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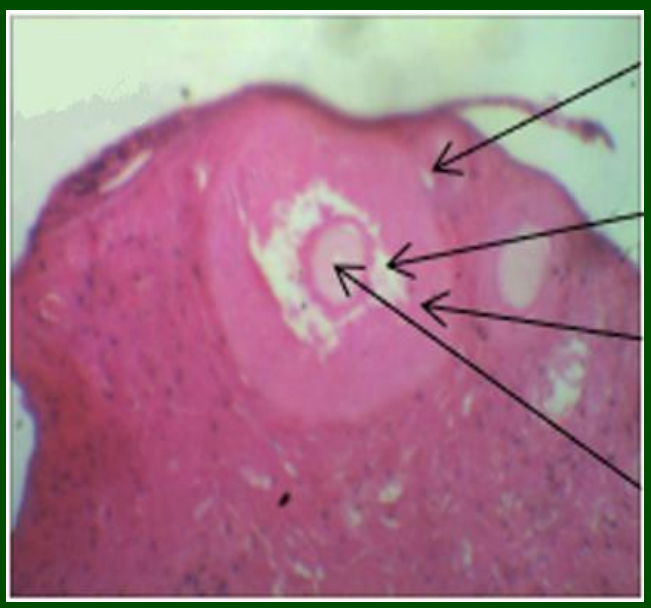

Histology of the Graafian follicles (zoom 400 x) in mice receiving *Moringa olifeira* leaf extract of 500 mg/kg BW

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CONTENT

Cover :
Histology of the Graafian follicles (zoom 400 x) in mice receiving *Moringa olifeira* leaf extract of 500 mg/kg BW

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AUTHOR GUIDELINES

Majalah Obstetri & Ginekologi publishes original articles on all aspects of obstetrics and gynecology. Articles can be classified as **original research, case series, review article, systematic review,** and **meta-analysis** that keep the readers informed of current issues, innovative thinking in obstetrics and gynecology. We welcome submissions that contribute to the advancement of knowledge in obstetrics and gynecology. Articles are considered for publication with the condition that they have not been published, submitted, or being under consideration for publication elsewhere. Manuscript must be written in American English with proper grammar. Authors should follow the **Author Guidelines** and the manuscript is arranged according to the **Manuscript Template**. Manuscript must be submitted through online submission by registered users. Authors can register themselves in the journal system. For further question contact us at: mog@journal.unair.ac.id.

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Case series highlights important innovations with wide applicability or previously unpublished complications of new techniques or medications. The authors must confirm in the manuscript that they have obtained **written permission** of those whose case is being presented. The manuscript should be approximately 3500 words. Total number of tables and figures are limited, advisably not more than five, and references are minimally 20 from the last 10 years before the date of submission. The text consists of **Abstract, Introduction, Case Series, Discussion, Conclusion,** and **Disclosures**. The Disclosures consist of **Acknowledgment, Conflict of Interest, Patient Consent for Publication, Funding,** and **Authors Contribution**.

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Rose ME, Huerbin MB, Melick J, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935(1-2):40-6.

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Butler SW. Secrets from the black bag. London: The Royal College of General Practitioners; 2005.

Chapter of an edited book

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

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For example:

Moir and Jessel maintain “that the sexes are interchangeable”.[1]
Numerous studies[20-22] have.....
Smith's research .....[21]
Smith and Jones’[22] research .....

Up to 3 authors eg. Smith, Jones and McDonald reported that .....[23]

More than 3 authors eg. Smith et al.[24] reports.

ORIGINAL RESEARCH

Nano-curcumin in the decrease of proteinuria in white rats (*Rattus norvegicus*) with preeclampsia

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ABSTRACT

Objective: Since preeclampsia is one of the most serious hypertensive disorders in pregnancy, as it occurs in 5-7% of all pregnancies, and causes around 70,000 maternal deaths and 500,000 fetal deaths worldwide each year, this study aimed to determine the effect of nano-curcumin on proteinuria in pregnant white rats (*Rattus norvegicus*) with preeclampsia.

Materials and Methods: In this study, 24 white rats (*Rattus norvegicus*) were randomly selected and divided into six groups. Inclusion criteria included healthy rats aged 8 weeks or older, with normal blood pressure and weight, while exclusion criteria included sick, deceased, or prematurely birthing rats, and those with high blood pressure. Treatment, administered over six days from gestational days 13-18, involved L-NAME and nano-curcumin injections. Groups included K- (no treatment) and K+, P1, P2, P3, and P4 (treated with L-NAME and varying nano-curcumin doses). Blood pressure and proteinuria were evaluated on gestation days 12, 15, and 19 to confirm the preeclampsia model and assess nano-curcumin's effect on proteinuria. Urine collected over 24 hours in metabolic cages preceded the rats' termination. Data analysis utilized IBM SPSS version 23, including the Shapiro-Wilk test, parametric independent sample t-tests, One-Way ANOVA tests, and LSD post-hoc tests to identify group differences.

Results: The results of this study showed that nano-curcumin had the effect of reducing proteinuria in white rats with preeclampsia. The significant results of the One-Way Anova test was p=0.001 ($p < 0.05$) and the LSD post-hoc test revealed that the effective dose was 25 mg/ml. It was found that higher nano-curcumin dose had a higher average of proteinuria.

Conclusion: Nano-curcumin can affect proteinuria in preeclampsia. The most effective dose is 25 mg/ml.

How to cite: Subandi, Sahara AI, Nurdiana. Nano-curcumin in the decrease of proteinuria in white rats (*Rattus norvegicus*) with preeclampsia. Majalah Obstetri & Ginekologi (Journal of Obstetrics & Gynecology Science). 2024;32(1):8-13. doi: 10.20473/mog.V32I12024.8-13.

Highlights:

1. The size of curcumin was modified to nano scale in order to enhance its bioavailability and facilitate its absorption in the body.
2. As a herbal medicine, nano-curcumin has the ability to reduce proteinuria and serve as a preventive measure against preeclampsia.

INTRODUCTION

Maternal Mortality Rate (MMR) is an indicator to determine the welfare and health status of a mother. In 2017 cases of maternal death during pregnancy until the postpartum period reached 295.000 cases. Based on the result of the 2015 SUPAS MMR data, the cases was 305 per 100.000 birth.[1] Data from the Ministry of Health in 2020 showed that there was 1.110 cases of maternal death caused by several factors, including hemorrhage, infection, and hypertension.[2] Cases of hypertension in pregnancy are very high and have a risk of increasing the morbidity and mortality of pregnant women.[3]

Preeclampsia is one of the most serious hypertensive disorders. Preeclampsia causes around 70,000 maternal deaths and 500,000 fetal deaths every year worldwide.[4] Pregnant women with a preexisting history of hypertension are at a greater risk of developing preeclampsia compared to those without a history of hypertension.[5] Preeclampsia is a condition characterized by high blood pressure (≥140/90 mmHg) and proteinuria (>300 mg in a 24-hour period or =+1 on the dipstick test) in pregnant women who are at least 20 weeks gestational age.[6,7]

Preeclampsia occurs because there is an imbalance between free radicals and antioxidants in the body that can result in oxidative stress. Oxidative stress can increase the production of lipid peroxidation that will cause endothelial dysfunction resulting in impaired endothelial function, that is an increase in renal endothelial permeability so that proteinuria will occur.[8–11] One way to prevent preeclampsia is by using herbal medicines as an alternative treatment. One of the herbal medicines that can be used is turmeric. Curcumin, a primary bioactive compound found in turmeric, is safe and possesses therapeutic properties for treating a range of disorders, including preeclampsia. Curcumin works by influencing various molecular targets, by physically interacting with targets, or by modulating transcription factors of enzyme activity or gene expression.[12] Experimental studies have demonstrated that turmeric has the ability to inhibit cytokines, such as IL-8 and TGF-Q. Curcumin has immunomodulatory, stimulatory, immune, and antioxidant properties, so it is effective in protecting kidney cells from proliferation and fibrosis.[13,14] Curcumin has antioxidant compounds that can prevent oxidative stress and, as an anti-inflammatory, it can prevent endothelial dysfunction.

Despite its widespread availability in Indonesia and its numerous advantages, turmeric usage as an alternative medicine, particularly for curcumin, remains uncommon. In order to enhance the absorption of curcumin into cells, it is necessary to reduce its size to the nanoscale, resulting in nano-curcumin. This is due to the high bioavailability and normal metabolic rate of curcumin.[15] This study aimed to determine the effect of nano-curcumin administration on the decrease of proteinuria in pregnant white rats (*Rattus norvegicus*) with preeclampsia. This study was useful for the development of science and as a clinical research on the benefits of nano-curcumin.

MATERIALS AND METHODS

This study was an experimental study with a post-only control group design. This study had received ethical clearance from the Health Research Ethics Commission, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia, No. 226/EC/KEPK/10/2022. Data were obtained from proteinuria measurement with a urine dipstick test. The population of this study were white rats (*Rattus norvegicus*) and the samples were 24 rats selected by simple random sampling and divided into six groups. Inclusion criteria in this study included healthy rats with clear eyes, active movement, hair that does not fall out, and good appetite. The rats must be at least 8 weeks old, had a systolic blood pressure of 84-134 mmHg and diastolic less than 90 mmHg, and had a minimum weight of 150 grams. The exclusion criteria in this study were rats that were sick or died before treatment, gave birth before treatment, and had high blood pressure. Furthermore, the drop-out criteria included rats that were sick, died and/or gave birth during the study. Five rats were excluded from the study because they met the exclusion criteria and then six rats were excluded from the study because they met the drop-out criteria.

Data were collected for six days treatment at 13-18 days of gestation by injecting doses of L-NAME and nano-curcumin. The rats were grouped into group K- without treatment, and groups K+, P1, P2, P3, and P4 that were injected with L-NAME of 125 mg/kg body weight and nano-curcumin of 25 mg in group P1, 50 mg in group P2, 100 mg in P3, and 200 mg in P4. On gestation day 12 and 15, blood pressure and proteinuria were measured to confirm the success of the preeclampsia rat model. On gestation day 19, proteinuria was measured to determine the effect of nano-curcumin on proteinuria. Urine was collected in the metabolic cage for 24 hours, then the rats were terminated. Data were analyzed with IBM SPSS version 23 program and then the normality test was performed using the Shapiro-Wilk test. The parametric independent sample t-test and One-Way ANOVA test were performed if the data were normally distributed. Differences between groups were tested using the LSD post-hoc test.

RESULTS AND DISCUSSION

Increased blood pressure (BP) and proteinuria in rats injected with L-NAME

Injection of L-NAME has caused increase in rats' blood pressure and proteinuria (Table 1). Table 1 also shows that there is an increased blood pressure and proteinuria above normal after L-NAME administration measured at gestational age 12 and 15 days. The mean blood pressure elevation was ≥140/90 mmHg and proteinuria was ≥1 (0.3gr/L) after 24 hours of urine collection. L-NAME can change the condition of rats to pre-eclampsia. A previous study showed that L-NAME can cause preeclampsia by increasing blood pressure and damaging renal vascular endothelium, resulting in clinical symptoms of proteinuria.[16] The results of the independent simple t-test found significance level of 0.011 ($p < 0.05$), showing that in preeclampsia conditions the proteinuria was higher than in normal conditions. This was in line with a previous study that increased proteinuria continued to occur in preeclampsia pregnancies.[17,18]

The mechanism of action of L-NAME in rats entails a reduction in Nitric Oxide (NO) production due to the inhibition of Nitric Oxide Synthase (eNos). This inhibition has implications for the vasoconstriction of blood vessels, leading to elevated blood pressure in rats. Additionally, L-NAME exerts another effect by activating iNOS (inducible nitric oxide synthase), which prompts the rapid and uncontrolled production of Nitric oxide (NO). Subsequently, NO binds to superoxide, forming peroxynitrite, which oxidizes the formation of lipid peroxides. The accumulation of peroxynitrite exacerbates due to the interaction between NO and superoxide, resulting in heightened lipid peroxides or free radicals, leading to an imbalance in antioxidants and the onset of oxidative stress. Oxidative stress triggers inflammation in the vascular endothelium, culminating in vascular endothelial dysfunction. In compromised endothelium, the renal vascular endothelium's filtration capacity diminishes, leading to the inability to properly filter proteins by the glomerulus, resulting in proteinuria.[19]

Effect of nano-curcumin administration on proteinuria

Proteinuria serves as a key indicator in monitoring preeclampsia. The presence of protein in urine results partly from the physiological excretion of viscous glycoproteins by tubular cells, known as "Tamm-Horsfall protein." A pathological condition is declared when there is an excretion of protein in urine exceeding 300 mg per 24 hours. Proteinuria assessment involves immersing a dipstick test in urine collected over a 24-hour period. The onset of proteinuria stems from kidney vascular endothelial dysfunction, which impairs the glomerular filtration capacity due to oxidative stress.[19,20]

The administration of nano-curcumin was initiated for a span of 6 days between gestational ages 13-18 days, with varying doses allocated to each group: P4 received 200 mg/day, P3 received 100 mg/day, P2 received 50 mg/day, and P1 received 25 mg/day. The effect of nano-curcumin administration on proteinuria in rats was observed in the treatment groups. The effect of nano-curcumin administration in the treatment groups is presented by the average proteinuria levels recorded for each group, as detailed in Table 2. Notably, the highest average was noted in the K+ group (10 ± 3.56), whereas the lowest was observed in the K- group (0.112 ± 0.14). Across the four treatment groups, the average proteinuria levels were recorded as 0.425 ± 0.39 in P1, 5.3 ± 2.22 in P2, 6 ± 2.58 in P3, and 8 ± 2.6 in P4. The average in the K+ group surpassed that of the four groups treated with varying doses of nano-curcumin (P1=25 mg, P2=50 mg, P3=100 mg, P4=200 mg). Among the treatment groups, the highest average was observed in the P4 group (8 ± 2.6), while the lowest was noted in the P1 group (0.425 ± 0.39).

