	174 ± 23.0[c]	216 ± 18.0[ab]	22.1 ± 1.8[b]
APAP+BA	383 ± 28.0[b]	30.9 ± 5.1[b]	399 ± 3.08[b]	147 ± 13.0[bc]	26.8 ± 2.4[b]

*Data are the least square means ± SE. Different superscripts within columns differ ($p < 0.05$).
[1]KIM-1 = kidney injury molecule; YKL-40 = glycoprotein 39 or chitinase-3-like protein; IL-18 = interleukin 18; SOD = superoxide dismutase; MDA = malondialdehyde.
[2]BA was administered via oral gavage at a dose of 25 mg/kg for 15 days (Nader and Baraka 2012). APAP, after its dissolution in hot saline, was administered on the last day to produce nephrotoxicity via a single oral gavage at a dose of 1 g/kg (Dokumacioglu *et al.* 2017).

TABLE 3. Effect of BA treatment on the histopathology and immunohistochemistry of renal tissues from rats exposed to APAP-induced nephrotoxicity*

Groups[2]	Parameters[1]					
	Hyperemia	Degeneration	Necrosis	Inflam. cells	IL1β	8–OHdG
Control	0 (0–1)[c]	0 (0–1)[c]	0 (0–0)[c]	0 (0–0)[c]	0 (0–0)[c]	0 (0–1)[c]
APAP	2 (2–3)[a]	2 (2–3)[a]	2 (1–2)[a]	2 (1–2)[a]	2.5 (2–3)[a]	3 (2–3)[a]
BA	0 (0–1)[c]	1 (0–1)[c]	0 (0–0)[c]	0 (0–0)[c]	0 (0–0)[c]	0.5 (0–1)[c]
APAP+BA	1 (0–2)[b]	1.5 (1–2)[b]	0.5 (0–1)[b]	1 (0–1)[b]	1 (1–1)[b]	1.5 (1–2)[b]

*Data are the median score (minimum–maximum). Different superscripts within columns differ ($p < 0.05$).
[1]IL1β = interleukin 1 beta; 8-OHdG = 8-hydroxy-2'-deoxyguanosine.
[2]BA was administered via oral gavage at a dose of 25 mg/kg for 15 days (Nader and Baraka 2012). APAP, after its dissolution in hot saline, was administered on the last day to produce nephrotoxicity via a single oral gavage at a dose of 1 g/kg (Dokumacioglu *et al.* 2017).

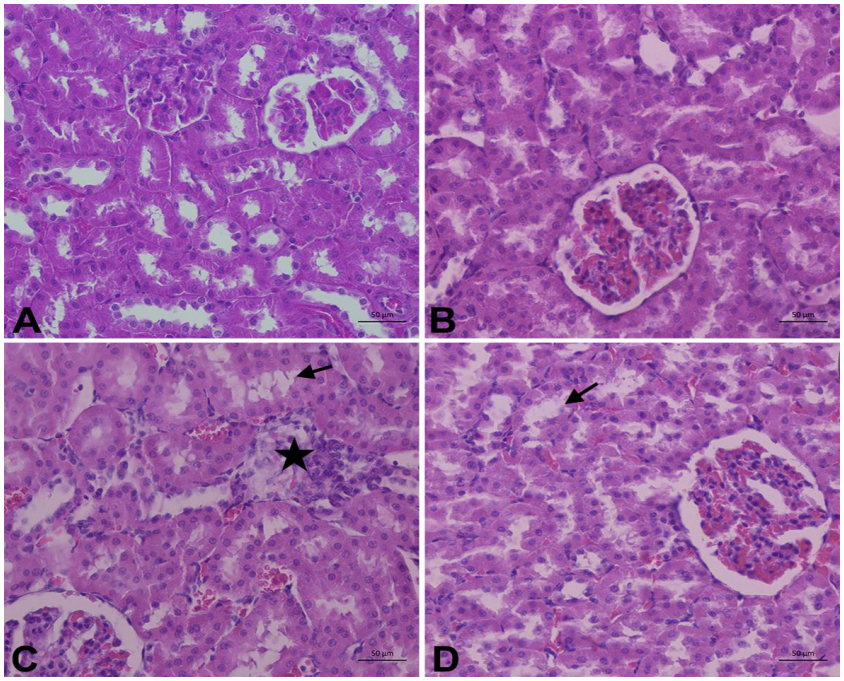

FIGURE 1. Effect of BA treatment on the histopathology of renal tissue in rats exposed to APAP-induced nephrotoxicity. HxE, Bar: 50 µm. A–B) No histopathological lesions in the healthy rats not given BA (control) and given BA (BA group). C) Inflammatory cell infiltration, degeneration, and necrosis in the epithelial cells of proximal tubules in rats with APAP-induced nephrotoxicity (APAP group). The star on the figures indicates inflammatory cell infiltration, and the black arrow shows degeneration and necrosis. D) Moderate histopathological changes were observed in rats with APAP-induced nephrotoxicity and treated with BA (Group APAP + BA).

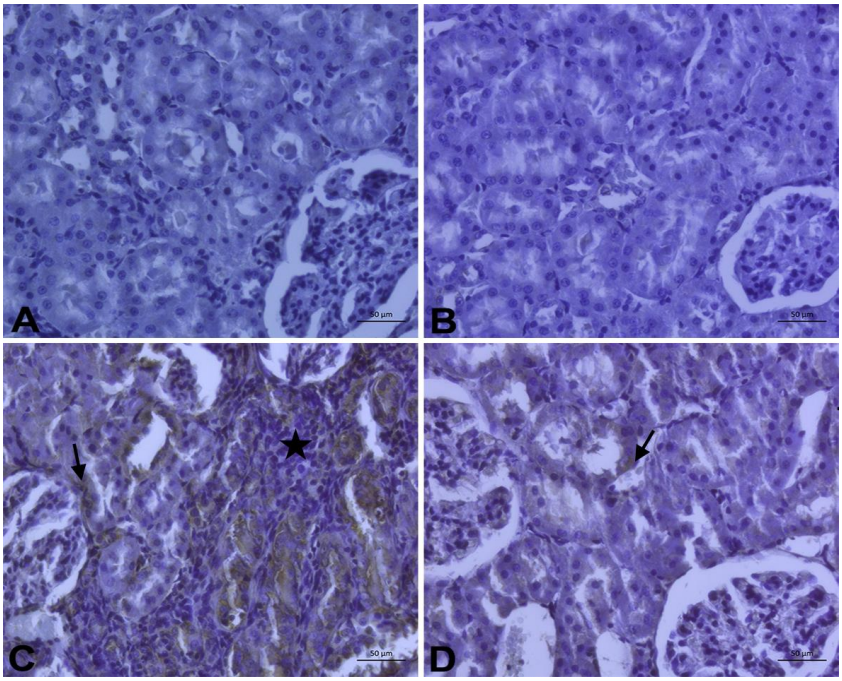

FIGURE 2. Effect of BA treatment on the immunohistochemistry of IL-1β expression in rats exposed to APAP-induced nephrotoxicity. Immunopositive stained epithelial cells, mesengial cells, and endothelial cells of blood vessels. The star on the figures indicates inflammatory cell infiltration, and the black arrow shows degeneration and necrosis. Bar: 50 µm.

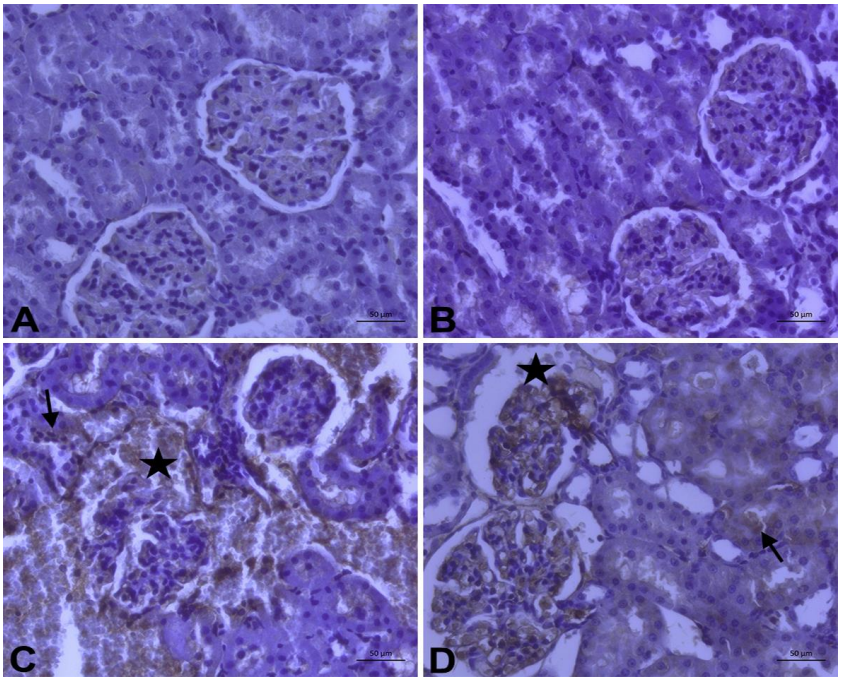

FIGURE 3. Effect of BA treatment on the immunohistochemistry of 8-OHdG expressed in rats exposed to APAP-induced nephrotoxicity. Immunopositive stained epithelial cells, mesengial cells, and endothelial cells of blood vessels. The star on the figures indicates inflammatory cell infiltration, and the black arrow shows degeneration and necrosis. Bar: 50 µm.