Table 1. Results of blood pressure measurements and proteinuria at 12- and 15-days' gestation

Groups	Blood Pressure (mmHg)				Proteinuria (gr/L)	
	G12		G15		G12	G15
	Systolic	Diastolic	Systolic	Diastolic		
K-	118.25±9.88	83±6.63	121.25±12.53	87.5±7.05	0±0.08	0.1±0.09
K+	119±5.10	86±5.94	15.15±8.70	118.75±13.67	0.2±0.09	11.8±3.95
P1	117±6.16	76.75±5.85	146.75±4.50	109.25±10.18	0.2±0.17	3.75±0.96
P2	116.25±17.78	79±13.39	147.75±31.86	115.5±23.69	0.2±0.09	6.8±3.77
P3	118.5±16.62	85.5±7.14	151.25±9.00	117.75±19.60	0.2±0.09	7.8±2.87
P4	115.25±13.07	81.75±7.89	149±17.22	125.75±15.48	0.2±0.09	10.3±.40

Proteinuria occurs due to imbalanced levels of free radicals and antioxidants, precipitating oxidative stress. The oxidative stress provokes inflammation in the vascular endothelium, ultimately leading to vascular endothelial dysfunction. Consequently, in compromised endothelium, the filtration capacity of the renal vascular endothelium diminishes, resulting in the failure to adequately filter proteins by the glomerulus, thereby manifesting as proteinuria.[21]

Table 2. Results of proteinuria measurements at 19 days' gestation

Group	Rat number-	Proteinuria (g/L)	Average (g/L)
K-	1 2 3 4	0 0.3 0 0.15	0.112±0.14
K+	1 2 3 4	7 15 10 8	10±3.56
P1	1 2 3 4	1 0.1 0.3 0.3	0.425±0.39
P2	1 2 3 4	8 3 4 6	5.3±2.22
P3	1 2 3 4	3 5 7 9	6±2.58
P4	1 2 3 4	10 8 5 9	8±2.16

Subsequently, the One-Way ANOVA test was initiated following a homogeneity test, yielding a significance level of 0.056 ($p > 0.05$). The outcomes of the One-Way ANOVA test for proteinuria demonstrated significance with $p=0.001$ ($p < 0.05$), indicating significant difference among the sample groups. This substantiates the effect of nano-curcumin administration on proteinuria in white rats with preeclampsia. Previous studies have shown that oxidative stress within the body can be ameliorated through exogenous antioxidants, with curcumin being one of the sources. Curcumin exhibits the capacity to permeate target cells, effectively mitigating free radicals such as Reactive Nitrogen Species (RNS) or Reactive Oxygen Species (ROS) by harmonizing antioxidant and free radical levels within the body through the inhibition of enzymes responsible for augmenting free radical production. Consequently, this impedes the onset of oxidative stress, thereby averting inflammation in the vascular endothelium of the kidney and enhancing the glomerular filtration function.[22,23] Nano-formulated curcumin emerges as a viable therapeutic option due to its high bioavailability, enabling faster and more effective curcumin action on the targeted disease or organ.[24]

The LSD post-hoc analysis was conducted to identify differences among groups, with a significance level set at $p < 0.05$. Table 3 summarizes the test outcomes, revealing a significant difference between the K- group and others. The p-values in the K+ group were 0.000, in P2 0.004, in P3 0.001, and in P4 0.000, showing significant differences. Moreover, the p-value in the K+ group significantly differed from those in K- ($p=0.000$), P1 ($p=0.000$), P2 ($p=0.007$), and P3 ($p=0.019$). The p-value in the P1 group was significantly difference from those in K+ ($p=0.000$), P2 ($p=0.006$), P3 ($p=0.002$), and P4 ($p=0.000$). In P2 group, the value was significantly different from those in K- ($p=0.004$), K+ ($p=0.007$), and P1 ($p=0.006$), while insignificantly different from those in P3 ($p=0.636$) and P4 ($p=0.094$). Group P3 exhibited significant differences from K- ($p=0.001$), K+ ($p=0.019$), and P1 ($p=0.012$), but not from P2 ($p=0.636$) and P4 ($p=0.215$). The p-value in group P4 was significantly different from those in K- ($p=0.000$) and P1 ($p=0.000$), but not significantly from those in K+ ($p=0.215$), P2 ($p=0.094$), and P3 ($p=0.215$). Consequently, the dose in P1 group (25 mg) exhibited the most significant changes compared to other groups' doses.

The highest average proteinuria was observed in group P4, reaching 8 ± 2.16, close to the average of the positive control (K+) group at 10 ± 3.56. Group P4 received a combination of L-NAME and nano-curcumin at a dose of 200 mg/day, while the positive control group only received L-NAME. This suggests that higher doses of curcumin may potentially increase proteinuria levels. Notably, nano-curcumin exhibits an LD50 of 5000 mg/kg body weight. Experiments conducted on normal male and female subjects using doses of 50 mg, 100 mg, and 200 mg resulted in an increase in albumin, BUN, and creatinine levels, which was 0.1 in each group. Despite its LD50 of 5000 mg/kg body weight, nano-curcumin administration to normal rats can augment albumin levels.[25] Various studies elucidate that repeated administration of antioxidants in high doses can transform antioxidants into pro-oxidants, thereby amplifying free radicals and potentially damaging body cells. Additionally, nanoparticles have the capability to permeate blood vessel walls or infiltrate body cells, particularly those with sizes ranging from 20-50 nm, thereby exerting direct effects on target cells. Nano-curcumin, owing to its hydrophilic properties, readily dissolves and penetrates the bloodstream.[26,27]

Table 3. Results of post-hoc comparison test (LSD)

Groups	K-	K+	P1	P2	P3	P4
K-		0.000*	0.843	0.004*	0.001*	0.000*
K+	0.000*		0.000*	0.007*	0.019*	0.215
P1	0.843	0.000*		0.006*	0.002*	0.000*
P2	0.004*	0.007*	0.006*		0.636	0.094
P3	0.001*	0.019*	0.002*	0.636		0.215
P4	0.000*	0.215	0.000*	0.094	0.215	

The strength and limitations of the study

This study demonstrated the efficacy of curcumin as an alternative for reducing proteinuria, offering a clear and standardized measurement methodology aligned with established guidelines. The research effectively met its objectives, yielding valuable outcomes. Nonetheless, limitations were observed, particularly regarding the ultrasound tool utilized for the rats. Additionally, dropout rates were notable due to factors such as mortality, birthing, and illness among the rat subjects, potentially influenced by undisclosed external variables.

CONCLUSION

Nano-curcumin has an effect on decreasing proteinuria in white rats (*Rattus norvegicus*) with preeclampsia. The most effective dose in reducing proteinuria is 25 mg. Future research is expected to be able to analyze the effect of nano-curcumin at doses below 25 mg on proteinuria and to examine the right dose for humans.

DISCLOSURES

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Conflict of interest

There is no conflict of interest

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Author contribution

S: Supervised result, discussion, and funded this research. AIS: Collected data, designed the study, collected literature, analyzed the data, drafted this manuscript. N: Supervised and discussion. This manuscript has been reviewed and approved by all authors.

REFERENCES

1. WHO, UNICEF, UNFPA. Trends in maternal mortality 2000 to 2017: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division [Internet]. 2019 [cited 2023 Apr 28]. Available from: https://apps.who.int/iris/handle/10665/327595.
2. BPS – Statistics Indonesia. Angka Kematian Ibu Menurut Pulau [Internet]. 2015 [updated 2018 Jun 5; cited 2023 Apr 28]. Available from: https://www.bps.go.d/id/statistics-table/2/MTM0OSMy/angka-kematian-ibu-menurut-pulau.html
3. Ministry of Health, Republic of Indonesia. Profil Kesehatan Indonesia Tahun 2020 [Indonesian Health Profile 2020]. Jakarta: Ministry of Health, Republic of Indonesia [Internet]. [cited 2023 Apr 28]. Available from: https://www.kemkes.go.id/id/profil-kesehatan-indonesia-2020
4. Rana S, Lemoine E, Granger JP, et al. Pre-eclampsia: Pathophysiology, challenges, and perspectives. Circ Res. 2019;124(7):1094-112. doi: 10.1161/CIRCRESAHA.118.313276. Erratum in: Circ Res. 2020 Jan 3;126(1):e8. PMID: 30920918.
5. Fox R, Kitt J, Leeson P, et al. Preeclampsia: Risk factors, diagnosis, management, and the cardio-vascular impact on the offspring. J Clin Med. 2019;8(10):1625. doi: 10.3390/jcm8101625. PMID: 31590294; PMCID: PMC6832549.
6. Fauzia S, Sari RDP, Rahmanisa S. Hubungan tingkat preeklampsia dengan kejadian bayi berat lahir rendah (BBLR) di RSUD Dr. H. Abdul Moeloek Provinsi Lampung periode 1 Oktober 2015 - 1 Oktober 2016 [Correlation between preeclampsia and low birthweight in Dr. H. Abdul Moeloek Hospital, Lampung]. Jurnal Kesehatan dan Agromedicine. 2019;6(2):296-8. Available from: https://juke.kedokteran.unila.ac.id/index.php/agro/article/view/2402

7. Mersha AG, Abegaz TM, Seid MA. Maternal and perinatal outcomes of hypertensive disorders of pregnancy in Ethiopia: systematic review and meta-analysis. BMC Pregnancy Childbirth. 2019;19(1): 458. doi: 10.1186/s12884-019-2617-8. PMID: 31796036; PMCID: PMC6889359.
8. Kurniati E, Rusnawati. Body mass index with preeklampsia events on mother. Jurnal Life Birth. 2020;2(2):86-92. Available from https://ojs.stikespanritahusada.ac.id/index.php/jlb/article/view/279
9. Staff AC. The two-stage placental model of pre-eclampsia: An update. J Reprod Immunol. 2019; 134-135:1-10. doi: 10.1016/j.jri.2019.07.004. Epub 2019 Jul 8. PMID: 31301487.
10. Rumopa H, Wagey FW, Suparman E. Malondi-aldehyde levels in preeclampsia before and after delivery. Indones J Obs Gynecol. 2018;6(3):143–8. doi: 10.32771/inajog.v6i3.777.
11. Toboła-Wróbel K, Pietryga M, Dydowicz P, et al. Association of oxidative stress on pregnancy. Oxid Med Cell Longev. 2020;2020:6398520. doi: 10.1155/2020/6398520. PMID: 33014274; PMCID: PMC7512072.
12. Wulandari G, Mulyani Y, Sulaeman A. Review: Peran kunyit (*Curcuma longa*) sebagai terapi hipertensi dan mekanismenya terhadap ekspresi gen. Majalah Farmasi dan Farmakologi. 2021; 25(2):51–8. doi: 10.20956/mff.v25i2.13287.
13. Salehi B, Stojanović-Radić Z, Matejić J, et al. The therapeutic potential of curcumin: A review of clinical trials. Eur J Med Chem. 2019;163:527-45. doi: 10.1016/j.ejmech.2018.12.016. Epub 2018 Dec 7. PMID: 30553144.
14. Vanaie A, Shahidi S, Iraj B, et al. Curcumin as a major active component of turmeric attenuates proteinuria in patients with overt diabetic nephropathy. J Res Med Sci. 2019;24:77. doi: 10.4103/jrms.JRMS_1055_18. PMID: 31523263; PMCID: PMC6734668.
15. Fahrumnisa AR. Ekstrak kunyit (*Curcuma longa*) sebagai tatalaksana sindrom polikistik ovarium [Curcuma longa extract for the management of PCOS]. Jurnal Ilmiah Kesehatan Sandi Husada. 2019;8(2):115–20. doi: 10.35816/jiskh.v10i2.125.
16. Liu R, Pei Q, Shou T, et al. Apoptotic effect of green synthesized gold nanoparticles from Curcuma wenyujin extract against human renal cell carcinoma A498 cells. Int J Nanomedicine. 2019; 14:4091-103. doi: 10.2147/IJN.S203222. PMID: 31239669; PMCID: PMC6556565.
17. Liu T, Zhang M, Mukosera GT, et al. L-NAME releases nitric oxide and potentiates subsequent nitroglycerin-mediated vasodilation. Redox Biol. 2019;26:101238. doi: 10.1016/j.redox.2019.101238. Epub 2019 Jun 4. PMID: 31200239; PMCID: PMC6565607.
18. Morikawa M, Mayama M, Saito Y, et al. Severe proteinuria as a parameter of worse perinatal/neonatal outcomes in women with preeclampsia. Pregnancy Hypertens. 2020;19:119-26. doi: 10.1016/j.preghy.2019.12.013. Epub 2020 Jan 10. PMID: 31972468.
19. Shu W, Li H, Gong H, et al. Evaluation of blood vessel injury, oxidative stress and circulating inflammatory factors in an L-NAME-induced preeclampsia-like rat model. Exp Ther Med. 2018; 16(2):585-94. doi: 10.3892/etm.2018.6217. Epub 2018 May 24. PMID: 30112025; PMCID: PMC6090470.
20. Gerasimova EM, Fedotov SA, Kachkin DV, et al. Protein misfolding during pregnancy: New approaches to preeclampsia diagnostics. Int J Mol Sci. 2019;20(24):6183. doi: 10.3390/ijms20246183. PMID: 31817906; PMCID: PMC6941028.
21. Morikawa M, Yamada T, Yamada T, et al. Pregnancy outcome of women who developed proteinuria in the absence of hypertension after mid-gestation. J Perinat Med. 2008;36(5):419-24. doi: 10.1515/JPM.2008.062. PMID: 18605971.
22. Abd El-Hack ME, El-Saadony MT, Swelum AA, et al. Curcumin, the active substance of turmeric: its effects on health and ways to improve its bio-availability. J Sci Food Agric. 2021;101(14): 5747-62. doi: 10.1002/jsfa.11372. Epub 2021 Jul 14. PMID: 34143894.
23. Rafiee Z, Nejatian M, Daeihamed M, et al. Application of different nanocarriers for encapsulation of curcumin. Crit Rev Food Sci Nutr. 2019; 59(21):3468-97. doi: 10.1080/10408398.2018.1495174. Epub 2018 Oct 4. PMID: 30001150.
24. Karthikeyan A, Senthil N, Min T. Nanocurcumin: A promising candidate for therapeutic applications. Front Pharmacol. 2020;11:487. doi: 10.3389/fphar.2020.00487. PMID: 32425772; PMCID: PMC7206872.
25. Sandhiutami NMD, Dewi RS, Khairani S, et al. Safety evaluation of curcumin nanoparticle formula in mice and antioxidants potency in-vitro. Jurnal Ilmu Kefarmasian Indonesia. 2022;20 (1):63-72. doi: 10.35814/jifi.v20i1.1187.
26. Kotha RR, Luthria DL. Curcumin: Biological, pharmaceutical, nutraceutical, and analytical aspects. Molecules. 2019;24(16):2930. doi: 10.3390/molecules24162930. PMID: 31412624; PMC ID: PMC6720683.
27. Aulia D, Graharti R. Hubungan diabetes melitus dengan kejadian preeklampsia di RSUD DR. H. Abdul Moeloek Provinsi Lampung Periode 1 Januari - 30 Juni 2018 [Correlation between diabetes mellitus and preeclampsia in Abdul Moeloek Hospital, Lampung]. Medula. 2018;8(2):180–6.

ORIGINAL RESEARCH

Moringa oleifera extract affects the diameter of the Graafian follicles in female *Mus musculus*

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ABSTRACT

Objective: This study aimed to determine the effect of Moringa leaf extract (*Moringa oleifera* Lam.) on the diameter of Graafian follicles in female mice (*Mus musculus*).

Materials and Methods: This study used experimental design, employing a cohort of 24 female mice of 20-25 grams in weight, aged between 2-3 months, and in good health. These subjects were divided into three treatment groups and subjected to oral doses of Moringa leaf extract at 300 mg/kg BW, 400 mg/kg BW, and 500 mg/kg BW over a 14-day period. The study procedures involved the preparation of the experimental animals, preparation of Moringa leaf extract, treatments administration, and the preparation of histological specimens. Subsequently, the diameters of Graafian follicles within each treatment group were measured. Data analysis were performed using the ANOVA test ($p < 0.05$) followed with the Least Significance Difference (LSD) test utilizing the IBM SPSS software.

Results: There were variations in Graafian follicle diameters across the experimental groups. The average diameters were 180.944 µm in the control group, 239.942 µm in treatment group 1, 315.006 µm in treatment group 2, and 396.650 µm in treatment group 3. This indicated that dose administration starting from 300 mg/kg, 400 mg/kg, and 500 mg/kg had an effect on the size of the follicle and antrum diameter. The number of granulosa cells was found to increase, as well as the size of the ovum.

Conclusion: Moringa leaf extract in different doses has a significant positive effect on increasing the diameter of the Graafian follicles in female mice.

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Highlights:

1. This study unveils a dose-dependent relationship between Moringa leaf extract and increased Graafian follicle size in female mice.
2. The significant positive effect of Moringa leaf extract on Graafian follicles suggests promising implications for fertility interventions, offering hope for individuals seeking natural treatment to address infertility challenges.

INTRODUCTION

Fertility refers to the ideal functioning of the reproductive organs in facilitating the development of egg follicles, including primary, secondary, tertiary, and Graafian follicles, leading to the formation of ova, ovulation, and the synthesis and release of steroid hormones.[1] Graafian follicles consist of a central nucleus cell surrounded by a cell membrane and many follicular cells. The cell's nucleus possesses the capability to undergo development and maturation, ultimately resulting in the formation of an egg, also known as an ovum.[2] Insufficient nutrition disrupts follicle growth, which in turn affects the fertilization process.

Several plant compounds offer advantages in addressing reproductive issues. *Moringa oleifera* Lam., also known as Moringa, is a very nutritious plant that plays a key role in enhancing fertility. It is has been recognized that a quantity of 25 grams of Moringa leaf powder is sufficient to fulfill the daily nutritional requirements of children as follows: 42% protein, 125% calcium, 60% magnesium, 41% potassium, 71% iron, 272% vitamin A, and 22% vitamin C.[3] Furthermore, Moringa is rich in zinc, vitamin C, and antioxidants, including flavonoids. It also includes β-carotene, which is a precursor to vitamin A, as well as vitamins B complex, C, D, and K.[4]

Several studies have investigated the effect of Moringa leaf extract on the reproductive abilities of male and female mice (*Mus musculus*). A study conducted by Gunawati et al.[4] examined the impact of Moringa leaf on male mice (*Mus musculus*). This study observed a rise in the generation of spermatogenic cells.

Balumbi et al.[5] did a study utilizing Moringa leaf extract to determine the duration of the estrus cycle in mice. The study demonstrated that the administration of Moringa leaf extract resulted in a normal length of the estrus cycle in the treatment group, as opposed to the control group which had a cycle length of 4-5 days. A study conducted by Narulita et al.[1] demonstrated that the leaves of the Moringa plant had the highest nutritional value. Moringa leaves provide a superior nutritional composition compared to other plant components, hence it is reasonable to anticipate its usefulness in increasing the size of the ovaries and enhancement of their functionality.

In a study conducted by Alfian,[6] the diameter of the Graafian follicles was evaluated using papaya seed extract. The findings indicated that there was no statistically significant difference between the treatment and control groups. This study also measured the diameter of the Graafian follicles but, different from the previous studies, this study used Moringa leaf extract. This study aimed to assess the effect of Moringa leaves on the diameter of Graafian follicles in female mice.

MATERIALS AND METHODS

This study was a true experimental study using a completely randomized design (CRD).[7] The period of the study was four months, from July to October 2022 at the Laboratory of the Department of Biology, Faculty of Teacher Training and Education, Halu Oleo University, Kendari, Southeast Sulawesi, Indonesia. The protocol of this study was approved by the Research Ethics Committee of the Institute for Research and Community Services, Halu Oleo University with number: 185d/ UN29.20.1.2/PG/2022.

The population in this study was 45 female mice acclimatized for 2 weeks at the Laboratory of the Department of Biology Education of Halu Oleo University. The mice were subsequently randomized to 24 female mice using simple random sampling with the sample criteria of 20-25 grams of weight, age of 12-13 weeks, in good health and not physically disabled. The rats were allocated into four groups of control group (K), treatment group 1 (P1), treatment group 2 (P2), and treatment group 3 (P3), each consisting of 6 mice. The mice were acclimatized for 1 week, kept in rectangular cages of 38 cm x 27 cm x 13 cm covered with wire. The pedestal in the cage was wood shavings that were changed twice a week. During maintenance, the mice were given an intake of 6 grams of pellets/day and water ad libitum through a drinking bottle.

Preparation of extract from *Moringa oleifera* leaves

The Moringa leaves were dried in an oven for 12 hours at a temperature of 50ºC. The dried Moringa leaves were blended until becoming powder. The dry powder was measured at 1000 grams, added with 96% ethanol as much as 3 liters, then the extraction process was carried out by maceration method for 24 hours. The extract was filtered, then the Moringa leaf filtrate was concentrated using a rotary evaporator.

Animal treatment

Moringa leaf extract was administered in the morning (07.00 am) with different doses. Healthy adult female mice (2-3 months) were randomized into four groups and treated as follows: Control group (K), comprising 6 samples, receiving distilled water only; treatment group 1 (P1), consisting of 6 samples receiving a dose of 300 mg/kg BW; treatment group 2 (P2), 6 samples receiving

a dose of 400 mg/kg BW; and treatment group 3 (P3), consisting of 6 samples receiving a dose of 500 mg/kg BW. The extract was administered for 14 days which was carried out directly by the researchers and on day 15, the female mice were dissected to remove their ovaries. The treatment was given for 14 days considering three estrus cycles. This was in accordance with research conducted by Nugroho[8] where the normal average estrous cycle of female mice was 4-5 days. Dosage refers to previous studies conducted by Balumbi, et al.[5] in female mice test animals to see ovarian morphometry and estrus cycle. Moringa leaf extract (*Moringa oleifera* Lam.) was mixed with 0.2% Na-CMC. This was because Moringa leaf extract can be dispersed well in Na-CMC.

Moringa leaf extract administration to the mice was done using syringe equipped with a blunt tip needle, which had been filled with 0.5 ml of Moringa leaf extract liquid. The skin on the nape of the mouse was pulled with the middle finger and thumb of the left hand, and the little finger hold the tail of the mouse. The handheld tool was hold in the right hand and then the extract was injected into the mouse mouth. The administration of Moringa leaf extract to the mice was done by the assigned members of the research team.

Histology preparations

The removed ovaries were put in histological preparations. The preparations were fixed with Bouin's solution for approximately two days, and then washed with 70% alcohol (1 x 60 minutes). The next process was dehydration using 90% alcohol solution for one night, then transferred to 96% alcohol and absolute alcohol for 1 x 60 minutes, respectively. After the dehydration process was complete, it was followed by the purification process by soaking the ovarian organs using a toluol solution for one night, then paraffin infiltration was carried out by immersing the ovarian organs into a mixture of toluol and paraffin in a ratio of 1:1 for 30 minutes followed by pure paraffin I, II, and III for 45 minutes, respectively. The subsequent process was embedding and implanting the ovarian organs into the paraffin, then the position was set in the direction of transverse cutting and they were allowed to freeze, forming a block to be cut with a microtome. Then, the paraffin block was mounted on a holder, placed on a microtome, cut in 6 µm thickness, forming a ribbon. From the slices, the best one was selected, then it was placed on a slide with Mayer's albumin smear and put in a slide warmer for 24 hours to make the attachment stronger.

The procedure of staining and mounting were as follows: First was the deparaffinization. The slide containing the slices of the ovary was dipped in xylol solution until the paraffin was dissolved for one minute, then dried on filter paper. Then the hydration, during which the dried object glass was put into alcohol with decreasing concentrations starting from absolute alcohol, 96%, 90%, 80%, 70%, 60%, 50%, 40%, 30%, and distilled water for one minute each. Subsequently, the objects were placed in a staining jar containing hematoxylin Ehrlich for seven minutes and washed with running water for 10 minutes. They were subsequently being put into 30%, 50%, 60%, and 70% alcohol each for one minute, then into Eosin-Y for ten minutes, rinsed with 70%, 80%, 90%, 96% alcohol, and absolute alcohol for one minute each. Finally, the preparation was put in a xylol solution for 15 minutes, then dried on filter paper, mounted with Canada balsam, and covered with a cover slip.

Graafian follicles diameter calculation

Subsequently, observations were made under a microscope to see and calculate the diameter of de Graff follicles in each treatment group. The data on the number of the Graafian follicles' diameters were then analyzed using SPSS statistics version 25 software. The method of calculation was the same as by Alfian,[6] that was by measuring the outer layer of theca cells (if any) and/or the granulosa cell layer. The formula is:

$$x = \frac{X1 + X2}{2}$$

Notes:
x=Average diameter length
X1=Longest diameter of the follicle
X2=Shortest diameter of the follicle

Statistical analysis

The data on mean and standard deviation were obtained when carrying out the data normality test with the Kolmogorov-Smirnov test. The obtained data were normally distributed and the subsequent data homogeneity test using Levene statistic test showed that the obtained data were homogeneous. This was done as a prerequisite test for using the parametric statistical test (ANOVA test). After testing the hypothesis with the Analysis of Variance, it was found that the result was significant ($p < 0.05$) so that it was continued with the Least Significance Difference (LSD) test which obtained significant differences between each treatment by means of the SPSS application program.

RESULTS AND DISCUSSION

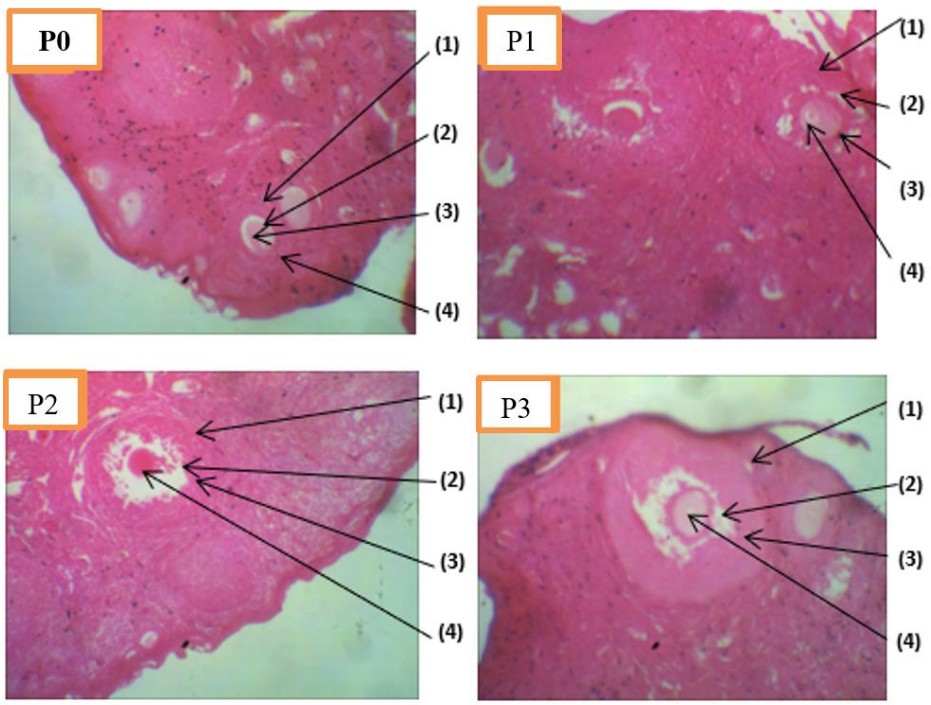
Diameter of the Graafian follicles

Each treatment was assessed by measuring the average diameter of the Graafian follicles in the mice (*Mus musculus*). The administration of Moringa leaf extract has a significant effect on the enlargement of the Graafian follicles' diameter in mice. The control group exhibited the smallest growth, with an average increase of 180.944 µm. In comparison, the groups that received Moringa leaf extract showed larger increases in the average diameter of their follicles. Specifically, the increase was 239.942 µm in the group that received a treatment of 300 mg/kg BW, 315.006 µm in the group receiving a treatment of 400 mg/kg BW, and the highest increase of 396.650 µm was observed in the group receiving 500 mg/kg BW.

However, in the image of the Graafian follicles in group P1 that received an extract dosage of 300 mg/kg BW, the follicle diameter increased due to a modest enlargement of the antrum and an increase in the ovum fiber. In addition, the image of Graafian follicles in group P2, which was administered an extract of 400 mg/kg BW, showed an increase in follicle diameter due to an enlargement of the antrum and an increase in granulosa cells. The ovum also enlarged. In the treatment group P3, the image of Graafian follicles shows a significant rise in the diameter of the follicle and its antrum. Additionally, there was an increase in the number of granulosa cells and the size of the ovum. Subsequently, the testing in this study employed the Analysis of Variance (ANOVA) parametric test, and the outcomes are displayed in Table 2.

Table 1. Effect of *Moringa olifeira* extract on the diameter of the Graafian follicle in mice after 14 days post-treatment

	Treatment Groups				p value
	P0 (n=6)	P1 (n=6)	P2 (n=6)	P3 (n=6)	(0.05)
Average diameter (µm) of the Graafian follicle of mice	180.944	239.942	315.006	396.650	0.000



Notes: (1). Theca externa, (2). Antrum, (3). Granulosa cell, (4). Ovum.

Figure 2. Histology of the Graafian follicles (Zoom 400x). Control (K), 300 mg/kg BW (P1), 400 mg/kg BW (P2), dan 500 mg/kg BW (P3).

Table 2. The results of Analysis of Variance (ANOVA) test on the Graafian follicles diameter

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	157260.559	3	52420.186	97.504	.000
Within Groups	10752.447	20	537.622		
Total	168013.006	23			

Table 3. The results of Tukey's honestly significant difference (HSD) test

(I) Treatment	(J) Treatment	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
Control	P1	-85933.33333*	23459.24872	.008	-151594.2743	-20272.3924
	P2	-144330.66667*	23459.24872	.000	-209991.6076	-78669.7257
	P3	-242641.66667*	23459.24872	.000	-308302.6076	-176980.7257
P1	Control	85933.33333*	23459.24872	.008	20272.3924	151594.2743
	P2	-58397.33333	23459.24872	.092	-124058.2743	7263.6076
	P3	-156708.33333*	23459.24872	.000	-222369.2743	-91047.3924
P2	Control	144330.66667*	23459.24872	.000	78669.7257	209991.6076
	P1	58397.33333	23459.24872	.092	-7263.6076	124058.2743
	P3	-98311.00000*	23459.24872	.002	-163971.9409	-32650.0591
P3	Control	242641.66667*	23459.24872	.000	176980.7257	308302.6076
	P1	156708.33333*	23459.24872	.000	91047.3924	222369.2743
	P2	98311.00000*	23459.24872	.002	32650.0591	163971.9409

*. The mean difference is significant at the 0.05 level.