Compared with the control group, the APAP administration increased renal KIM-1, YKL-40, IL-18, and MDA levels by 117%, 127%, 228%, and 100%, respectively ($p < 0.05$, Table 2) and decreased renal the SOD level by 64% ($p < 0.05$, Table 2). The BA treatment completely restored renal KIM-1, YKL-40, and MDA levels and partially restored renal IL-18 and SOD levels in the rats subjected to renal damage induction.

Tissue analysis

Nephrotoxicity induction by APAP administration was successful, as reflected by the dramatic increases in the scores for hyperemia, degeneration, necrosis, and infiltration of inflammatory cells (macrophages and lymphocytes) in the intertubular region (Table 3; Figures 1A, 1B, and 1C). BA treatment was partially effective in ameliorating these histopathological parameters (Table 3; Figure 1D).

Biomarker expression

Responses to immunopositivity for IL-1β (Table 3; Figure 2) and 8-OHdG (Table 3; Figure 3) among the experimental groups were similar to the histopathological findings. APAP administration resulted in immunopositivity for IL-1β and 8-OHdG of the kidney tubular epithelial cells, mesengial cells, and endothelial cells of blood vessels, which were partially alleviated by the BA treatment (Table 3; Figures 2 and 3).

DISCUSSION

APAP is one of the nonsteroidal anti-inflammatory drugs and has a widespread clinical use. When it is used at high doses, however, APAP can cause acute toxicity in organs involved in its metabolism and elimination, particularly in the liver and kidneys.[22] Kidneys are dynamic organs having important roles in maintaining body homeostasis, water, and acid–base and electrolyte balance. Some biochemical and physiological properties of the kidney make it more susceptible to ischemic and toxic damage compared with other organs.[23] This experiment questioned whether BA treatment alleviates APAP-induced nephrotoxicity using biochemical and histopathological markers pertinent to kidney damage.

Many studies indicated elevated BUN and creatinine levels as the evidence of renal dysfunction.[24] Naguib *et al*.[25] and Das *et al*.[26] reported increases in BUN and creatinine levels upon the hepatorenal damage induction by paracetamol. In agreement with previous studies, APAP-induced nephrotoxicity was associated with elevations in BUN, creatinine, ALT, and ALP concentrations. APAP is a nephrotoxin and can induce nephrotoxicity at a single dose of its administration.[27,28] In APAP intoxication, increased levels of N-acetyl-p-benzoquinoneimine lead to increased formation of superoxide radicals (O_2^-) and hydrogen peroxide (H_2O_2).[29] Kidney damage induced by nephrotoxins may result in chronic renal failure, nephrotic syndrome, tubular dysfunction, and acute renal failure due to triggering by oxidative stress.[23,30] MDA, an important indicator of oxidative stress, is formed by the peroxidation of polyunsaturated fatty acids. Lipid peroxidation is the chemical reaction initiated by free radicals and involves the oxidation of polyunsaturated fatty acids on the membrane structure. Reactive

aldehydes, including MDA, cause cross-linking and polymerization in membrane components, which eventually leads to alterations in membrane functions, involving deterioration in membrane structure, ion transport, and enzyme activity.[31] SOD is an endogenous antioxidant enzyme protecting the cells responsible for oxygen metabolism from the adverse effects of superoxide radicals. In the literature, SOD activity was shown to decrease in acute kidney injuries.[32,33] Double MDA concentration and decreased SOD concentration in the APAP group can be attributed to the lipid peroxidation reaction and decreased antioxidant protection system success of renal damage. BA has been suggested to exhibit antioxidant properties, thus attenuating the development of oxidative stress in experimental animal models. BA has antioxidant effects, which can protect kidney cells from oxidative damage caused by free radicals. Oxidative stress contributes to kidney damage. Thus, the antioxidant properties of BA may support kidney health. BA can help protect cells against oxidative damage by reducing MDA levels and inducing SOD activity. These effects can potentially mitigate the negative effects associated with kidney damage.[34,35]

Severe inflammatory response also occurs in kidney damage resulting from oxidative stress.[36] The study by Ucar *et al*.[37], in which kidney damage was induced by APAP administration, revealed increases in the levels of inflammatory cytokines. Inflammation underlies the pathogenesis of many acute or chronic kidney diseases, and IL-18 is a useful marker for the diagnosis of diseases and prediction of their severity and prognosis.[38,] In agreement with the study of Shen *et al*.[39], a dramatic increase in IL-18 concentration was observed in rats exposed to kidney damage upon APAP administration.

KIM-1 is found at very low levels in the proximal tubules of the normal kidney. However, its level increases in damaged epithelium.[40,41] It is one of the proteins most induced in the kidneys following acute kidney injury[42,43] and considered a prominent biomarker.[44] The KIM-1 response upon APAP administration is similar to those reported by Kim *et al*.[45] and Coban *et al*.[28] We observed the positive effects of BA on KIM-1 in our study. No research investigated the relationship between BA and KIM-1. However, some studies suggested that BA may have a protective effect on kidneys by reducing oxidative stress[46] and inflammation[47], which can lead to decreased KIM-1 levels. KIM-1 is a biomarker used to detect early signs of kidney injury, and its reduction may indicate improved kidney function. Further research is needed to fully understand the potential relationship between BA and KIM-1.

YKL-40, identified as a new inflammatory marker, plays an important role in inflammation, angiogenesis, extracellular matrix remodeling, and fibrosis development.[48,49] Puthumana *et al*.[50] reported that YKL-40 levels increased to limit kidney damage and support adaptive repair mechanisms. The YKL-40 level became more than doubled in the APAP group, which was accompanied by increased cytokine levels because inflammatory cytokines stimulate the synthesis.[51,52] YKL-40 is a marker of inflammation and tissue remodeling and associated with various pathological conditions, including kidney diseases. However, no current evidence suggests that BA has a direct effect on YKL-40 levels or activity. In our study, we observed the positive effects of BA on YKL-40. We believe that the positive effect of BA on YKL-40 levels resulted from its capability to halt the inflammatory process. Decreased inflammation may have led to a decrease in YKL-40 levels. Further research is needed to explore any potential relationship between BA and YKL-40 in kidney disease or other conditions.

The APAP-induced renal damage was evident, as reflected by histopathological findings, such as degeneration in kidney tissues and necrosis and hyperemia in epithelial cells. Moreover, immunohistochemical findings revealed the increased expressions of IL-1β and 8-OHdG. Inflammation and oxidative stress play important roles in the pathophysiology of many kidney diseases and their complications.[53] Acute kidney injury, as a result of long-term use of APAP, is one of the most common conditions. Natural ingredients with high antioxidant potency may help protect renal tissues from the APAP-induced nephrotoxicity.

BA may have various positive effects on kidneys. Some studies suggest that BA can help the kidneys function in a healthy way by protecting kidney cells from oxidative stress and inflammation.[46,54] In addition, BA is being investigated as a potential treatment option for some kidney diseases, such as kidney inflammations and kidney stones. Khataylou[54] showed that BA markedly decreased the production of proinflammatory cytokines.

BA supplementation provides nephron-protective effects through ameliorating oxidative stress and inflammatory response.[55] Lingaraju *et al*.[55] reported that BA administration increased renal antioxidant activity by suppressing inflammatory cytokines. BA reduced oxidative stress and inflammation in renal tissue. An experimental study examining the effects of BA on renal fibrosis reported that BA prevents fibrosis by inhibiting nuclear factor-κB activation.[56] The BA treatment completely and partially ameliorated the serum parameters. These positive effects on metabolic profile were accompanied by an enhanced antioxidant status. The beneficial effects of BA treatment were also notable in histopathological and immunohistochemical evaluations.

CONCLUSIONS

Acute APAP exposure generated inflammation and oxidative stress in tissues, as reflected by the increases in

specific (KIM-1, YKL-40, and IL-18) and general (SOD and MDA) biomarkers involved in the pathophysiology of nephrotoxicity. Overall, BA treatment was partially effective in ameliorating renal damage. Studies investigating the effect of BA on kidney injury are limited. Our study is one of the few research investigating the effect of BA on kidney injury, which makes the topic innovative and interesting. Our study can contribute new information to the literature regarding the effect of BA on kidney injury. This can provide an important scientific contribution for researchers and healthcare professionals. The study results suggested that BA ameliorated the oxidative stress and inflammatory response of APAP-induced renal damage by reducing the KIM-1/YKL-40/IL-18 signaling pathway. Future research should consider different treatment dosages and durations of BA treatment for kidney injury.

CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests nor personal relationships that could have appeared to influence the work reported in this paper.

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Comparison of Maturation Stages of Natural Killer Cell Differentiation Culture from Cultured and Freshly Isolated Umbilical Cord Blood Hematopoietic Stem Cells

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Comparison of Maturation Stages of Natural Killer Cell Differentiation Culture from Cultured and Freshly Isolated Umbilical Cord Blood Hematopoietic Stem Cells

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Abstract

Background: Natural killer (NK) cells originate from the differentiation of hematopoietic stem cells (HSCs) in the common lymphoid progenitor pathway, and HSCs can be obtained from umbilical cord blood (UCB). Comparative studies of NK cell differentiation between cultured and freshly isolated HSCs are important in the development of NK cell therapy for cancer. This study aimed to compare the maturation stages of NK cell differentiation between cultured and newly isolated HSC samples using interleukin-2 in the absence of feeder cells.

Methods: Differentiation cultures were divided into two groups according to HSC source. Giemsa staining and flow cytometry were performed to determine the maturation stages and the presence of NKp46 receptors, respectively.

Results: Giemsa staining revealed that the cultured HSC samples produce a higher number and more mature (stage 5) NK cells than the freshly isolated HSC samples. Flow cytometry showed that the NKp46 mean fluorescence intensity significantly differed between the two samples, and a high level of NKp46 activation receptor was found in the isolated samples on day 35.

Conclusions: The cultured HSC samples could produce more mature NK cell populations than the freshly isolated HSCs, which will be beneficial for the therapy applications of NK cells derived from UCB HSCs.

Keywords: cell differentiation, hematopoietic stem cells, maturation stage, natural killer cells, umbilical cord blood

INTRODUCTION

Stem cells are unspecialized cells that come from the human body and have the ability to self-renewal and differentiate into various types of cells. Hematopoietic stem cells (HSCs) are stem cells that play a role in hematopoiesis in the adult human body. They can be isolated from an adult's red bone marrow and peripheral blood after mobilization byb granulocyte-colony stimulating factor (G-CSF). The ability of HSCs to differentiate into various types of blood cells in abundance can be used to treat multiple types of hematologic cancer.[1] HSCs from umbilical cord blood (UCB) provides the following advantages in clinical applications: (i) low risk of infection due to exposure to an operating theater and prior screening for infections from the mother; (ii) less incidence of graft versus host disease, and (iii) minimal requirement for identical human leukocyte antigen matching.[2]

Natural killer (NK) cells act as antivirals and antitumor as part of innate immunity.[3] They can be detected in varying amounts from primary lymphoid tissues (spinal cord and thymus), secondary lymphoid tissues (mucosa-associated lymphoid tissue, tonsils, and spleen), liver, uterus, and lungs and normally circulate in peripheral blood at a percentage of 5%–15%.[4] NK cells are derived from the differentiation of HSCs in the common lymphoid progenitor pathway, which determines the development of progenitor cells into B or NK/T cells. The presence of CD56 indicates that the final development stage of NK

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cells is the mature (adult) stage, namely, CD56 ^{bright} (stage 4) and stage 5 (CD56^{dim}).[3,5]

NK cell differentiation cultures generally use feeder layers and cytokines. As a feeder layer, the stromal cell line provides microenvironment factors for the maturation of NK cells.[6] Feeder cells increase the number of NK cells for cancer immunotherapy applications but are less beneficial for clinical use for safety reasons, i.e., viral or other intracellular pathogen transmission. Cytokines for NK differentiation culture is the optimal way to obtain a sufficient number of NK cells for cancer immunotherapy applications. Cytokines are necessary for the development, proliferation, and activation of mature NK cells.[7] Dezell *et al*. used various cytokine combinations, including IL-3, IL-7, IL-15, stem cell factor, and Flt-3 ligands, and obtained stage 4 (CD56^{bright}) NK cells on the 35th day.[8] However, their protocol is costly for the further ex vivo expansion of NK cells. This circumstance causes difficulty in the use of UCB HSC-derived NK cells for cancer immunotherapy.

Modification is warranted to develop a simple differentiation protocol capable of producing NK cells at an adult stage; however, comparative studies on the effectiveness of NK cell differentiation with cultured HSCs or freshly isolated HSCs are limited. The differentiation ability and maturation stage of NK cells from HSC cultured samples could be compared with those of NK cells from freshly isolated HSCs to determine the success of the NK cell differentiation protocol.[9] Therefore, this study aimed to compare the maturation stages of NK cell differentiation from HSC cultured or freshly isolated HSCs using a modification of the Dezell protocol. The differentiation protocol in this study used no feeder cells and a single daily cytokine IL-2 supplementation for the culture medium from day 21 to day 35 of differentiation. Gene markers perforin (PRF) and granzyme B (GRB) are generally expressed in some stage 4 NK cells and most stage 5 NK cells. Their expression can be triggered by IL-2 stimulation. The presence of IL-2Rα receptors on activated NK cells can increase the interaction of IL-2 on NK cells.[10] This study used Giemsa staining, flow cytometry, and qRT-PCR to evaluate the maturation stages of differentiated NK cells.

METHODS

Materials

This research was conducted at the Stem Cell and Tissue Engineering (SCTE) Laboratory, Indonesia Medical Education and Research Institute, FK UI, Central Jakarta, from October 2021 to July 2022. This in vitro experimental study compared two treatment groups: HSC samples isolated directly from UCB and HSC samples cultured for 2 weeks and then continued with a culture of differentiation into NK cells for 5 weeks.

HSCs were isolated from two fresh UCB samples (100–120 mL) from patients who underwent cesarean section deliveries at the National Central General Hospital Dr. Cipto Mangunkusumo (RSUPNCM). Sampling was conducted in accordance with the code of ethics (Protocol Number: 21-10-1076) reviewed by the Faculty of Medicine, University of Indonesia. The samples were extracted by a team of ob-gyn doctors at RSUPNCM working with a collaborating researcher, Dr. Gita Pratama Sp. OG(K). For each sample, the number of wells was repeated between 12 and 9 wells on a 12-well plate with two harvesting times for sample analysis on days 14 and 35.

HSC isolation

MNC was isolated from fresh UCB by Ficoll gradient density and centrifugation. The mixture of UCB and Ficoll (ratio volume 1:1) was centrifuged (400 *g,* 10 min, 22°C (*no brake*)). The buffy coat was transferred to a new tube, then washed with PBS with a volume ratio (1:1), and centrifuged (650 *g,* 10 min, 22°C (*low brake*: acc: 5; dcc: 5)). MNC CD34+ antibody was isolated following the immunomagnetic principle of the EasySep kit. Finally, the cells were counted using the Neubauer Improved Counting Chamber.

HSC culture

HSCs were suspended in medium culture (RPMI 1640 + 15% PRP (platelet-rich plasma) + 10% HSA (human serum albumin)) and cultured in each well of a 12-well plate. The method used was derived from optimization in the SCTE copyright laboratory with registration number EC00202201784. The medium was changed every 2 days for up to 2 weeks.

NK cell culture

NK differentiation culture medium was prepared by modification without coculture with immortal liver embryo cell lines and administration of IL-2. The culture medium was prepared using HAM F12:DMEM basal medium with a volume ratio of 1:2 (v/v). The supplements added consisted of 20% (v/v) human serum of blood type A, 50 M ethanolamine, 20 ng/mL ascorbic acid, sodium selenite (Na_2SeO_3), and 100 g/mL pen–strep antibiotics. IL-2 cytokine was added between 21 and 35 days to increase NK cell maturation.[8]

Flow cytometry

Flow cytometry tubes were prepared and labeled "unstained" and "stained" for each NK differentiation culture well and then added with 100 µL of cell suspension. Meanwhile, 3 mM PE-Cy7 conjugated NKp46 was added to the stain tube and resuspended by pipetting up and down. The stain tube was incubated for 15–30 min in the dark. After incubation, 100 µL of PBS was added to each stain and unstained tube. Finally, the sample was analyzed using BD FACS Aria III to obtain the mean fluorescence intensity (MFI). This value is related to the number of antibodies that recognize and attach to cell antigens.[11]

Giemsa staining

Giemsa staining was performed on the 14th and 35th day of harvesting cells to determine the potential of HSCs for differentiation into NK cells. In brief, 200 µL of cell suspension was obtained from each well and dripped on a glass slide, which were then soaked with the methanol-fixative solution and allowed to stand in a staining jar for 30 min. The glass slide was dripped with 5% Giemsa solution and again allowed to stand for 20–30 min. Furthermore, the preparation was rinsed using running water and placed on an upright shelf until it dried. The dried preparations were stored in a preparation box prior to observation using an OPTILAB microscope. Five fields of view were photographed for each slide in each sample repetition to tabulate the number of NK cells present at each stage and compare the stage. The maturation stage of differentiated NK cells was compared with that of NK cells following the method of Freud *et al*.[3]

RNA isolation and cDNA synthesis

RNA was isolated from NK cell culture following the Quick-RNA™ Miniprep Plus Kit reagent protocol [Zymo Research]. NK cells derived from culture and isolation samples were prepared in triplicate. Each sample was derived by incorporating 3–4 wells on 12-well plates for each set of NK differentiation cultures. Purity was measured using a nanodrop to determine the A260/A280 ratio. cDNA synthesis was carried out using the master mix composition in accordance with the TOYOBO manual. The mixture was incubated in a thermal cycler for cDNA synthesis at 37°C for 15 min, at 50°C for 5 min, and at 98°C for 5 min.

The three primers were designed with Primer Blast Tools NCBI, selected and optimized in IMERI. The primers were *actin B*, *granzyme B*, and *perforin* (Table 1). The components of the qRT-PCR mix mixture were entered following the Bioline manual. Amplification began with one cycle of reverse transcription enzyme activation of 45 °C for 10 min, one cycle of polymerase enzyme activation of 95 °C for 2 min repeated 40 times, denaturation at 95 °C for 5 s, and extension of annealing at 56 °C for 10 s and 72 °C for 30 s. CT value on qRT-PCR was processed using the Livak formula.