The statistical analysis presented in Table 2 demonstrates that the administration of Moringa leaf extract, at varying doses, had a considerably favorable impact on the diameter of the Graafian follicles in mice (*Mus musculus*). There were significant differences seen in each treatment group.

Table 3 demonstrates that the control group does not show a statistically significant effect on the diameter of the Graafian follicles. The treatments administered at doses of 300 mg/kg BW and 400 mg/kg BW exhibited had resulted a slightly different effect. However, the administration of a dose of 500 mg/kg BW in treatment group 3 had a significant effect on the size of the Graafian follicles.

The treatment was administered for a duration of 14 days, by considering the three estrus cycles. According to Nugroho et al.[8], their research revealed that the typical estrous cycle of female mice lasts for 4-5 days. The doses administered in this study were based on a previous research conducted by Balumbi, et al.[5], which examined the ovarian morphometry and estrus cycle in female mice experimental animals. The Moringa (*Moringa oleifera* Lam.) leaf extract was combined with a 0.2% solution of sodium carboxymethyl cellulose (Na-CMC) because of the favorable dispersibility of the Moringa leaf extract in Na-CMC.

The findings indicated that there were different in the Graafian follicles among the different treatments. The treatment group P3 exhibited the greatest disparity when administered a dosage of 500 mg/kg BW of Moringa leaf extract. In addition, the diameter of the Graafian follicles demonstrated a progressive increase in correlation with the increasing dosage of Moringa leaf extract, as compared to the control group. The results of our study indicated that the administration of Moringa leaf extract at a dosage of 500 mg/kg BW led to an enlargement of the longest Graafian follicle in the left ovary of the mice. The average diameter of the Graafian follicles was measured to be 396.65 micrometers.

The alterations in the ovaries are influenced by the hormonal response that occurs as a result of the changes in the estrous cycle. Balumbi, et al.[5] reported that the inclusion of Moringa leaf extract in the diet enhances the estrous cycle due to the presence of essential elements in Moringa leaves that support development and growth. Rani et al.,[3] discovered that the inclusion of vitamin E in Moringa leaves can enhance reproductive success. The growth of the follicle is determined by its diameter and the oocyte. Vitamin E acts as an antioxidant and enhances the production of steroid hormones during the oocyte maturation.[9,10] The increase of the follicle's antrum is a result of the proliferation of granulosa cells, leading to an increase in diameter of the follicle's basement membrane. The antrum is filled with fluid that contains the estrogen hormone secreted by the granulosa cells. The estrogen hormone is produced by the theca interna cells of the ovarian follicles. The estrogen influences the period of puberty in female animals. Female animals undergoing puberty are

showing signs of sexual desire or estrus, and ovulate their egg cells.[11]

Yuliani et al.[12] conducted phytochemical analysis and found that Moringa leaves contain antioxidants such as flavonoids, saponins, tannins, and terpenoids. Flavonoids belong to the isoflavone group. Isoflavones are compounds that promote the synthesis of estrogen and possess a structural similarity to the hormone estrogen. Flavonoids are a group of isoflavone compounds that directly bind to the estrogen receptor due to their chemical structure, which closely resembles that of 17-ß estradiol in the body. The most prevalent compound is 17-ß estradiol. In a separate study, both female and male mice demonstrated an increase in the width of their seminiferous tubules when administered a dose of 0.55 mg/kg of Morinaga leaf extract. This effect was attributed to the presence of flavonoids.[13] Additionally, it can impede NFkβ and apoptosis via the TNF-α pathway, hence facilitating the development of Graafian follicles.[14] Furthermore, it is worth noting that not only are the leaves of the Moringa plant highly beneficial, but the extract derived from the bark of Moringa can also serve as an active element with antifertility properties.[15]

The hormone is produced by the theca interna cells, granulosa cells of the ovarian follicles, and the corpus luteum.[16] Dafaalla et al.[17] reported that Moringa leaf extracts had a substantial impact on the synthesis of testosterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH). The Moringa leaf is rich in ascorbic acid and possesses potent antioxidant properties. Ascorbic acid has a crucial function in safeguarding the brain and cerebrospinal fluid against the harmful effects of free radicals, thereby ensuring their protection from damage. Additionally, it supports the regular production of LH and FSH hormones by the pituitary gland in the brain. The *Moringa oleifera* is thought to possess therapeutic properties, functioning as an antioxidant, and exhibiting anti-inflammatory, antibacterial, antifungal, and various other advantages.[18]

A study conducted by Balumbi et al.[5] revealed that Moringa leaf extract can act as estrogen receptors in the body, leading to an increase in estrogen levels in the blood. This increase in estrogen stimulates the hypothalamus to secrete GnRF (Gonadotropin Releasing Factor), which in turn increases the production of FSH hormone. The FSH hormone then stimulates the development of primary and secondary follicles, transforming them into Graafian follicles. Furthermore, increased blood estrogen levels result in a sudden increase of LH (luteinizing hormone) in the bloodstream. This disorder causes an increase in the number of cells in the ovaries, leading to a change in the size of the follicle. According to a study conducted by Amelia et al.[19], the administration of Moringa leaf ethanol extract to mice was found to have a positive effect on enhancing the development of the folliculogenesis process. However, in mice with an endometriosis model, there was also an increase in folliculogenesis when Moringa leaf ethanol was administered at a dosage of 0.35 mg/kg BW.[10] A separate investigation carried out by Fathil demonstrated that Moringa enhances the concentrations of reproductive hormones (testosterone, luteinizing hormone, follicle stimulating hormone) in mice.[20]

The main limitation of this study was in the production of the histological preparations. Prior to conducting the main investigation, it would have been advisable to conduct a preliminary study in order to improve the process of sample preparation and enhance the accuracy of microscopy observations. The findings of this study suggest that incorporating *Moringa oleifera* Lam. leaves into the diet or using them as herbal supplements (traditional herbal medicine) can have positive effects on reproductive performance, particularly in humans. This implies that there is a practical application for the consumption of *Moringa oleifera* Lam. leaves in improving reproductive health.

CONCLUSION

The extract of Moringa leaves (*Moringa oleifera* Lam.) has a significant effect on increasing the diameter of the Graafian follicles in mice (*Mus musculus*). This is due to the presence of vitamin E in Moringa leaves, which stimulates granulosa cells to produce estrogen hormone, thereby facilitating the process of folliculogenesis.

DISCLOSURES

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Conflict of interests

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Author contributions

AD and SH contributed to preparing and checking the completeness of tools and materials for laboratory sample examination; MB and MR contributed to controlling the condition of the samples and treating the samples according to the research design; LD and JF, contributed to observing, measuring, and administering respective doses of Moringa leaf extract up to the completion of the study; RH and R contributed to assisting data collection, data measurement, tabulation of research results, editing and administering research approval, and the documentation of research results. All authors have read and approved the contents of the final manuscript.

REFERENCES

1. Narulita E, Prihatin J, Anam K, et al. Perubahan kadar estradiol dan histologi uterus mencit (*Mus musculus*) betina dengan induksi progesteron sintetik [Change of mice estradiol level and histology by synthetic progesterone injection]. Majalah Ilmiah Biologi Biosfera. 2017;34(3):117-22. doi: 10.20884/1.mib.2017.34.3.487.
2. Ningtyas, NSI. Pengaruh pemberian minyak buah merah (*Pandanus conoideus* Lam.) terhadap histopatologi folikel de Graaf pada mencit (*Mus musculus*) model infertil [Effect of red fruit oil on Graafian follcles histopathology in infertile mice]. Jurnal Sangkareang Mataram 2017;3(3):36-8. Available from: https://www.sangkareang.org/index.php/SANGKAREANG/article/view/178
3. Rani KC, Jayani NIE, Darmasetiawan NK, et al. Modul pelatihan kandungan nutrisi tanaman kelor [Training module on nutrition content of Morinaga plant]. Surabaya: Fakultas Farmasi Universitas Surabaya; 2019. p. 12.
4. Gunawati LS, Berata IK, Setiasih NL. Eka. Struktur histopatologi testis tikus wistar dengan aktivitas berlebih yang diberikan ekstrak daun kelor [Testicular histopathological structure of overactive Wistar rats receiving Moringa extract]. Indonesia Medicus Veterrinus. 2019;8(5):637-46. Available from: https://ojs.unud.ac.id/index.php/imv/article/view/57009
5. Balumbi M, Fachruddin, Risman M. Morfometri ovarium setelah pemberian ekstrak daun kelor (*Moringa oleifera* LAM) [Ovarian morphometry after Moringa extract administration]. Acta Veterinaria Indonesiana. 2021; 9:44-52. doi: 10.29244/avi.9.1.44-52.
6. Alfian MAJ, Sitasiwi AJ, Djaelani MA. Efek antifertilitas ekstrak air biji pepaya (*Carica papaya* l.) terhadap jumlah dan diameter folikel de graaf mencit (*Mus musculus*) betina [Antifertility effect of papaya seed water extract on the diameter of mice Graafian follicle]. Jurnal Pro-Life. 2018;5(1): 476-86. doi: 10.33541/jpvol6Iss2pp102
7. Sastroasmoro S, Ismail S, 2014. Dasar-dasar metodologi penelitian klinis [Basic clinical research methodology]. 5th edition. Jakarta: Sagung Seto; 2014.
8. Nugroho RA. Mengenal mencit sebagai hewan coba laboratorium [Mice as experimental animals]. Samarinda: Mulawarman University Press; 2018.
9. Tahapari E, Darmawan J, Robisalmi A, et al. Penambahan vitamin E dalam pakan terhadap kualitas reproduksi induk ikan nila (*Oreochromis niloticus*) [Improving the reproductive quality of tilapia (*Oreochromis niloticus*) broodstock through vitamin E addition in feed]. Jurnal Riset Akuakultur. 2019. 14(4):243-52. doi: 10.15578/jra.14.4.2019.243-252
10. Antina RR. Ekstrak etanol *Moringa oleifera* Lam terhadap folikulogenesis pada mencit model endometriosis [*Moringa oleifera* Lam. ethanol extract on folliculogenesis of endometrial model mice]. Jurnal Biosains Pascasarjana. 2017; 19(3): 246-59. doi: 10.20473/jbp.v19i3.2017.246-259.
11. Pramesti NA, Restuadi TI, Yudhana A, et al. Pengaruh pemberian ekstrak kedelai (*Glycine max*) terhadap jumlah pertumbuhan folikel ovarium mencit (*Mus musculus*) [The effect of soybean extract (*Glycine max*) on total growth of ovarian follicles in mice (*Mus musculus*)], Jurnal Medik Veteriner. 2018; 1 (3): 120-7. doi:org/10.20473/jmv.vol1.iss3.2018.120-127
12. Yuliani NN, Dienina DP. Uji aktivitas antioksidan infusa daun kelor (*Moringa oleifera*, Lam.) dengan metode 1,1-diphenyl-2-picrylhydrazyl (DPPH) [Antioxidant activity test of Moringa infusion using 1,1-diphenyl-2-picrylhydrazyl (DPPH) method]. Jurnal Info Kesehatan. 2015;13(2):1060-82. Available from: https://jurnal.poltekeskupang.ac.id/index.php/infokes/article/view/98.
13. Laoung-On J, Saenphet K, Jaikang C, et al. Effect of *Moringa oleifera Lam*. leaf tea on sexual behavior and reproductive function in male rats. plants (Basel). 2021;10(10):2019. doi: 10.3390/plants10102019. PMID: 34685828; PMCID: PMC8537186.
14. Lestari, Y.D. Hendarto, H. Widjiyati. Pengaruh ekstrak etanol daun kelor (*Moringa oleifera* Lam.) terhadap apoptosis sel granulosa pada mencit (*Mus musculus*) model endometriosis [Effect of Moringa leaf ethanol extract on the apoptosis of granulosa cells in endometrial model mice]. Jurnal Biosains

Pascasarjana. 2018:20(1):1-8. doi: 10.20473/jbp.v20i1.2018.1-8.
15. Aisyah S, Adnan A. Pengaruh ekstrak kulit batang tumbuhan kelor (*Moringa oleifera*) terhadap angka konsepsi mencit (*Mus musculus*) ICR jantan [Effect of Moringa bark on male mice conception rate]. Biogenesis: Jurnal Ilmiah Biologi. 2016; 4(1):58-63. doi: 10.24252/bio.v4i1.1470.
16. Mahmudati N. Kajian biologi molekuler peran estrogen/fitoestrogen pada metabolisme tulang usia menopause [Molecular biology study on estrogen/ phytoestrogen in menopause-age bone metabolism]. Proceeding Biology Education Conference. 2011;8(1). Available from: https://jurnal.uns.ac.id/prosbi/article/view/7364.
17. Dafaalla MM, Hassan AW, Idris OF, et al. Effect of ethanol extract of Moringa oleifera leaves on fertility hormone and sperm quality of male albino rats. World Journal of Pharmaceutical Research, (1–11), World Journal of Pharmaceutical Research. 2016;5(1). Available from: https://www.cabidigitallibrary.org/doi/full/10.5555/20163075003
18. Shabnam F, Rani I, Vivek D, et al. Therapeutic benefits of miracle tree *Moringa oleifera*: A complete overview. Current Traditional Medicine. 2023; 9(2):82-92. https://www.eurekaselect.com/article/124802
19. Amelia D, Santoso B, Purwanto B, et al. Effects of *Moringa oleifera* on insulin levels and folliculogenesis in polycystic ovary syndrome model with insulin resistance. Immunol Endocr Metab Agents Med Chem. 2018;18(1):22-30. doi: 10.2174/1871522218666180426100754. PMID: 30369967; PMCID: PMC6174639.
20. Fathil NM. The histological and physiological study of *Moringa oleifera*. Minar Journal. International Journal of Applied Sciences and Technology. 2022;4(3):276-98. doi: 10.47832/2717-8234.12.30

ORIGINAL RESEARCH

Level of knowledge on preeclampsia following health education through a WhatsApp group

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ABSTRACT

Objective: Hypertension in pregnancy, including preeclampsia, is the third most common cause of maternal mortality in Indonesia. One of the problems is low preeclampsia knowledge in the community. WhatsApp, as a social media platform, could facilitate spearheading promotive and preventive efforts, especially for high-risk mothers in the community. This study aimed to analyze the difference in levels of knowledge after receiving education through WhatsApp groups.

Materials and Methods: This was a pre-experimental study using one group pre-test and one post-test design. The sample size was 58 high-risk pregnant women in one of the Public Health Centers in Surabaya. Respondents completed a preeclampsia knowledge questionnaire before and after receiving health education via WhatsApp group for 12 days. The results were analyzed using the Wilcoxon signed rank test, Mann-Whitney U-Test, and Kruskal Wallis test.