Data analysis

Data from microscopic observations were displayed in the form of images with a scale to indicate the presence of cells in the culture. Data from Giemsa staining were shown in graphical form to assess the stages of NK cell maturation and tabulate the number of NK cells at each stage. C_T data from qRT-PCR were processed using the Livak formula. Data were analyzed using the normality test, homogeneity test, and t-test to determine differences in the treatment groups using IBM SPSS Statistics 20. Nonnormally distributed and nonhomogeneous data on the expression of perforin, granzyme B, and actin B were analyzed using the nonparametric Mann–Whitney test to determine differences between the two groups.

TABLE 1. Primer sequence

No	Gene	Primer Sequence (5'–3')
1	*ACTB*	F: CATCCGCAAAGACCTGTACG R: CCTGCTTGCTGATCCACATC
2	*PRF*	F: ACAGCTTCAGCACTGACACG R: GATGAAGTGGGTGCCGTAGT
3	*GRZB*	F: CCCTGGGAAAACACTCACAC R: TTACACACAAGAGGGCCTCC

RESULTS

Microscopic observations showed that the HSC structure was round and small (Figure 1a). According to a previous study, HSC morphology is rounder and brighter than its background.[12] NK cell microscopic morphology derived from HSC culture or freshly isolated HSCs showed the morphology of cells that make up colonies (Figures 1b–c). This finding indicated that the HSCs differentiated into other cells. The observed NK cell structure was in the form of a colony due to aggregation in both samples. NK cells have adhesion molecules as a markers of differentiation. One type of such adhesion molecule is very late activation antigen-4 (VLA-4), which triggers the aggregation of NK cells through the LFA-1/ICAM-1 adhesion signaling pathway. VLA-4 expression may increase with the stimulation of recombinant IL-2.[13] The results of Giemsa staining for the cultured and freshly isolated HSC samples showed no difference between the NK cells observed on the 14th and 35th day (Figures 2a–d). Each stage can be distinguished by the size of the cell and the cytoplasmic-to-nucleus ratio of each NK cell. Stage 5 NK cells have a smaller cytoplasmic-to-nucleus ratio than stage 4 NK cells. Granules are prevalent in the cytoplasm of cells at stage 5, although they cannot be observed in each stage 5 NK cell. NK cells in stage 3 are easier to distinguish because they are larger than NK cells in stages 4 and 5.

On the 35th day, stage 5 NK cells were the most abundant in both samples. The number of NK cells in the HSC culture was more than that in the freshly isolated HSC sample (Figure 3). The increase in stage 5 NK cells number on day 35 and the decrease in stages 3 and 4 NK cells on day 35 indicated that NK cells underwent maturation toward stage 5. The stages of maturation of NK cells were in accordance with the research conducted by Grzywacz *et al*., who found NK cells at stages 3, 4, and 5 in CD34+ cord blood samples.[14]

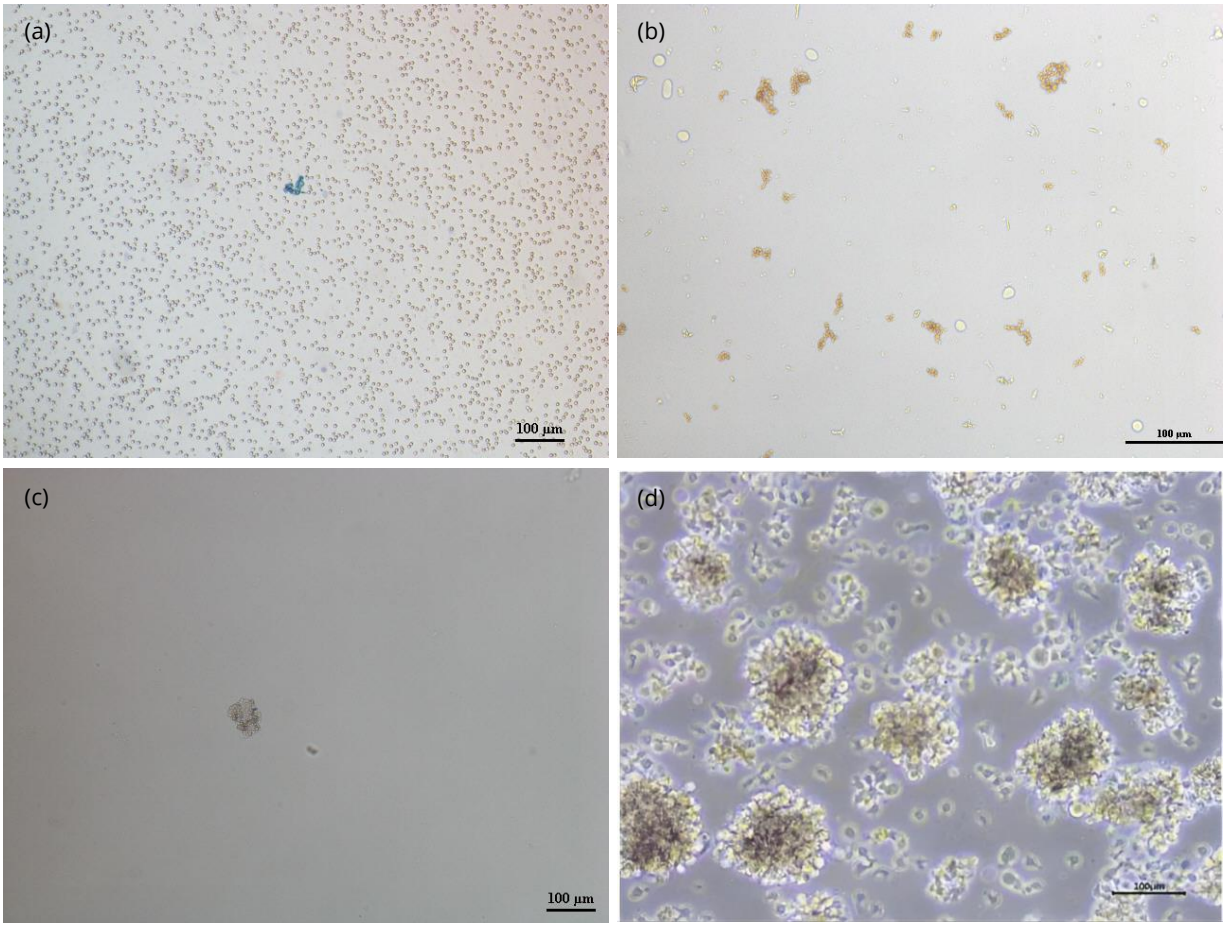
The decrease in stage 3 and 4 NK cells and and the increase in stage 5 NK cells between days 14 and 35 showed that the number of stage 3 ($p > 0.05$; p: 0.70) and 5 ($p > 0.05$; p: 0.97) NK cells was not significantly different

between the two sources. However, the number of stage 4 NK cells significantly differed between the two samples ($p < 0.05$; p: 0.01). Therefore, the number of NK cells commonly found in the HSC culture was influenced by the initial amount of HSCs placed in the well plate (seeding).

Flow cytometry showed the percentage of NKp46 on day 35 of each group sample (Figure 4). The results conformed to the findings of Dezell *et al*.[8] who reported the presence of NKp46 receptors on the 35th day.

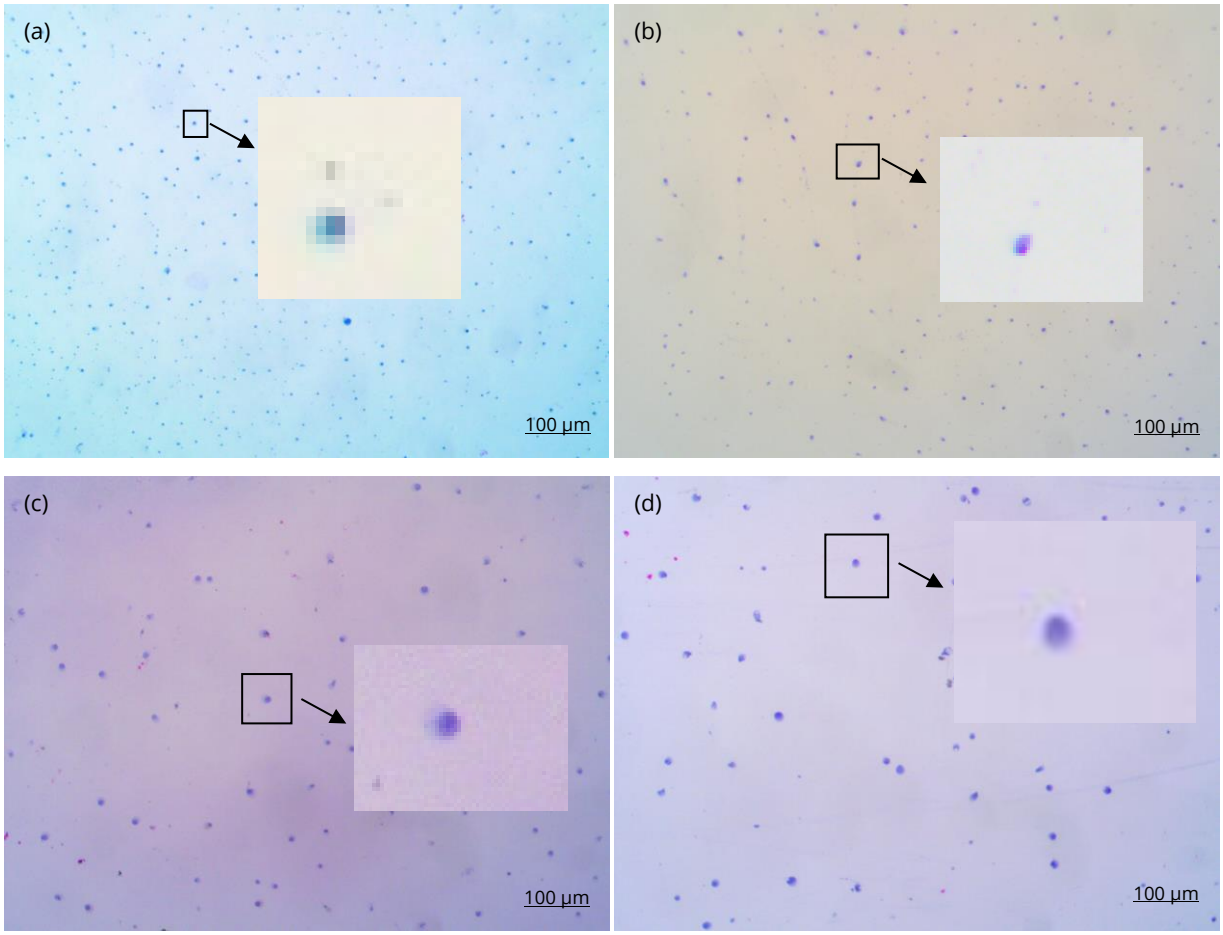
Considering that the percentage of NKp46 reached 100% in both sample groups, the researchers also look into differences in MFI value from each sample (Table 2). Most of the HSC culture samples had MFI in the range of 198–4309, and most of the freshly isolated HSC samples had MFI in the range of 999–7788. Significant difference in MFI ($p < 0.05$; $p = 0.003$) was observed for the NK cells derived from different HSC samples. The high MFI values of the isolated samples indicated that more NKp46 receptors accumulated on day 35 compared with those in the cultured HSC samples. This finding revealed that the differentiation of cultured HSCs in serum-free medium is better than that of freshly isolated HSCs.[9] The administration of IL-2 in vitro can trigger an increase in the expression of NCRs such as NKp46 receptors.[15]

qRT-PCR results showed no significant difference in the PRF expression of NK cells between the two types of HSC samples ($p > 0.05$; p: 0.38); however, significant difference in GRB expression was observed ($p > 0.05$; p: 0.00). This result suggested that PRF and GRB can be expressed in NK cells derived from the differentiation of UCB HSCs.[16] When the samples (differentiation treatment with HSC culture) were compared with positive control (PC), i.e., NK cells, the expression shown was higher. This finding was further reinforced by the greater CD34+ expression (negative controls) showing than NK cells (PC). Therefore, these results cannot be applied to determine the potential differentiation of NK cells from two types of HSC sources.



Magnification 10 x 10, scale bar 100 µm. (a) Morphological Structure of HSC. (b) Results of NK Cell Culture with HSC Isolated Samples. (c) NK Cell Culture Results with HSC Culture Samples. (d) Culture of NK101 in a Culture Medium (Yang *et al*. 2019:5).

FIGURE 1. NK culture microscope observation results for 35 days



Magnification 10 x 10, scale bar 100 µm. (a) Observation of Giemsa on day 14th of HSC Culture samples. (b) Observation of Giemsa on the 35th day of HSC Culture samples. (c) Observation of Giemsa on day 14th of HSC isolation samples. (d) Observation of Giemsa on the 35th day of HSC. isolation samples.

FIGURE 2. Microscopic view by Giemsa staining of culture and isolation samples

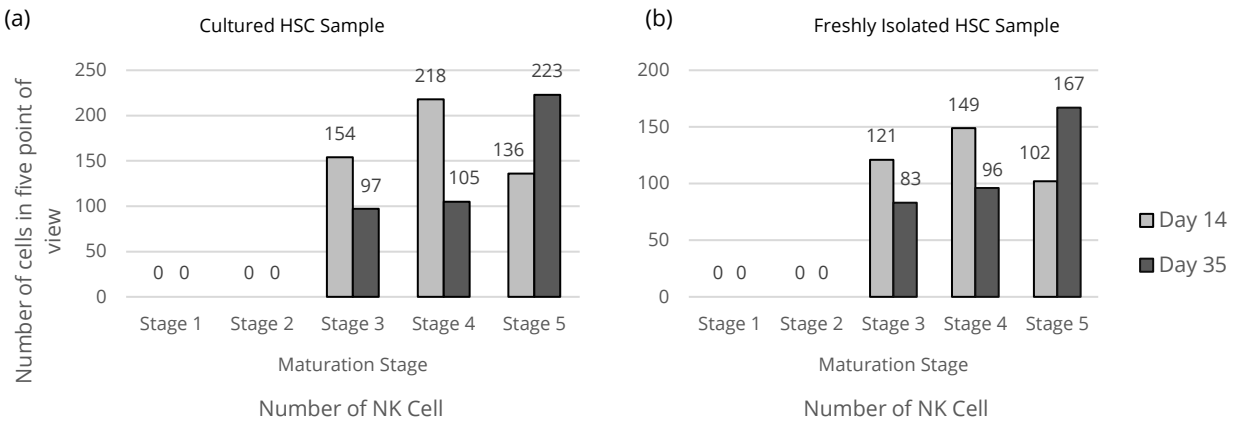
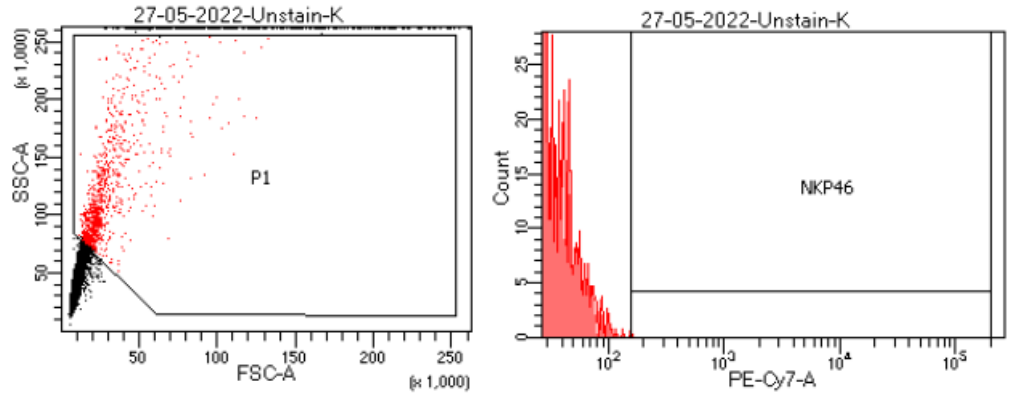
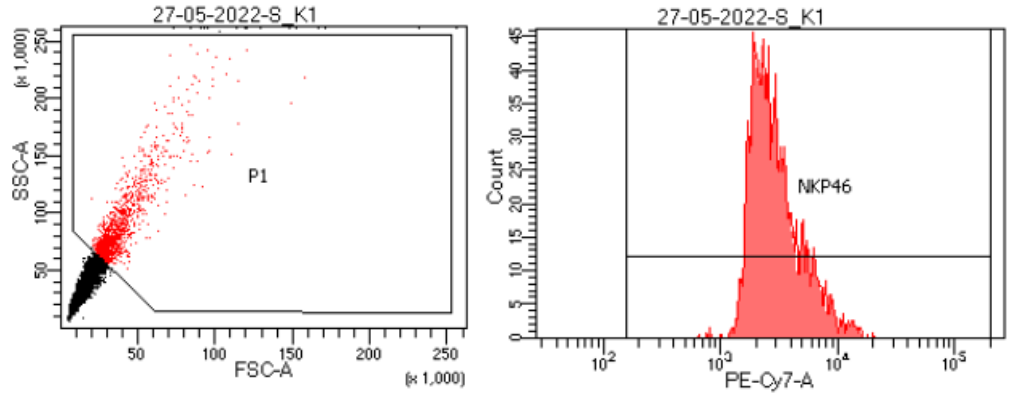


FIGURE 3. Graph of NK cell maturation stages from HSC culture and isolation samples. (a) NK Cell Maturation Stages from HSC Culture Samples. (b) NK Cell Maturation Stage from HSC Isolated Samples.