Results: Most respondents had good knowledge about preeclampsia before and improved after intervention. All respondents had a difference in knowledge before and after the intervention ($p < 0.001$). The only factor that showed a difference in the initial knowledge level about preeclampsia was previous exposure to preeclampsia information ($p=0.014$).

Conclusion: Health education through WhatsApp groups can be considered to be provided as it has been proven effective in increasing the knowledge among high-risk pregnant women about preeclampsia.

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Highlights:

1. WhatsApp groups can effectively overcome the constraints of antenatal care in delivering health education to pregnant women.
2. The scope of health information about pregnancy should be expanded as this study has shown that it enhances their level of knowledge.

INTRODUCTION

Preeclampsia is the leading cause of maternal morbidity and mortality worldwide. This complication results in more than 70,000 maternal deaths and 500,000 fetal deaths each year globally.[1] In 2021, hypertension in pregnancy including preeclampsia-eclampsia became the third largest contributor to maternal mortality in Indonesia, with as many as 1077 cases.[2] It is expected that 90% of maternal mortalities were classified as preventable deaths.[3] Preeclampsia is the main target of one of the preventable pregnancy complications in Indonesia.[4] Prevention can be done by increasing knowledge about pregnancy danger signs that are found to be related to the ability for better early risk detection in pregnancy.[5] This is especially important for at-risk individuals to have adequate knowledge about pre-eclampsia.[6]

Primary health facilities spearhead promotive and preventive efforts related to health problems. Based on data from the Surabaya City health profile in 2020,[7] the Medokan Ayu Health Center had the lowest coverage of the first antenatal visit compared to other public health centers in Surabaya, which was 49.81%. Likewise, the fourth visit was 79.64%, which was still below the average coverage of antenatal visits in Surabaya.[7] Based on internal data, 14 cases of preeclampsia were recorded in December 2022. The low coverage of antenatal visits is a concern. Mothers who had four or more antenatal visits and visited since the first trimester were likely to have good preeclampsia knowledge.[8] In addition, the method chosen to improve the knowledge needs to be reconsidered. With face-to-face consultations, the health information conveyed was limited due to the short time.[9] Providing health education can be continued online to save time, energy, and costs.[10]

The widespread use of the internet has changed the way people seek health information and communicate with health care providers, including pregnant women who are highly motivated to seek information through online sources.[11] The increased utilization of social media for health education in the community is due to its efficacy in overcoming the limitations of access to information and health support of traditional health services.[12] Increasingly, mothers prefer online media, especially social media groups, to enable interaction and bonding.[13] Therefore, it is necessary to analyze the effect and the effectiveness of the WhatsApp group as a source of information for pregnant women.

MATERIALS AND METHODS

This research was a quantitative study using pre-experimental one group pre-test post-test design. This study was conducted at Medokan Ayu Health Center, Surabaya, Indonesia, in August – September 2023. The population of this study was high-risk pregnant women who attended antenatal visits during that period. There were 58 respondents who participated until completion. This study had received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Airlangga, Surabaya, numbered 118/EC/KEPK/FKUA/2023.

The variables obtained in this study were preeclampsia knowledge besides basic characteristics of the mothers: maternal age, educational background, employment status, gravida status, gestational age, high-risk pregnancy, and previous exposure to preeclampsia information. Health education was conducted by delivering information about preeclampsia through text, posters, and videos six times for 12 days. The knowledge before and after the intervention was evaluated. Knowledge about preeclampsia was measured using a questionnaire with 29 questions that had been tested for validity and reliability. Knowledge scores were classified as good knowledge (76-100), moderate knowledge (56-75), and poor knowledge (<56). The non-parametric test with SPSS version 25 was the Wilcoxon signed rank test to analyze the difference between prior and subsequent knowledge. Mann-Whitney U test and Kruskal Wallis test were conducted to analyze the difference in knowledge based on maternal characteristics.

RESULTS AND DISCUSSION

During the study periods, 174 high-risk pregnant women were attending antenatal care in Medokan Ayu Public Health Center, Surabaya, among them 58 pregnant women who fulfilled the inclusion criteria and were willing to join the study, were recruited. The characteristics of the samples are presented in Table 1.

In this study, most of the respondents aged between 20-35 years old, had the highest education at the secondary education level, were not employed, multigravida, were in their second trimester of pregnancy, and had heard about preeclampsia. The most widely accessed source of health information is social media.

The mean score of knowledge about preeclampsia was found to have increased by 22.625%. More than half of the respondents (56.90%) had good pre-test knowledge and almost all of the respondents (89.67%) had good knowledge after the intervention. The results showed a significant difference in pre-test scores on the variable of previous exposure to preeclampsia information (p=0.014).

Table 1. The profile of the high-risk pregnant women

Characteristics	Participants (58) N (%)
Maternal Age	
< 20	2 (3.4)
20 - 35	47 (81.0)
> 35	9 (15.5)
Education	
Elementary school	5 (8.6)
Junior high school	7 (12.1)
Senior high school	33 (56.9)
Diploma/S1/S2/S3	13 (22.4)
Employment Status	
Unemployed	48 (82.8)
Employed	10 (17.2)
Gravida Status	
Primigravida	16 (27.6)
Multigravida	42 (72.4)
Gestational Age	
1st trimester	6 (10.3)
2nd trimester	31 (53.4)
3rd trimester	21 (36.2)
High-risk pregnancy	
Hypertensive disorder	4 (6.9)
Miscarriage	11 (19.0)
Cesarean section delivery	20 (34.5)
Preeclampsia knowledge before intervention	
Known	31 (53.4)
Did not know yet	27 (46.6)
Sources of health information about pregnancy	
Social media	47 (81.0)
Health workers	19 (32.6)
Parents	10 (17.2)
Family	2 (3.4)
Friends	3 (5.2)
Neighbors	1 (1.7)
Internet search engines	2 (3.4)
Television	1 (1.7)

Table 2. Preeclampsia knowledge score

Knowledge scores	N (%)	Mean ± SD	Minimum-Maximum
Pre-test			
Poor	11 (18.97)		
Moderate	14 (24.14)	72.53 ± 20.17	6.90-96.55
Good	33 (56.90)		
Post-test			
Poor	2 (3.45)		
Moderate	4 (6.90)	88.94 ± 13.01	31.03-100.00
Good	52 (89.67)		

The mean score of knowledge was higher among pregnant women who had received information about preeclampsia. There were no significant differences in knowledge scores according to other variables, either for the pre-test or post-test scores. The finding of better knowledge among those who had received information about preeclampsia indicates that all of the information that had been shared either through social media, consultation with health workers, or from other people, could indeed improve their knowledge. Respondents who had heard about preeclampsia before had better knowledge.[14] Enhanced counseling with health workers is linked to higher levels of knowledge about preeclampsia.[15] The lack of quality and quantity of antenatal consultation is a reason for only 30% of mothers being informed about preeclampsia.[16]

Table 3. Distribution of knowledge level based on characteristics

Characteristics	Pre-test			p-value	Post-test			p-value
	Poor	Moderate	Good		Poor	Moderate	Good	
	N (%)	N (%)	N (%)		N (%)	N (%)	N (%)	
Maternal age								
< 20	0 (0.0)	0 (0.0)	2 (100.0)	0.854[b]	0 (0.0)	0 (0.0)	2 (100.0)	0.172[b]
20 - 35	9 (19.1)	12 (25.5)	26 (55.3)		2 (4.3)	4 (8.5)	41 (87.2)	
> 35	2 (22.2)	2 (22.2)	5 (55.6)		0 (0.0)	0 (0.0)	9 (100.0)	
Education								
Elementary school	1 (20.0)	2 (40.0)	2 (40.0)	0.497[b]	1 (20.0)	0 (0.0)	4 (80.0)	0.348[b]
Junior high school	4 (57.1)	0 (0.0)	3 (42.9)		1 (14.3)	2 (28.6)	4 (57.1)	
Senior high school	6 (18.2)	8 (24.2)	19 (57.6)		0 (0.0)	2 (6.1)	31 (93.9)	
Diploma/S1/S2/S3	0 (0.0)	4 (30.8)	9 (69.2)		0 (0.0)	0 (0.0)	13 (100.0)	
Employment Status								
Unemployed	10 (20.8)	11 (22.9)	27 (56.3)	0.489[a]	2 (4.2)	3 (6.3)	43 (89.6)	0.421[a]
Employed	1 (10.0)	3 (30.0)	6 (60.0)		0 (0.0)	1 (10.0)	9 (90.0)	
Gravida Status								
Primigravida	2 (12.5)	7 (43.8)	7 (43.8)	0.238[a]	0 (0.0)	2 (12.5)	14 (87.5)	0.678[a]
Multigravida	9 (21.4)	7 (16.7)	26 (61.9)		2 (4.8)	2 (4.8)	38 (90.5)	
Gestational Age								
1st trimester	2 (33.3)	1 (16.7)	3 (50.0)	0.437[b]	0 (0.0)	0 (0.0)	6 (100.0)	0.844[b]
2nd trimester	6 (19.4)	8 (25.8)	17 (54.8)		1 (3.2)	4 (12.9)	26 (83.9)	
3rd trimester	3 (14.3)	5 (23.8)	13 (61.9)		1 (4.8)	0 (0.0)	20 (95.2)	
Hypertensive disorder history								
Yes	0 (0.0)	1 (25.0)	3 (75.0)	0.569[a]	0 (0.0)	0 (0.0)	4 (100.0)	0.864[a]
No	11 (20.4)	13 (24.1)	30 (55.6)		2 (3.7)	4 (7.4)	48 (88.9)	
Miscarriage history								
Never	10 (21.3)	13 (27.7)	24 (51.1)	0.372[b]	2 (4.3)	4 (8.5)	41 (87.2)	0.516[b]
Once	1 (12.5)	1 (12.5)	6 (75.0)		0 (0.0)	0 (0.0)	8 (100.0)	
Twice	0 (0.0)	0 (0.0)	2 (100.0)		0 (0.0)	0 (0.0)	2 (100.0)	
Thrice	0 (0.0)	0 (0.0)	1 (100.0)		0 (0.0)	0 (0.0)	1 (100.0)	
Previous cesarean section delivery								
Yes	3 (15.0)	4 (20.0)	13 (65.0)	0.402[a]	1 (5.0)	0 (0.0)	19 (95.0)	0.784[a]
No	8 (21.1)	10 (26.3)	20 (52.6)		1 (2.6)	4 (10.5)	33 (86.8)	
Preeclampsia knowledge before intervention								
Known	1 (3.2)	10 (32.3)	20 (64.5)	0.014[a]	1 (3.2)	1 (3.2)	29 (93.5)	0.050[a]
Did not know yet	10 (37.0)	4 (14.8)	13 (48.1)		1 (3.7)	3 (11.1)	23 (85.2)	

[a]Mann Whitney Test
[b]Kruskal Wallis Test

The finding of better knowledge among those who had received information about preeclampsia indicates that all of the information that had been shared either through social media, consultation with health workers, or from other people, could indeed improve their knowledge. Respondents who had heard about pre-eclampsia before had better knowledge.[14] Enhanced counseling with health workers is linked to higher levels of knowledge about preeclampsia.[15] The lack of quality and quantity of antenatal consultation is a reason for only 30% of mothers being informed about preeclampsia.[16]

According to the maternal age, neither the statistical analysis nor the percentage tendencies showed difference in preeclampsia knowledge. However, based on the educational background, a pattern was seen that the higher the level of education, the more mothers had good knowledge. Mothers who did not receive formal education had lower knowledge about preeclampsia.[8] In addition, the percentage of poor knowledge was found to be higher in non-working women. Working women are more likely to obtain information because they often interact with friends and through mass media.[17] Based on parity, there was no significant difference in knowledge, but the increase in primigravida post-test scores was found to be slightly higher than multigravida. This may be because primigravida have a higher need for information due to their changing life period.[18] They tend to seek more specific pregnancy information and more advice regarding their pregnancy compared to multigravida.[19]

Good knowledge was more prevalent in mothers with a history of hypertension in pregnancy and miscarriage, but the difference was not significant due to the small number of respondents who had such a history. Various complications that have been experienced by pregnant women become important experiences for them. Pregnant women who have experienced obstetric complications have better knowledge of preeclampsia and tend to be aware of their condition.[8]

Table 4. Differences in knowledge before and after intervention

Pre-Test	Post-Test			Total
	Poor N (%)	Moderate N (%)	Good N (%)	
Poor	1 (9.1)	3 (27.3)	7 (63.6)	11 (100.0)
Moderate	1 (7.1)	1 (7.1)	12 (85.7)	14 (100.0)
Good	0 (0.0)	0 (0.0)	33 (100.0)	33 (100.0)
Total	2 (3.4)	4 (6.9)	52 (89.7)	58 (100.0)

Wilcoxon sign ranked test ($p<0.001$)

Most respondents had good preeclampsia knowledge in the pre-test and improved after being given health education through the WhatsApp group. The Wilcoxon Sign Ranked Test results showed a difference between knowledge before and after providing education through the WhatsApp Group.

The increased level of knowledge illustrates the efficacy of using WhatsApp groups to broaden the community's knowledge, specifically pregnant women. This study shows the necessity of special emphasis when providing information about preeclampsia, especially related to symptoms, risk factors, and complications regarding preeclampsia. Many respondents still lacked of knowledge that first pregnancy, too young maternal age, and having a history of high blood pressure in previous pregnancies are risk factors for preeclampsia. A similar result in a previous study, was that only a few respondents had adequate knowledge about risk factors, complications, and symptoms of preeclampsia.[6] This condition needs to be a concern because more women will immediately seek medical care when they recognize the possible consequences of the experienced symptoms.[6] Identifying risk factors is important as prevention and treatment during early pregnancy may support the health of the mother and child in the short and long term.[20]

Symptoms such as epigastric pain were largely unknown to the respondent. This result was also reported in another study, which found serious symptoms including epigastric pain and blurred vision were not recognized by patients.[16] This finding may explain why all of the preeclampsia cases were found to be advanced.[16] Most pregnant women are suffering the main preeclampsia symptoms but they do not realize the actual condition and do not seek health care immediately.[21]

Although almost all items were increased in terms of correct answers after health education, there was one item that showed a decrease in correct answers. This finding indicates that not all respondents received the information points or maybe there was an error in understanding the information. This self-directed learning process cannot be monitored by the provider, which may be vulnerable to different understandings.[10] Therefore, it is important to provide an open forum for discussion.[10]

Most respondents reported utilizing social media as a source of pregnancy-related health information. Through WhatsApp, it is possible to obtain some advice, ask for any doubts, interact with participants, and exchange their experiences, needs, and knowledge.[22] Real-time interactions among participants and health professionals quickly and efficiently can be facilitated through social media.[23] During the provision of the educational materials about preeclampsia, there was active interaction between each respondent and the researcher.

Health education through WhatsApp saves energy, money, and time. It can solve the problem of limited consultation time during antenatal visits to deliver information. Even though it is considered beneficial, due to the flexibility, it is difficult for the provider to control the learning process hence there may be delays in receiving feedback.[10] This study found out four respondents opened the material later. This shows that there was still a potential for ineffectiveness in a few respondents due to the delay in receiving information and limitations in monitoring.