(a)

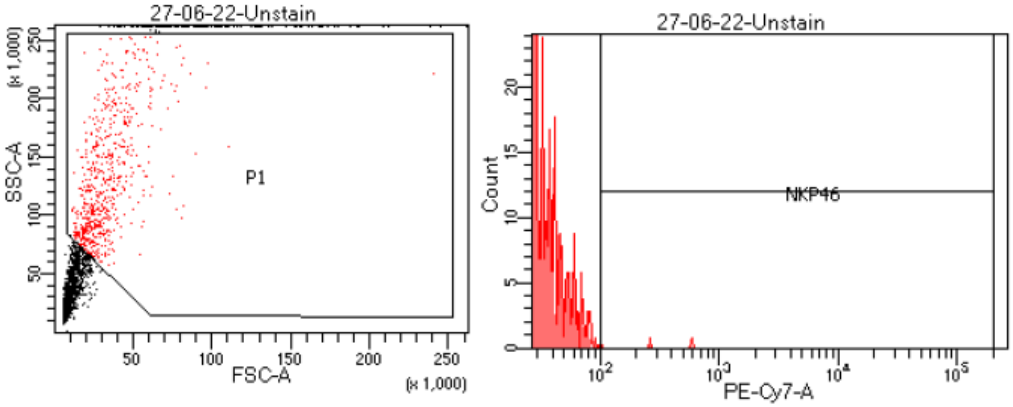


Tube: Unstain-K			
Population	#Events	%Parent	%Total
All Events	5,835	####	100.0
P1	967	16.6	16.6
NKP46	0	0.0	0.0



Tube: S_K1			
Population	#Events	%Parent	%Total
All Events	10,000	####	100.0
P1	1,147	11.5	11.5
NKP46	1,147	100.0	11.5

(b)



Tube: Unstain			
Population	#Events	%Parent	%Total
All Events	2,297	####	100.0
P1	674	29.3	29.3
NKP46	2	0.3	0.1

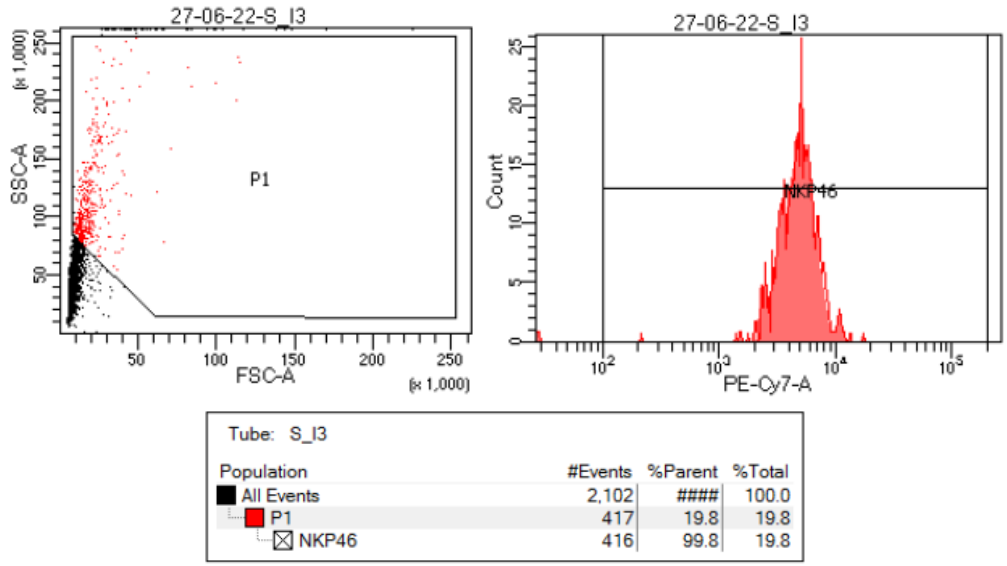


FIGURE 4. Percentage of NKp46 day 35 NK cell culture from (a) HSC culture samples (b) freshly isolated HSC samples

TABLE 2. MFI value differences from day 35 differentiation to day 14 differentiation

Group	Repetition	Differences in MFI value (d35–d14)	Mean	SEM
HSC culture	1	450	1343.25	386.25
	2	2159		
	3	3153		
	4	300		
	5	4309		
	6	852		
	7	507		
	8	2284		
	9	334		
	10	403		
	11	198		
	12	1170		
Freshly isolated HSC	1	4048	3841	639.03
	2	999		
	3	3816		
	4	7788		
	5	4118		
	6	1822		
	7	3439		
	8	3555		
	9	4984		

DISCUSSION

Modifying the existing NK differentiation protocol without using coculture and an immortal liver embryonic cell line with IL-2 can produce stage 5 NK cells on day 35. Dezell *et al*.[8] obtained matured NK cells that were previously in stage 4 after 35 days using stromal cells. In the early weeks, NK cells are predominantly in stage 4 ($CD56^{bright}$) with several types of cytokines, especially without the presence of a feeder layer.[3,17] This finding was supported by the number of stage 4 NK cells at 2 weeks of culture. Maturation can be triggered by the stimulation of IL-2 given in the 3rd week. NK cells that differentiated from UCB HSCs were shown to respond to cytokines, such as IL-2, similar to NK cells in peripheral blood and cord blood.[18]

The determination of the maturation stages of NK cells using Giemsa staining is not necessarily accurate due to subjectivity factors. Determining the stages of development can be performed using other methods, one of which is flow cytometry. One of the markers to decide on the adult stages of NK cells is CD56. $CD56^{bright}$ shows immature adult stage NK cells (stage 4), and $CD56^{dim}$ shows the most mature NK cells (stage 5).[19]

The number of cultured HSCs is greater than that of isolated HSCs. HSC culture serves for cell expansion, so the number of cells produced is high. Meanwhile, the amount of HSC in cord blood becomes limited under isolation. Therefore, the number of NK cells derived from HSC cultures is more significant compared with that from the isolated samples. Calculating the number of NK cells after the culture is terminated is necessary to ensure whether the number of NK cells produced is different according to the HSC-type sample. In general, the number of NK cells is calculated using the trypan blue method adjusted to the percentage of the population of each NK cell using specific receptor markers through flow cytometry.[20]

The low expression of NKp46 can be affected by the presence of reactive oxygen species (ROS).[21] The increase in ROS leads to enhanced proliferation and differentiation activity in HSC.[22] Culturing HSC samples increases the number of cells so that cell proliferation will take place and increase the presence of ROS. An increase in ROS will

trigger toxicity in HSCs, such as DNA damage.[23] The expression of NKp46 receptors can also be affected by microRNA (miRNA) regulation.[24] Cultured HSC samples are known to be hypermethylated, which can alternate the regulation of HSC gene expression and trigger the loss of potential differentiation in most of their progenitor cells. Although NK cells have the same immunophenotypes as other NK cells, they are not necessarily functional.[25] Therefore, further functional tests must be carried out to determine the activity of NK cells from differentiation cultures from both types of HSC samples.

C_T values in some samples could not be determined due to the lack of target genes in the samples[26] influenced by low RNA purity or low RNA concentration. Hence, the obtained data are not representative, except for the negative control that is relatively pure (A260/A280: 2). In addition, the RNA concentration obtained in this study was valued at <5 µg, which is below the recommended range (10–15 µg) for optimal cDNA synthesis. Therefore, the results of qRT-PCR were affected.[27]

On the basis of observations from Giemsa staining, NK cells derived from cultured and freshly isolated UCB HSCs can produce NK cells at stage 5. Therefore, many NK cells can be produced using simple materials (one cytokine and no feeder cells). This synthesis method of NK cells is safer for clinical applications because it reduce some of the possible side effects caused by feeder cell contamination.[9,28] NK cells derived from cord blood are limited and generally immature, making them less beneficial for clinical applications. Some studies have reported successful expansion and functionality of NK cells from UCB HSC with various protocols using the combination of cytokines and feeder cells.[30] In the current work, NK cell differentiation cultures from cultured UCB HSCs can also increase the number of NK cells required for clinical applications.

CONCLUSIONS

Observations from Giemsa staining showed that NK cell differentiation culture without feeder cells and using IL-2 produced more stage 5 NK cells after 35 days for HSC culture samples than for freshly isolated HSC samples. The obtained NK cells also have the NKp46 receptor on day 35. These results show that HSC culture can enrich mature NK cells produced in vitro, which can later be used for immunotherapy applications. In addition, HSC culture can enrich the number of mature NK cells, which can later be used for immunotherapy applications. Functional test on the ability of NK cells is warranted for their future clinical applications.

CONFLICT OF INTEREST

The authors declare that no conflicts of interest arise in the scientific dissemination of this paper.

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Potential Use of the Gel Extract of Butterfly Pea Flower as Topical Therapy to Prevent Photodamage by Downregulating TNF-α and Caspase-3 Expression Levels in UVB-Exposed Rats

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Potential Use of the Gel Extract of Butterfly Pea Flower as Topical Therapy to Prevent Photodamage by Downregulating TNF-α and Caspase-3 Expression Levels in UVB-Exposed Rats

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Abstract

Background: Prolonged exposure to UVB radiation causes DNA damage in skin cells by raising the levels of reactive oxygen species, resulting in the production of inflammatory factors and skin issues. Plant extracts are frequently used to counteract photodamage due to their antioxidant properties. One example is the floral extract of the butterfly pea plant, which contains flavonoid antioxidants. However, the effect of the extract on inflammatory factors is unknown. This study investigated how tumor necrosis factor-alpha (TNF-α) and caspase-3 expression changed when a butterfly pea flower extract gel was applied topically to UVB-exposed animals.

Methods: Experimental and control groups were tested. The healthy group was not exposed to UVB. The negative controls and treatments 1 and 2 were exposed daily for 5 days at a minimal erythema dose of 160 mJ/cm^2 and then treated with a gel-based extract containing 5% and 10% of the extract, respectively. A 96% ethanol solution was used during the maceration step for the extraction. Real-Time Quantitative Reverse Transcription PCR was used to examine gene expression levels in the skin tissue on day 14.

Results: The expression levels of TNF-α and caspase-3 decreased in the treatment group, and higher doses of the extract had a greater effect.

Conclusions: The gel extract considerably reduced the UVB-induced TNF-α and caspase-3 production in rats.

Keywords: butterfly pea flower, caspase-3, TNF-α, UVB

INTRODUCTION

UVB radiation is the UV light that penetrates the epidermis and reaches the upper part of the dermis where it induces DNA damage to the skin cells by increasing the concentration of reactive oxygen species (ROS).[1] Excessive ROS production increases inflammation characterized by the release of various proinflammatory molecules, such as tumor necrosis factor-alpha (TNF-α).[2] UV irradiation changes dermal collagen through the collagen breakdown pathway (matrix metalloproteinase proteins [MMPs]), and by inhibiting the procollagen synthesis pathway resulting in the loss of collagen content.[3] UV-induced ROS damage DNA, and induce lipid peroxidation and protein degradation in skin cells. Additionally, ROS reduce the activities of antioxidant enzymes in the skin, including superoxide dismutase and glutathione peroxidase.[4]

Prolonged production of TNF-α induces ROS that cause oxidative damage to DNA through the NADPH-oxidase 1 pathway,[5] thereby activating the p53 gene, which leads to caspase-3 expression and triggers apoptosis in skin cells, including fibroblasts.[6,7] Several studies have revealed that chronic UVB exposure causes oxidative stress, thereby activating the phosphorylation of mitogen-activated protein kinases, as well as the p38, JNK, ERK, and p53 pathways, which trigger the expression of MMPs and degradation of the extracellular matrix, such as collagen.[8,9] Treatments with various chemical agents, such as retinoic, kojic, glycolic acid, hydroquinone, or alpha arbutin, are the main choices but these chemical agents can cause side effects, such as skin irritation, contact dermatitis, genotoxicity, and skin cancer.[10]

All parts of the butterfly pea flower (*Clitorea ternatea*. L) plant,[11] including the roots, seeds, and leaves have been used medicinally and are recognized to have various inflammation-reducing effects.[12] The petals of the butterfly pea flower are a source of anthocyanins and various types of flavonoids with antioxidant effects. Recent studies have reported that butterfly pea extract has high antioxidant activities that inhibit the production of ROS and reduce inflammation, which inhibits the increase in MMP,[12,13] prevents fibroblast cell apoptosis, and inhibits the decrease in collagen.[14] Another study

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demonstrated that anthocyanins are strong antioxidants that reduce ROS if administered topically or orally.[15] However, no study has examined the role of butterfly pea extract on the expression levels of TNF-α and caspase-3 in the skin with low collagen levels due to UVB exposure.[15] Thus, this study examined the effect of topically applied butterfly pea flower extract gel on the expression levels of TNF-α and caspase-3 in Wistar rats exposed to UVB.

METHODS

Materials and instruments

The following materials were used in this study: butterfly pea extract, water-based gel, rat caspase-3 primer set (F: 5'-GTGGAACTGACGATGATATGGC-3'; R: 5'-CGCAAAGTGACTGGATGAACC-3' and TNF-α F: 5'-AAATGGGCTCCCTCTCATCAGTTC-3'; R: 5'-TCTGCTTGGTGGTTTGCTACGAC-3'), RNAlater solution, and neutral-buffered formalin. The instruments used were a microscope (Olympus, Tokyo, Japan), UVB tool (25 watts), micropipettes, glass objects and tools, refrigerator (4 °C), freezer (−20 °C and −80 °C), probe sonicator, vortex, and Falcon tubes.

Preparation of the butterfly pea flower extract

The butterfly pea flowers were purchased from Balai Besar Penelitian dan Pengembangan Tanaman Obat dan Obat Tradisional Tawangmangu, Central Java, Indonesia, and extracted at the Integrated Laboratory of Diponegoro University. The extraction was completed using the maceration method with methanol. The filtrate was evaporated to dryness to obtain the flower extract.

Qualitative phytochemical analysis

The crude extract was screened to detect the secondary metabolites. Alkaloids were detected using the Wagner method, flavonoids using the Willstatter method, tannins using 1% $FeCl_3$, and triterpenoids using the Lieberman–Burchard method.

UVB-exposed rats

All animal experiments were approved by the Bioethics Commission for Medical/Health Research, Faculty of Medicine, Sultan Agung Islamic University, Semarang No. 304/VIII/2022/Komisi Bioetik. Twenty-four male Wistar rats (*Rattus novergicus*; age, 3 months old; weight, 200 g) were procured from the Faculty of Medicine, Islamic University of Sultan Agung. The rats were quarantined for 3 days and evaluated before the study began. All rats received a standard diet and water *ad libitum* and were divided into four groups consisting of six rats each. The first, second, and third groups included rats having collagen exposed to UVB. The fourth group was not exposed to UV radiation. The hair on the left dorsum of the rats was shaved to maximize the effect of UVB exposure on the skin. UVB was provided five times at an intensity of 160 mJ/cm^2/day, for a total dose of 800 mJ/cm^2.

Preparation of the topical gel therapy

The skin surface was treated topically to modify the epidermis and dermis. Topical therapy doses of 5% and 10% were prepared in a water-based gel. The topical gel extract was administered to the rats once a day for 2 weeks after UVB exposure on day 6. Total RNA was extracted from a 50 mg skin tissue sample using the FAVORGEN RNA isolation kit. cDNA was prepared from 25 µg of total RNA in the skin samples using the ReverTra Ace™ qPCR RT Master Mix.

Polymerase chain reaction analysis was conducted to determine the gene expression levels of TNF-α, caspase-3, and the housekeeping gene glyceraldehyde-3-phosphate dehydrogenase using rat-specific primers and SYBR Green DNA polymerase. The reaction was run for 40 cycles at 60 °C for the annealing process.

Statistical analysis

Data analysis was performed using SPSS software (version 20.0; SPSS Inc., Chicago, IL, USA). Comparative analyses were performed using one-way analysis of variance followed by a post-hoc test to detect differences between the groups. A p-value <0.05 was considered significant.

RESULTS

Bioactive compounds in the butterfly pea flower extract

The qualitative test was a phytochemical screening method carried out using colorimetry. The secondary metabolites (phytochemical compounds) were assessed by visualizing the colors produced by each compound. The phytochemical screening included tests such as, flavonoid, alkaloid, saponin, tannin, steroid, and triterpenoid tests.

This type of phytochemical screening analysis provides valuable information regarding the presence of the important classes of phytochemicals in an extract. The results indicated that flavonoids could be a potential source of antioxidant activity in butterfly pea flower extract. A quantitative flavonoid test was performed to analyze the total flavonoid contents in the ethyl acetate and ethanol extracts of butterfly pea flowers. The total flavonoid levels were measured three times and the results are shown in Table 1. The average total flavonoid content in a butterfly pea flower extract sample was 682,0238.

TABLE 1. Total flavonoids in the butterfly pea flower extract

Extract Concentration	Total Flavonoid Compound
1000 ppm	690,2143
1000 ppm	671,6429
1000 ppm	684,2143

Butterfly pea flower extract gel increases collagen density in the skin of UVB-exposed rats

Collagen density profile in UVB-exposed rats

The rats were stimulated with UVB light for 5 days at an intensity of 160 mJ every 15 min and then euthanized under anesthesia. Mason's trichrome staining was used to examine UVB-exposed rat skin tissue. The UVB-exposed rats expressed less collagen than the healthy rats. As shown in Figure 1, the healthy rat skin displayed greater collagen density (blue hue) than the rat skin exposed to UVB radiation.

Expression levels of TNF-α and caspase-3 in dermal fibroblasts

The effect of the butterfly pea flower extract topical gel on relative TNF-α mRNA expression level was analyzed using Real-Time Quantitative Reverse Transcription PCR. The expression levels of TNF-α and caspase-3 mRNA decreased significantly in the dorsal skin of the treatment group than in the control group. However, the expression levels of TNF-α and caspase-3 mRNA were higher in the UVB group than in the treatment group.