Despite the overall results, this study certainly had limitations. Experimental studies with additional control groups and randomized respondents with a wider study population may show better results. Furthermore, it is necessary to determine the length of the education period concerning memory retention of the information provided. Apart from the limitations, the results clearly showed the effectiveness of WhatsApp as an educational platform for pregnant women with several findings that can be used as suggestions for its implementation and serve as a basis for further development. Considerations for future researchers include comparing or combining various health education media especially those that are suitable for the present era and investigating their effects on health outcomes.

CONCLUSION

Health education through WhatsApp groups can be utilized as a possible solution to the limited consultation time during antenatal care as it has been proven to be effective in increasing the knowledge about preeclampsia among high-risk pregnant women.

DISCLOSURES

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Conflict of interest

There is no conflict of interest to declare.

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Author Contribution

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting, and approval for publication of this manuscript.

REFERENCES

1. Rana S, Lemoine E, Granger JP, et al. Preeclampsia: Pathophysiology, Challenges, and Perspectives. Circ Res. 2019;124(7):1094-112. doi: 10.1161/CIRCRESAHA.118.313276. Erratum in: Circ Res. 2020 Jan 3;126(1):e8. PMID: 30920918.
2. Ministry of Health, Republic of Indonesia. Profil kesehatan Indonesia tahun 2021 [Health Profile of Indonesia year 2021]. Kementerian Kesehatan Republik Indonesia; 2022. 538 p.
3. Baharuddin M, Amelia D, Suhowatsky S, et al. Maternal death reviews: A retrospective case series of 90 hospital-based maternal deaths in 11 hospitals in Indonesia. Int J Gynaecol Obstet. 2019;144 Suppl 1:59-64. doi: 10.1002/ijgo.12736. PMID: 30815870.
4. Pribadi A. Zero mother mortality preeclampsia program: opportunity for a rapid acceleration in the decline of maternal mortality rate in indonesia. International Journal of Women's Health and Reproduction Sciences. 2021;9(3):160–3. doi: 10.15296/ijwhr.2021.30.
5. Mardiyanti I, Nursalam N, Devy SR, et al. The independence of pregnant women in early detection of high risk of pregnancy in terms of parity, knowledge and information exposure. Journal of Public Health in Africa. 2019 Oct 30;10(s1). doi: 10.4081/jphia.2019.1180.
6. Fondjo LA, Boamah VE, Fierti A, et al. Knowledge of preeclampsia and its associated factors among pregnant women: a possible link to reduce related adverse outcomes. BMC Pregnancy Childbirth. 2019;19(1):456. doi: 10.1186/s12884-019-2623-x. PMID: 31791264; PMCID: PMC6888941.
7. Ministry of Health, Republic of Indonesia. Profil kesehatan kota Surabaya Tahun 2020 [Health profile of the Surabaya City year 2020]. Kementerian Kesehatan Republik Indonesia; 2021.
8. Mekie M, Addisu D, Bezie M, et al. Knowledge and attitude of pregnant women towards pre-eclampsia and its associated factors in South Gondar Zone, Northwest Ethiopia: a multi-center facility-based cross-sectional study. BMC Pregnancy Childbirth. 2021;21(1):160. doi: 10.1186/s12884-021-03647-2. PMID: 33622291; PMCID: PMC7903706.
9. Wayan A, Ady Wirawan IM, Indraguna Pinatih GN, et al. The exploration of antenatal education method and its problems in Denpasar Regency, Indonesia: A qualitative study. Open Access Maced J Med Sci. 2021;9(E):990–8. doi: 10.3889/oamjms.2021.7041.
10. Jayanti TN, Hermayanti Y, Solehati T. Perbandingan efektivitas pendidikan kesehatan antara media cetak dan media elektronik terhadap mual muntah pada ibu hamil. Jurnal Keperawatan Muhammadiyah. 2021;6(4). doi: /10.30651/jkm.v6i4.10291.
11. McCarthy R, Byrne G, Brettle A, et al. Midwife-moderated social media groups as a validated information source for women during pregnancy. Midwifery. 2020;88:102710. doi: 10.1016/j.midw.2020.102710. Epub 2020 May 15. PMID: 32485501.
12. Stellefson M, Paige SR, Chaney BH, et al. Evolving role of social media in health promotion: Updated responsibilities for health education specialists. Int J Environ Res Public Health. 2020; 17(4):1153. doi: 10.3390/ijerph17041153. PMID: 32059561; PMCID: PMC7068576.
13. Gleeson DM, Craswell A, Jones CM. Women's use of social networking sites related to childbearing: An integrative review. Women Birth. 2019;32(4): 294-302. doi: 10.1016/j.wombi.2018.10.010. Epub 2018 Dec 31. PMID: 30606628.
14. Hamade R, Mohsen A, Kobeissy F, Karouni A, Akoum H. Knowledge of Preeclampsia Among Pregnant Women. CWHR. 2022 Nov;18(4):e07102

1197060. doi: 10.2174/15734048176662110070940 58
15. Joshi A, Beyuo T, Oppong SA, et al. Preeclampsia knowledge among postpartum women treated for preeclampsia and eclampsia at Korle Bu Teaching Hospital in Accra, Ghana. BMC Pregnancy Childbirth. 2020;20(1):625. doi: 10.1186/s12884-020-03316-w. PMID: 33059625; PMCID: PMC7566025.
16. Romuald R, Ratsiatosika TA, Martial RA, et al. The women knowledge, attitude, and perceptions of pre-eclampsia and eclampsia in Madagascar. Int J Reprod Contracept Obstet Gynecol. 2019;8(4): 1233. doi: 10.18203/2320-1770.ijrcog20191177.
17. Gardelia RA, Solehati T, Mamuroh L. The knowledge of pregnant women about pre-eclampsia at the tarogong public health center, Garut Regency. JMCRH. 2019;2(1). doi: 10.36780/jmcrh.v2i1.60.
18. Vogels-Broeke M, Daemers D, Budé L, et al. Sources of information used by women during pregnancy and the perceived quality. BMC Pregnancy and Childbirth. 2022;22(1):109. doi: 10.1186/s12884-022-04422-7.
19. Lanssens D, Thijs IM, Dreesen P, et al. Information resources among flemish pregnant women: cross-sectional study. JMIR Form Res. 2022;6(10): e37866. doi: 10.2196/37866. PMID: 36222794; PMCID: PMC9597425.
20. Wainstock T, Sergienko R, Sheiner E. Who is at risk for preeclampsia? Risk factors for developing initial preeclampsia in a subsequent pregnancy. J Clin Med. 2020;9(4):1103. doi: 10.3390/jcm9041103. PMID: 32294887; PMCID: PMC7230304.
21. Tamma E, Adu-Bonsaffoh K, Nwameme A, et al. Maternal hypertensive mother's knowledge, attitudes and misconceptions on hypertension in pregnancy: A multi-center qualitative study in Ghana. PLOS Glob Public Health. 2023;3(1): e0001456. doi: 10.1371/journal.pgph.0001456. PMID: 36962923; PMCID: PMC10021865.
22. Ribeiro ELDS, Silva AMND, Modes PSSDA, et al. WhatsApp use in a health education group with women. Rev Gaucha Enferm. 2023;44:e20220232. English, Portuguese. doi: 10.1590/1983-1447.2023.20220232.en. PMID: 37646757.
23. Omar MA, Hasan S, Palaian S, et al. The impact of a self-management educational program co-ordinated through WhatsApp on diabetes control. Pharm Pract (Granada). 2020;18(2):1841. doi: 10.18549/PharmPract.2020.2.1841. Epub 2020 May 3. PMID: 32477434; PMCID: PMC7243744.

SCOPING REVIEW

The impact of complementary therapies on dysmenorrhea in young women

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ABSTRACT

Objective: The study's objective was to obtain latest data on alternative therapy for dysmenorrhea in adolescent females of reproductive age.
Materials and Methods: A scoping review was conducted using the PRISMA ScR protocol. A search was conducted on PubMed, Science Direct, and Wiley, yielding 848 studies. Ten literature studies were identified that satisfied the criteria for population, exposure, and outcome. The studies also incorporated inclusion criteria, focusing on women of reproductive age who had dysmenorrhea.
Results: Out of 848 articles, 32 were considered potentially relevant and met the inclusion criteria. The articles indicated that teenagers commonly used warm compresses and herbal drinks as supplementary therapies to alleviate dysmenorrhea due to their perceived effectiveness and comfort. Other complementary therapies for the condition included massage, relaxation, herbal products, self-care practices, acupuncture, and therapeutic methods.
Conclusion: Herbal and warm water compress are the most commonly applied alternative therapies for treating dysmenorrhea.

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Highlights:

1. Complementary treatments have been shown to greatly reduce the intensity of dysmenorrhea pain.
2. The use of medicinal plants, herbal concoctions, or compresses might reduce dysmenorrhea discomfort more effectively than taking medications like mefenamic acid, ibuprofen, piroxicam, etc.

INTRODUCTION

Dysmenorrhea is characterized by irregular uterine contractions and lower abdominal pain, caused by increased prostaglandin production and release from the endometrium during menstruation. Dysmenorrhea affects women of childbearing age and adolescent girls more than other age groups. Women who are menstruating often report experiencing lower abdomen pain that extends to the hips and thighs. Possible additional symptoms may include headache, agitation, nausea, vomiting, and diarrhea. Menstrual pains typically begin a few days before the onset of menstruation and progressively diminish after the period begins.[1,2].

According to the World Health Organization, 90% of women experience dysmenorrhea (menstrual discomfort) monthly, with 10%–15% of them describing the pain as severe.[2] Adolescents, as defined by the World Health Organization, are those aged 10 to 19 years old. Over 50% of women in every country will develop dysmenorrhea at some stage in their life. Research shows that 45% to 90% of American teenage girls suffer from dysmenorrhea, while 90% of Swedish women under 19 and 67% of Swedish women over 24 experience this condition.[3] Furthermore, research shows that menstrual discomfort is highly prevalent in Indonesia, with 54.89% of women reporting experiencing the condition and 9.36% attributing it as the reason.[4-6]

Pharmaceutical and non-pharmaceutical treatments are the main categories of treatment for dysmenorrhea. Mefenamic acid, ibuprofen, piroxicam, and other nonsteroidal anti-inflammatory drugs (NSAIDs) can be utilized for pharmacological treatment of menstrual discomfort. Complementary and alternative medicine (CAM) can serve as a non-pharmacological therapy. Complementary and alternative medicine (CAM) is widely used and has increased over time in numerous countries. Complementary and alternative medicine (CAM) or "complementary health approaches" encompass various medical and healthcare treatments and products that fall outside the scope of conventional medicine. Complementary therapies not only improve health but are also more affordable and readily available.[7] This study aimed to collect current information on alternative therapies for dysmenorrhea in adolescent females of reproductive age.

MATERIALS AND METHODS

The scoping review technique was used as methodology in this in-depth review. The research's reference materials were obtained from a variety of articles.[8] This study used an evidence-based approach for scoping reviews by adopting the design of Tricco et al. (2018), which consists of six stages: stage one is identifying research questions, stage two is to find relevant articles, stage three is selecting articles, stage four is charting the data, stage five is combining the data, summarizing the findings, and stage six is presenting the findings.[9] To find questions for the scoping review, it is necessary to use efficient search methods to develop questions for literature search. The search method used in this review was PEO, which stands for Population, Exposure (intervention), and Outcome (results). The population in this review was teenage girls, the intervention was the complementary therapy and the outcome was the effect of the complementary therapy. The inclusion and exclusion criteria used to define article eligibility are described in Table 1.

Review in this study, the authors used PubMed, Wiley Online Library, and Science Direct as their search engines to look for studies on the impact of complementary therapy on young women's dysmenorrhea discomfort. To focus the search on teenage girl we used Boolean operators using the words Teenage Girl* OR Adolescent* girls OR young women*. The focus complementary therapy used Complementary therapy* OR Treatment traditional*, and the focus on dysmenorrhea used the words Primary dysmenorrhea* OR secondary dysmenorrhea*.

This scoping review found 72 articles from the PubMed database, 210 articles from Wiley Online Library, and 581 articles from Science Direct. All searches were conducted on January 8, 2023. The next step, all articles obtained with a total of 863 articles were entered into Zotero software and we found 15 duplicate articles. After the duplicate articles were discarded, the article review was started by selecting the titles and reading the abstracts to find articles suitable for the research and adjusted to the inclusion and exclusion criteria. We found 273 non-research studies, and 19 articles were found not using English and Indonesian, while 11 articles could not be accessed. Screened by title and abstract to as many as 545 articles, there were 34 articles found by filtering the completeness of the article, and 511 articles with records were excluded. From 34 articles found, there were 24 articles with full text, but 14 articles were excluded because they did not answer the research question. Finally, the results obtained were 10 articles, which were used in this study.

Table 1. Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
1. Articles published in the last 5 years	1. Articles published are not scientific journals
2. Complete and accessible article	2. Reviews, opinion articles
3. Articles in Indonesian and English	3. Thesis, term paper, dissertation thesis
4. International and National Publications	4. Books
5. Quantitative research articles, qualitative	

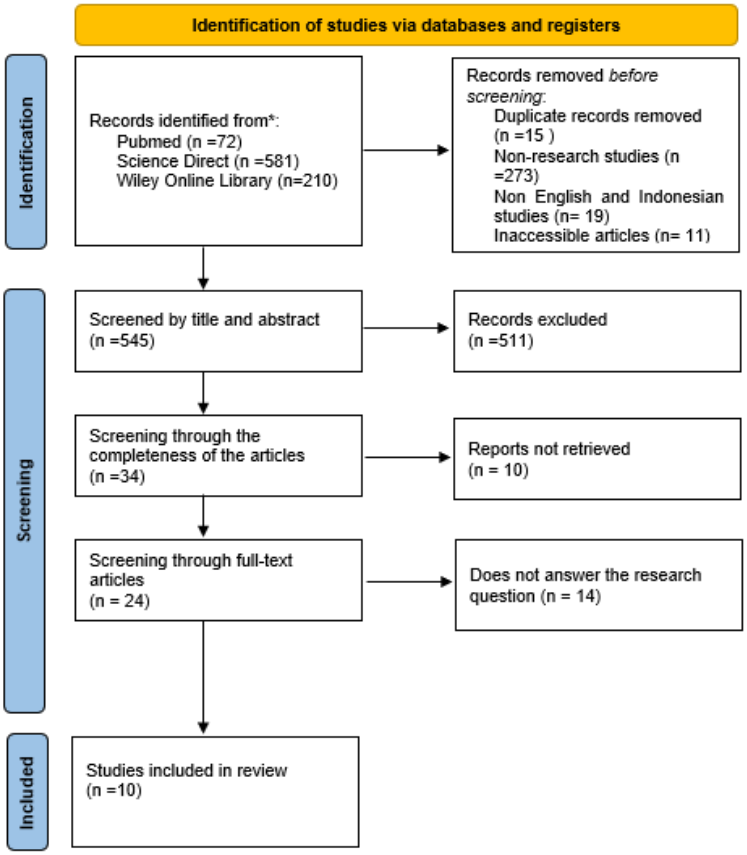

Figure 1. PRISMA flowchart

Critical assessment is the process of carefully, methodically, and accurately analyzing things. The author evaluated the articles using the Joana Briggst Institute (JBI) critical assessment tool. At this point, the author utilized the grades A, B, and C to assess the articles' quality. Every article was examined independently by the researchers to see if it might be used as a reference for further research. Further careful and meticulous assessment of every article later revealed the final values as shown in Table 2.