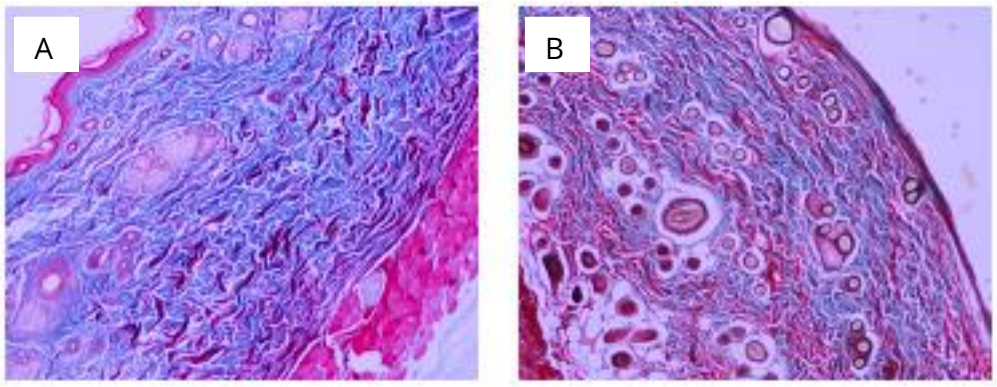
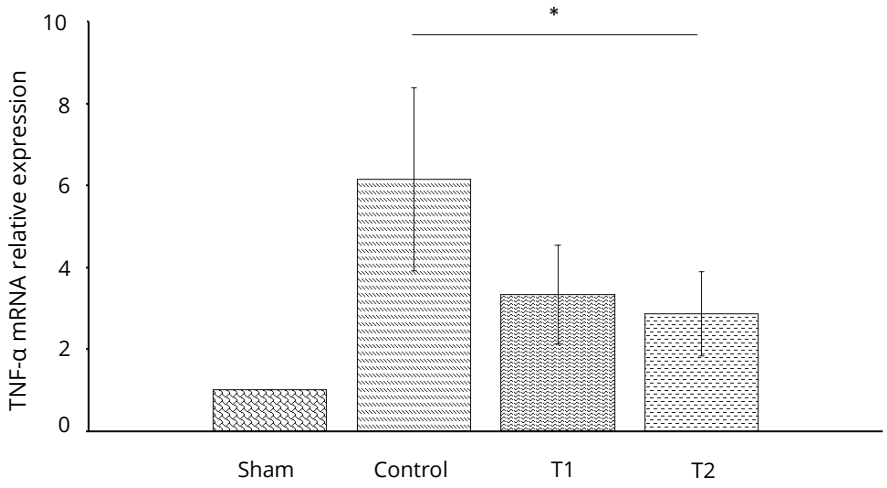
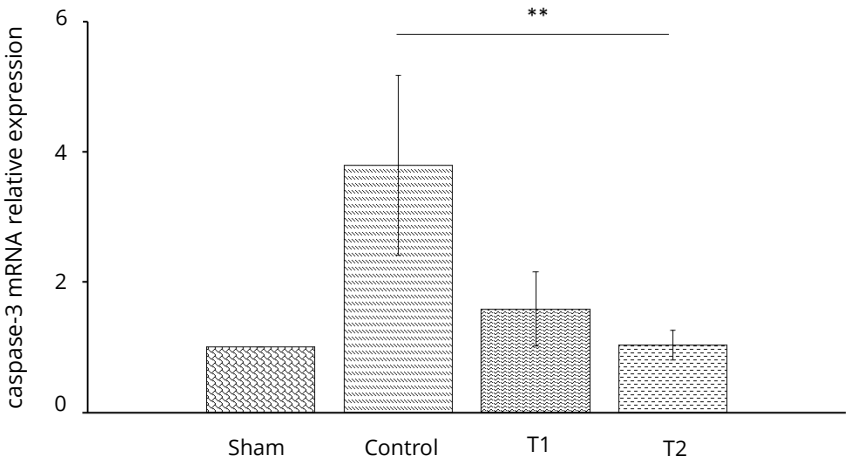


FIGURE 1. (A) Healthy rat collagen (B) Reduced collagen density caused by UVB exposure of rat skin tissue.



*significant difference in the control group ($p < 0.05$); indicates a significant difference in the UVB group (N = 6 per group).

FIGURE 2. Relative expression levels of TNF-α in the dorsal skin observed using real-time polymerase chain reaction: **(Sham)** group not exposed to UV radiation, **(Control)** group with UV-exposed collagen loss, **(T1)** group with collagen exposed to UVB-treated topical gel from 5% of butterfly pea extract, **(T2)** and group with collagen exposed to UVB-treated topical gel from 10% extract of butterfly pea.



*significant difference in the control group ($p < 0.01$); indicates a significant difference in the UVB group (N = 6 per group).

FIGURE 3. Relative expression levels of caspase-3 in the dorsal skin observed using real-time polymerase chain reaction. **(Sham)** group not exposed to UV radiation, **(Control)** group with UV-exposed collagen loss, **(T1)** group with collagen exposed to UVB-treated topical gel from 5% of butterfly pea extract, **(T2)** and group with collagen loss exposed to UVB-treated topical gel from 10% of butterfly pea extract.

The results of the TNF-α gene expression level analysis on day 14 after UVB exposure are shown in Figure 2. The results show that the gel topical therapy based on the butterfly pea flower extract decreased the expression of TNF-α in rat UVB-exposed skin. TNF-α gene expression level in T2 was significantly different from that of the control and healthy groups ($p < 0.05$) but was not significant compared with T1 ($p > 0.05$). The data also shows that T1 was not significantly different from the control ($p > 0.05$) but was significantly different from the healthy rats ($p < 0.05$).

The results of the caspase-3 gene expression level analysis on day 14 after UVB exposure are shown in Figure 3. The results show that the topical gel therapy based on the butterfly pea flower extract decreased the expression of caspase-3 in rat UVB-exposed skin. Caspase-3 gene expression was significantly different in T2 from that of the control and healthy groups ($p < 0.05$) but was not significant compared with T1 ($p > 0.05$; Mann–Whitney). The data also shows that T1 was not significantly different from the control ($p > 0.05$) but was significantly different from the healthy rats ($p < 0.05$).

DISCUSSION

UV radiation increases ROS production and activates signal transduction pathways leading to tissue damage. In addition, ROS produced by UVB irradiation increase the levels of inflammatory factors, such as TNF-α, which modulate cell apoptosis by activating caspase-3, causing a decrease in collagen and other skin problems.[17,18]

The butterfly pea flower has been proposed to have potent antioxidant activities. The antioxidant capacity of a coffee extract is determined by its high flavonoid contents, such as anthocyanins, quercetin alkaloids, saponins, and tannins. Anthocyanins are a class of flavonoids that are potential photoprotective agents because they absorb UV rays 31.99 and act as antioxidants and anti-inflammatory compounds.[12,19]

In the present study, applying 10% butterfly pea flower extract gel topically inhibited photodamage by downregulating the expression levels of the TNF-α and caspase-3 genes and significantly reducing the TNF-α levels ($p < 0.05$). The flavonoids in the butterfly pea flower extract may have caused the decrease in the TNF-α level. A previous study reported the role of anthocyanins in the activation of Nrf-2, which directly inactivates NF-kB.[20]

Recent studies have suggested that NF-B plays a crucial role in the development of skin inflammation due to UVB exposure. Inhibiting NF-kB expression may suppress skin inflammation in response to UVB radiation. Based on previous studies, activating NF-kB triggers the release of inflammatory cytokines, such as interferon-γ, interleukin (IL)-6, and TNF-α.[21,22] The NF-kB signaling pathway is activated in response to different stimuli, including the cytokine TNF-α, which is secreted by local macrophages during infection and cellular stress caused by external factors, such as exposure to UV light. In the absence of activating stimuli, NF-kB dimers are retained in the cytoplasm in association with inhibitory members of the NF-kB inhibitory (IkB) protein family.[23,24]

UVB exposure releases the NF-KB bonds and inhibiting factors so that NF-kB is activated. Previous studies have reported the role of a butterfly pea flower extract in inhibiting the expression of NF-kB. Suppressing the

transcription factor NF-kB is associated with the cleavage of the inflammatory cytokine pathway, including TNF-α. This aligns with the results of this study, which found a decrease in TNF-α expression after the administration of butterfly pea flower extract gel.[25–27]

TNF-α signals the regulation of immune homeostasis and is involved in the regulation of cell death.[28] The TNF-α-associated apoptotic mechanism is closely related to a cascade of apoptotic cysteine proteases known as caspases, which are responsible for initiating and executing apoptosis. The death signal from the TNF-α receptor is transduced to the TNFRSF1A Associated Via Death Domain adapter protein, which uses the subsequent Fas Associated Via Death Domain adapter protein and regulates The death-inducing signaling complex to activate caspase-8 to caspase-3, leading to cell apoptosis. The decreased expression of TNF-α is correlated with the blocked production signal of the apoptotic enzymes, including caspase-3.[29]

Furthermore, a significant decrease in caspase-3 expression level was detected in the T2 group compared with the control group. This result may be due to the decrease in TNF-α expression level in group 2. This result aligns with the previous studies, stating that a decrease in caspase-3 and TNF-α expression levels in the skin tissue of UVB-exposed rats after administering butterfly pea flower extract gel has implications for stopping the death of the skin cells.

Mason's trichrome staining indicated that UVB exposure decreased collagen density in the test group of rats, indicated by a reduced blue hue on the stained slides. This finding demonstrates that an inflammatory response of the skin was successfully induced by UVB after 5 days of treatment at a level of 160 Mj/cm^2 for 15 min each day. UVB irradiation induced ROS production in the epidermis, which caused the release of IL-6, and overproduction of MMPs activated by the protein transcription factor AP-1. MMPs destroy collagen and decrease collagen density.

Based on the results of this study, administering butterfly pea flower extract maintained the firmness of the skin exposed to UVB by inhibiting TNF-α and caspase-3 expression levels; however, this study had several limitations, such as the collagen level was not verified in the skin.

CONCLUSIONS

The butterfly pea flower extract gel was useful as a topical treatment for photodamage caused by excessive decreases in caspase 3 and TNF-α gene expression levels on the UVB-exposed skin of rats. This study will serve as the basis for further applied research, leading to the production of photoaging products, such as hyperpigmentation therapy.

CONFLICTS OF INTEREST

None declared.

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