RESULTS AND DISCUSSION

For each publication included in this review study, the author's name, year and country, purpose, methodology, and findings were documented. All publications were examined for key themes, including characteristics of teenagers who underwent complementary therapy, the use of complementary therapy for comfort, and the effect of the complementary therapy. The articles were assigned with numbers A1–A10 to facilitate searching. After critically evaluating 10 publications, it was found that there were five cross-sectional quantitative articles (A1, A2, A3, A4, and A6) with high ratings, one qualitative article (A5) with a moderate rating, and the randomized controlled trials (RCTs) articles A7 and A8 were rated highly, while RCTs A9 and A10 had a lower rating.

The articles were grouped using article mapping according to their original characteristics, which was determined by research approaches and country-specific features. Ten articles used different research methodologies, comprising five cross-sectional studies, one qualitative study, and four randomized controlled trials (RCT). This scoping review included research publications from Turkey, China, and Spain as examples of articles from developed countries, and from Malaysia, Ghana, India, and Iran as examples of articles from developing countries.

According to the evaluation conducted with the JBI instrument, seven articles had very good grades (A1, A2, A3, A4, A6, A9, A10) and three articles had good grades (A5, A7, A8). The highest score was 9.3 (A), while the lowest score was 9 (B) in article A5. The review categorized publications based on three important themes: the characteristics of teenagers who underwent complementary therapy, the comfort the therapy offered, and its impact. Primary dysmenorrhea is a common gynecological condition among teenagers, with a high prevalence rate observed in articles A1, A2, A3, A4, A6, and A7 in theme 1 focusing on teenagers who were undergoing alternative therapy. Theme 2 articles focused on complementary therapies that can effectively treat dysmenorrhea and were considered safe for women's comfort. These articles comprised A1, A2, A5, A6, and A8 articles. Theme 3 focused on the impact of complementary therapies. Several alternative therapies were found to be useful in alleviating pain and suffering related to dysmenorrhea, as reported in articles A1, A2, A5, and A6.

Characteristics of the teenagers undergoing complementary therapy

Women are affected by primary dysmenorrhea since it is one of the most prevalent and significant gynecological issues. Women with a history of early menarche, menorrhagia, a family history of dysmenorrhea, and emotional disorders are found to have a greater prevalence of dysmenorrhea. All young female students who had dysmenorrhea used supplementary medicine. As much as 48.9% of female students were between the ages of 21 and 23, while 47.2% were between the ages of 18 and 20. The age of menarche for 68.9% of the students was under 10 years old. All students had a regular menstrual cycle and 68.9% of them had a menstrual cycle of more than 7 days (A3). As much as 48.9% of female students were between the ages of 21 and 23, while 47.2% were between the ages of 18 and 20. The age of menarche for 68.9% of the students was under 10 years old. All students had a regular menstrual cycle and 68.9% of them had a menstrual cycle of more than 7 days (A3). Among the female students, 48.9% were between the ages of 21 and 23, while 47.2% were between the ages of 18 and 20. The age of menarche for 68.9% of students was under 10 years old. All students had a regular menstrual cycle and 68.9% of them had a menstrual cycle of more than 7 days (A3).[10] We analyzed the distribution of those students' use of complementary and alternative medicines to treat dysmenorrhea. The quality of life, work position, and social obligations are all greatly impacted by dysmenorrhea. The most common method of managing dysmenorrhea is through the use of non-pharmacological treatments since pain management without or with minimum drug use is a significant healthcare aim (A6).[11-13]

Effect of complementary therapy on comfort

While painkillers were insufficiently effective to regulate or lessen pain (A5),[14] complementary therapies are safe and effective to relieve menstruation discomfort or dysmenorrhea, so that their impact on women's comfort was apparent (A1).[13] One of the complementary therapies is the use of ginger as a herbal remedy. It is a safe herbal remedy for treating dysmenorrhea so that it does not impede young women's activities (A8).[15] This demonstrates that those who experience dysmenorrhea are more interested in relieving their menstrual pain using those therapies than using medical treatment, and complementary therapy in treating dysmenorrhea is safe and effective for use in women or young women (A1).[13] The relationship between availability and cost can be a common reason for the use of those therapies. Complementary therapies are often used in conjunction with conventional medicine or as a method to help the patients feel more comfortable. It was also found that analgesic was ineffective for dysmenorrhea. In order to lessen pain, dysmenorrhea can be treated with either self-medication or complementary therapy.

Effect of complementary therapy on dysmenorrhea

Women who employ a variety of complementary therapies are believed to have pain and discomfort relief from dysmenorrhea (A2).[6] According to several research, using complementary and alternative therapies to treat dysmenorrhea in adolescents can have an impact on menstruation discomfort or dysmenorrhea (A1).[13] Strategies in complementary therapy treatments carried out for pain management include those that support relaxation, such as rest, heat, massage, music, and adopting antalgic positions and distraction techniques. Common techniques to promote relaxation and consequently reduce pain include physical rest, various forms of heat application such as hot baths, warm compresses, electric blankets or even drinking hot herbal tea can help influence the reduction of dysmenorrhea (A5).[14]

Transcutaneous electrical nerve stimulation (TENS) has been proposed as an effective method for reducing pain in primary dysmenorrhea. TENS is a cost-effective, portable technique that is noninvasive and has minimal hazards and with only a few contraindications. According to the numerical rating scale (NRS) for dysmenorrhea-related pain, the length of dysmenorrhea pain relief, and the quantity of ibuprofen pills used,

TENS demonstrated a larger benefit in pain relief (A10).[17]

The most popular strategy for treating dysmenorrhea is the use of non-pharmacological treatments including complementary therapies. Alternative non-pharmacological treatments for primary dysmenorrhea include self-care techniques such as exercise, rest, dietary changes, and use of cold medications. and hot compresses to relieve menstrual pain (A6).[11] Additionally, it has been demonstrated that complementary treatments, such as acupuncture, can lessen the symptoms of primary dysmenorrhea and are linked to substantially lower pain intensity (A7).[12]

This scoping review tried to understand how complementary therapy affected young women's dysmenorrhea. Menstrual pain before or during a period, known as dysmenorrhea, renders a woman unable to work or engage in other activities and forces her to sleep. Dysmenorrhea is a condition that causes cramps, pelvic pain, and abdominal pain throughout the menstrual cycle.[16] Dysmenorrhea has a detrimental impact on social interaction, psychological status, and daily physical activity, as well as daily work or school activities, such as absenteeism, loss of attention, and decreased participation or output.[13]

There are four types of self-care measures for primary dysmenorrhea: lifestyle improvements involving reducing physical activity, keeping warm, consuming warm beverages, and avoiding cold beverages and foods, as well as hot or greasy foods, caffeine, and sweet foods. Self-medication, including traditional Chinese medicine or Western medicine, is a method of symptom management. Self-regulation of negative emotions involves actions such as engaging in disruptive behaviors, expressing feelings, and self-talk to suppress them, as well as alternative therapies including heat therapy, massage, and acupuncture. The category of dysmenorrhea including communication with others includes interactions with the mother, other family members, acquaintances, classmates, or teachers to seek management guidance or medical help (A4).[20]

There are other types of complementary treatments that can be employed, including herbal remedies, relaxing techniques, drinking mineral water as a form of therapy, and combination therapies. Adolescents can be managed and have their quality of life improved with the use of complementary therapies because they are secure and efficient. Young women may receive complementary and alternative therapy. On the other hand, warm water compress therapy is a popular supplementary therapy that is utilized frequently nowadays due to its ease of use, safety and comfort it provides, and effectiveness.[13]

Warm compresses have been shown in a study by Yunianingrum & Widyastuti[18] to be effective in treating dysmenorrhea while Ariyanti et al., found that using warm water compresses or herbs as a complementary therapy had similar effects.[19] Herbal beverages are occasionally used by teenagers as a supplemental treatment to ease menstrual discomfort. Herbal beverages like tamarind, turmeric, hot ginger, honey, and coconut water are thought to ease menstruation cramps.[19] The best for reducing the symptoms of dysmenorrhea are fennel, hops, chamomile, lavender, lemon balm, mint, rose, papaya, lemongrass, and zataria. Other properties of each plant that support the activity of reducing symptoms of dysmenorrhea include curcuma, pawpaw, aloe vera, cinnamon, and lemongrass.[16] According to Chen et al.'s findings, supplementary therapy reduced dysmenorrhea by about 56.5%,[20] showing that supplementary therapy can influence dysmenorrhea or menstrual pain.

Because it is simple to use and has no detrimental impacts on health, complementary therapy was highlighted in this study. According to the results, probably it is the most popular therapy now since it has been shown to be simpler, more efficient, and safer to use in several studies, particularly when combined with warm compresses and herbal therapy employing medicinal plants like ginger, turmeric, and other similar plants.

Since Asian culture made up the majority of the research papers, they were unable to adequately describe other cultures that diverge from the norms and cultures that are discussed in the research articles. Furthermore, as this study only included one qualitative article, not enough information was available for all young women who treat their dysmenorrhea with alternative therapies. Furthermore, the JBI tool was utilized in this scoping review to appraise the articles' quality and the phases involved in creating a scoping review, which were verified by means of the PRISMA-ScR checklist.

Table 2. Chart of data studied

No	Author, year	Country	Aim	Type of Reseach	Data Collection	Participants	Results	JBI
A1	Abubakar et al., 2020[13]	Malaysia	This research determined the practices and perceptions of female students with dysmenorrhea towards complementary and alternative therapies (CAT)	Quantitative Cross Sectional	Questionnaire, and numeric rating Scale (NRS)	As many as 474 female students participated in this survey as responders.	The incidence of dysmenorrhea was 72.1%, and the most common CATs used by respondents were hot compresses/heating pads (47.5%) and massage (43.0%), both of which were used often. The use of CAT was most frequently done to lessen the need for analgesics (61.4%), for efficacy (37.3%), and on the advice of others (32.9%). Approximately 23 and 9% of respondents said CAT was "effective" and "more effective" than analgesics, respectively.	A
A2	Samba Conney et al., 2019[6]	Ghana	The purpose of this study was to evaluate the effectiveness of complementary and alternative medicine (CAM) in treating dysmenorrhea in teenage girls.	Quantitative Cross Sectional	The NRS, a semi-structured questionnaire comprising both open-ended and closed-ended items, was used to collect the data.	As many as 478 female students from Mporhor High School and Archbishop Porter Girls' Secondary School participated in this survey as responders..	Users of CAM used 32% mind-body techniques like relaxation, 31% alternative techniques like hot water therapy, 15% biological techniques like herbal products, and 22% manipulative and body-based techniques like exercise. Significant connections were found that might lead to higher quality of life (QoL).	A
A3	Duman and Yıldırım, 2022[10]	Turkey	Aimed to identify the risk factors for primary dysmenorrhea in female students as well as the impact of CAM use in preventing primary dysmenorrhea.	Quantitative Cross Sectional	Visual Analogue Scale (VAS)	In this study, 134 respondents were divided into two groups at random, having 67 respondents in each group.	The students' mean VAS ratings indicated that having a hot bath (4.61 ± 2.13) and applying heat to the stomach (4.33 ± 1.98) were the most effective mind-body approaches utilized to minimize primary dysmenorrhea.	A
A4	Chen et al., 2019[20]	China	The purpose of this study was to investigate the frequency of primary dysmenorrhea among Chinese female students as well as its features and self-care management techniques.	Quantitative Cross Sectional	Questionnaire	There were 2.555 female students selected utilizing multistage cluster random sampling as respondents for this study.	Self-care strategies commonly used to reduce dysmenorrhea are keeping warm (84.6%), drinking warm drinks (75.7%) and avoiding cold drinks and food (74.2%). As much as 34.8% self-medicated, those using Western medicine were 15.6%, traditional Chinese medicine 8.6%, or both 10.6%.	A

A5	Fernández-Martínez et al., 2022[14]	Spain	This study aimed to describe how Spanish students manage dysmenorrhea	Quantitative Case Study	Interview	In this study, 33 nursing students from Andalusia (Spain) participated as responders.	Four main themes were identified: (a) Pain management strategies; (b) using painkillers; (c) selecting the ideal treatment; (d) non-pharmacological treatments.	B
A6	Unnisa et al., 2022[11]	India	The aim of this study was to explore quality of life with non-pharmacological treatment for dysmenorrhea.	Quantitative Cross Sectional	Questionnaire, interview	Respondents in this study totaled 517 respondents	348 out of 517 participants finished the study; of these, 51.1% had average QOL, 33.3% had bad QOL, and 14.9% had good QOL. This shows that managing the adverse impacts on health-related issues can be accomplished by frequently implementing non-pharmacological approaches.	A
A7	Wang et al., 2019[12]	China	This study was conducted to evaluate the effectiveness of acupressure techniques to relieve pain in patients with primary dysmenorrhea compared with conventional pain treatment.	Quantitative Cross Sectional	Visual Analogue Scale (VAS)	The respondents in this study were 62 young women	The results of this study were that acupuncture was proven to be associated with significantly lower pain intensity and reduced severity of primary dysmenorrhea symptoms compared to ibuprofen ($p < 0.05$).	B
A8	Adib Rad et al., 2018[15]	Iran	This research was conducted with the aim of comparing the effects of ginger and Novafen in menstrual pain.	Quantitative Cross Sectional	Demographic questionnaires, the pain visual analog scale (PVAS), the multidimensional verbal rating scale (MVRS), and pictorial blood loss assessment charts (PBAC) were used in this study to gather data. Using PVA, the degree of dysmenorrhea was examined.	The respondents in this study were 168 female teenage students	The differences between the two groups each time did not show statistical significance ($p > 0.05$). Both drugs reduced menstrual pain. Ginger and Novafen are effective in relieving pain in women with primary dysmenorrhea. Therefore treatment with natural herbal medicines, non-synthetic medicines, to reduce primary dysmenorrhea is recommended	B

A9	Yu et al., 2018[21]	China	The purpose of this study was to compare the effectiveness of AHP with an acupoint placebo plaster (APP) administered to patients with primary dysmenorrhea in a waiting list control group.	Quantitative Cross Sectional	Visual Analogue Scale (VAS)	Respondents in this study were 180 women.	The findings of this study demonstrated that acupoint plasters are safe to use and that their therapeutic effects as complementary therapies are superior to those of medicines.	A
A10	Bai, et al. 2017[17]	China	This study looked at how transcutaneous electrical nerve stimulation (TENS) therapy affected women with primary dysmenorrhea in terms of pain reduction.	Quantitative Cross Sectional	Numeric Rating Scale (NRS)	As many as 134 people participated in the study as respondents.	According to the study's findings, TENS was a safe and effective way to treat pain in people with primary dysmenorrhea. Therefore, the quantity of ibuprofen tablets taken (P.01), the length of time the pain from dysmenorrhea was relieved (P.01), and the NRS (P.01). However, there was no discernible change in the 2 groups' WHOQOL-BREF scores for life quality.	A

CONCLUSION

Complementary therapies can help treat or lessen dysmenorrhea or period pain in young women. Studies on complementary therapies for teenagers with dysmenorrhea provided evidence for this. The use of non-pharmacological treatments found in complementary therapy programs is the most widely used approach to treating dysmenorrhea. Because complementary therapy is simple to apply and has no detrimental effects on health, its significance should be stressed. Herbs and warm water compress therapy are two additional complementary therapies that are frequently employed since they are efficient and secure in treating dysmenorrhea. Research is needed to understand how alternative therapies affect dysmenorrhea in teenage girls.

DISCLOSURES

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REFERENCES

1. Astuti D, Kulsum U. Pola menstruasi dengan terjadinya anemia pada remaja [Menstrual pattern and anemica incidence among adolescents]. Ilmu Keperawatan dan Kebidanan. 2020;11(2):314–27. doi: 10.26751/jikk.v11i2.832.
2. Sembiring JB, Kadir D, Tarigan R. Efektivitas terapi kombinasi pemberian seduhan kembang telang/butterfly pea (*Clittoria ternatea*) dan lamaze exercice terhadap penurunan nyeri haid (disminore) pada remaja putri [Effectiveness of combined therapy using butterfly pea infusion and lamaze exercise on dysmenorrhea reduction]. Healthy Tadulako Journal. 2022;8(1):44–51. doi: 10.22487/htj.v8i1.487
3. Budhi NGMAA, Aticeh, Follona W, et al. (2022). Effect of spice drinks (red ginger and cinnamon) on dysmenorrhea pain. International Journal of Science and Society. 2022;4(4):437-48. doi: 10.54783/ijsoc.v4i4.592.
4. Nurbaiti, Febrina R. Pranayama sebagai pengurangan nyeri menstruasi pada remaja putri di SMK Baiturrahim [Pranayama to reduce dysmenorrhea among female adolescents in SMK Baiturrahim]. 2022;4(3):355–60. doi: 10.36565/jak.v4i3.329.
5. Azizah N, Kusumawardani PA. Inhalasi aromaterapi lavender dengan penurunan intensitas nyeri dismenorea pada remaja. Proceeding Book of the Health National Conference; 2020 Mar 4; Mataram, Indonesia.
6. Samba Conney C, Akwo Kretchy I, Asiedu-Danso M, et al. Complementary and alternative medicine use for primary dysmenorrhea among senior high school students in the western region of Ghana. Obstet Gynecol Int. 2019;2019:8059471. doi: 10.1155/2019/8059471. PMID: 31885598; PMCID: PMC6899296.
7. Arini KN, Nyoman N, Witari D. Edukasi pemanfaatan terapi komplementer untuk mengurangi kejadian emesis gravidarum pada kehamilan pertama [Education on complementary therapy for reducing emesis gravidarum in first pregnancy]. Jurnal Abdi Mahosada. 2023 ;1(1):7–13. doi: 10.54107/abdimahosada.v1i1. 145
8. Munn Z, Peters MDJ, Stern C, et al. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol. 2018;18(1):143. doi: 10.1186/s12874-018-0611-x. PMID: 30453902; PMCID: PMC6245623.
9. Tricco AC, Lillie E, Zarin W, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169(7):467-73. doi: 10.7326/M18-0850. Epub 2018 Sep 4. PMID: 30178033.
10. Duman NB, Yıldırım F, Vural G. Risk factors for primary dysmenorrhea and the effect of complementary and alternative treatment methods: Sample from Corum, Turkey. Int J Health Sci (Qassim). 2022;16(3):35-43. PMID: 35599944; PMCID: PMC9092532.
11. Unnisa H, Annam P, Gubba NC, et al. Assessment of quality of life and effect of non-pharmacological management in dysmenorrhea. Ann Med Surg (Lond). 2022;81:104407. doi: 10.1016/j.amsu.2022.104407. PMID: 36147090; PMCID: PMC9486665.
12. Wang H, Cao Y, Jin X, et al. Effect of an acupuncture technique of penetrating through zhibian (BL54) to shuidao (ST28) with long needle for pain relief in patients with primary

dysmenorrhea: A randomized controlled trial. Pain Res Manag. 2019;2019:7978180. doi: 10.1155/2019/7978180. PMID: 31929849; PMCID: PMC6935824.
13. Abubakar U, Zulkarnain AI, Samri F, et al. Use of complementary and alternative therapies for the treatment of dysmenorrhea among undergraduate pharmacy students in Malaysia: a cross sectional study. BMC Complement Med Ther. 2020;20(1):285. doi: 10.1186/s12906-020-03082-4. PMID: 32948163; PMCID: PMC7501717.
14. Fernández-Martínez E, Pérez-Corrales J, Palacios-Ceña D, et al. Pain management and coping strategies for primary dysmenorrhea: A qualitative study among female nursing students. Nurs Open. 2022;9(1):637-45. doi: 10.1002/nop2.1111. Epub 2021 Oct 30. PMID: 34719126; PMCID: PMC8685831.
15. Adib Rad H, Basirat Z, Bakouei F, et al. Effect of Ginger and Novafen on menstrual pain: A cross-over trial. Taiwan J Obstet Gynecol. 2018;57(6):806-9. doi: 10.1016/j.tjog.2018.10.006. PMID: 30545531.
16. Fauziyah PN, Zuhrotun A. Review: Tumbuhan Berkhasiat Untuk Mengatasi Dismenorea [Review article: traditional plants for dysmenorrhea]. Kartika J Ilm Farm. 2020;7(2):79. doi: 10.26874/kjif.v7i2.284.
17. Bai HY, Bai HY, Yang ZQ. Effect of transcutaneous electrical nerve stimulation therapy for the treatment of primary dysmenorrheal. Medicine (Baltimore). 2017;96(36):e7959. doi: 10.1097/MD.0000000000007959. PMID: 28885348; PMCID: PMC6392990.
18. Yunianingrum E, Widyastuti Y, Margono. The effect of warm compress and aromatherapy lavender to decreasing pain on primary dysmenorrhea. Jurnal Kesehatan Ibu dan Anak. 2018;12(1):39–47.
19. Ariyanti KS, Sariyani MD, Winangsih R. Terapi non-farmakologis untuk mengurangi nyeri haid pada remaja di Tabanan [Non-pharmacological therapy to reduce dysmenorrhea among adolescents in Tabanan]. J Kebidanan Malakbi. 2022;3(2):58. doi: 10.33490/b.v3i2.612.
20. Chen L, Tang L, Guo S, et al. Primary dysmenorrhea and self-care strategies among Chinese college girls: a cross-sectional study. BMJ Open. 2019;9(9):e026813. doi: 10.1136/bmjopen-2018-026813. PMID: 31537555; PMCID: PMC6756436.
21. Yu S, Wen Y, Xia W, et al. Acupoint herbal plaster for patients with primary dysmenorrhea: study protocol for a randomized controlled trial. Trials. 2018;19(1):348. doi: 10.1186/s13063-018-2682-8. PMID: 29970155; PMCID: PMC6029355.

REVIEW ARTICLE

Benefits and safety of myomectomy during cesarean section

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ABSTRACT

Uterine myoma is a tumor in the uterus that is generally benign. There are many types of uterine myomas. These tumors can grow on the outer wall of the uterus, on the uterine muscle, or it can also be on the inner wall of the uterus. The most frequent kind of uterine tumor is myoma. Uterine myoma mostly occurs in women over thirty years of age. Its prevalence ranges from 5.4% to 77%, with uterine fibroids accounting for up to 5% of pregnancies. The myomectomy procedure is an option for women who still want children but are concerned about the possibility of subsequent surgical intervention. The myomectomy cesarean section is indicated if there were complications related to the myoma in a previous pregnancy. It also avoids the possibility of repeat laparotomy for fibroid removal in the future. Myomectomy surgery should be planned based on fibroids' location, size, and quantity, using suitable imaging. Myomectomy cesarean section can be an option compared to cesarean section without myomectomy, especially if it is performed by experienced surgeons with proper hemostatic techniques and performed in tertiary-level health facilities. This article discusses the details of the benefits and safety of myomectomy during cesarean section so that it might be considered before performing this procedure.

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Highlights:

1. Myomectomy during cesarean section is a recommended and safe procedure.
2. This procedure benefits the patient because it avoids a second operation and anesthesia complications and is cost-saving.

INTRODUCTION

Myoma is the most common benign tumor of the reproductive organs, influencing 20-40% of reproductive-age women. This disease can result in significant illness and reduce the quality of life. Currently, there are many medical and non-invasive therapies. Still, data on long-term side effects and safety in obstetrics are insufficient; therefore, only short-term treatment outcome data are available. The most frequent benign tumor in women is uterine myoma. Its prevalence ranges from 5.4% to 77%, with uterine fibroids accounting for up to 5% of pregnancies.[1,2] Uterine myoma in pregnancy is a condition that can

cause problems because it can induce abortion, bleeding, premature labor, postpartum hemorrhage, and uterine compression in pregnant women caused by the increased size of myomas influenced by hormones in pregnancy, as well as complications related to degenerative changes.[3]

Medical therapy options, especially for short-term treatment, relieving clinical symptoms, and effective long-term treatment for reducing the volume of uterine myomas and massive bleeding, have not been found to date.[4] Also, there are few clinical trial studies on available medical treatment options.[5] Therefore, the risk of obtaining a myoma at the time of cesarean section has also increased. Some disadvantages of the technique during myomectomy cesarean section are the potential for postoperative bleeding, hysterectomy or postoperative morbidity after myomectomy cesarean section.[6]

More than a century ago, myomectomy cesarean section was first pronounced by Bonney. Several studies stated the presence of uterine hypotonia. Other contra-indications include congenital disabilities and coagulopathy diseases. Furthermore, myomectomy cesarean section should be avoided in several cases, for example, intramural, fundal, cornual, and posterior uterine wall myomas with higher surgical complications.[7] However, current research reported that myomectomy during cesarean section is a recommended treatment in some cases.[8] As a result, this study aims to explore the benefit and safety of myomectomy during cesarean delivery.

UTERINE MYOMA

Uterine myoma is a tumor in the uterus that is generally benign. There are many types of uterine myomas. These tumors can grow on the uterus's outer wall, the muscle of the uterine, or it can also be on the uterus's inner wall.[8] The most prevalent kind of uterine tumor is myoma. Uterine myoma mostly occurs in women over thirty years of age.[9] Uterine myomas are monoclonal benign tumors originating from smooth muscle cells in the uterus. These tumors are well-defined and composed of cells of smooth muscle tissue, fibroid connective tissue, and collagen. Uterine myomas are solid, relatively round, have a rubbery consistency and smooth walls, and are covered with a capsule on the outside.[10]

The cause of myoma is not known with certainty. Uterine myomas originate from normal muscle cells, immature muscles in the myometrium or embryonic cells in the uterine blood vessel walls. Tumor cell growth starts from multiple cells that are very small and spread in the myometrium.[11] These cells will grow slowly but progressively over the years under the estrogen hormone. Growth hormone levels decrease during pregnancy, but a hormone with a similar structure and biological activity, named human placenta lactogen (HPL), is seen in this period and may result in the quick development of uterine myomas in pregnancy synergistically with the estrogen hormone.[12]

Epidemiological data globally shows that around 70% of cases of uterine myoma occur at the age of 50 years, of which around 30-40% of cases are in perimenopausal women, and 20-25% of cases in reproductive-age women.[13] Uterine myoma can occur in all races and are most common in blacks (18%).[14]

Management of uterine myomas or benign tumors of the uterine muscle includes observation, medication, and surgery. Observations are made if the patient has no symptoms, and it is hoped that during menopause, the tumor volume will shrink. Medical administration aims to reduce bleeding and tumor volume as a pre-operative procedure. Gonadotropin-releasing hormone (GnRH) agonists are one medication used to treat uterine fibroids. The mechanism of action is based on the downregulation of GnRH receptors, which reduces FSH and LH production and estrogen production. GnRH analogs can also be used preoperatively for the thirty-four months before surgery.[15] Types of surgery include hysterectomy and myomectomy. The surgery choice is adjusted to the patient's condition and wishes.[16]

Hysterectomy is recommended for uterine myoma patients over 40 years old and does not plan to have any more children. Myomectomy is recommended for patients who desire fertility-sparing.[15] According to The Society of Obstetricians and Gynecologists of Canada (SOGC), myomectomy surgery is a choice for women who still want to maintain reproductive function but has the potential for further intervention. Myomectomy surgery should be planned based on the location, size, and quantity of fibroids, as determined by adequate imaging.[17]

UTERINE MYOMA DURING PREGNANCY

Uterine fibroids during pregnancy are expected to become more common in the future years. The frequency of uterine myomas in pregnancy ranges from 0.1% to 12.5% and varies by ethnic group. Most women with uterine fibroids have no symptoms, but 10-30% have difficulties throughout pregnancy, labor, and the puerperium.[18]

Although steroid hormones are most likely involved in the genesis and proliferation of uterine myomas during

pregnancy, additional hormones and proteins released by the fetal, placental, and maternal compartments during early pregnancy may have a synergistic influence. Myomas can develop quickly during pregnancy because of the stimulation of hormonal and increased blood flow.[18]

Pregnancy loss, intrauterine growth retardation (IUGR), intrauterine fetal death (IUFD), early birth, placental abruption, and postpartum hemorrhage are all related to uterine myoma. Myomas with large sizes (>5 cm) are related to an increased risk of preterm birth and postpartum hemorrhage. The primary debate nowadays is whether or not to undertake myomectomy on big asymptomatic myomas. Although myomectomy does not affect obstetrical or newborn outcomes, eliminating big uterine myomas that induce uterine cavity, distortion can boost pregnancy rates and decrease miscarriage rates. According to research, patients should be educated about the likelihood of increasing negative obstetric outcomes and should be monitored often during pregnancy.[18,19]

MYOMECTOMY CESAREAN SECTION

Myomectomy cesarean section is a procedure for removing uterine myomas when a cesarean section is performed. Although the number of myomectomy procedures performed during cesarean sections is growing, there is still widespread worry about the potential morbidity and death associated with uncontrolled bleeding.[16]

Myomectomy is best performed during the first and second trimesters of pregnancy. Myomectomy in pregnancy increases the incidence of cesarean section. Myomectomy cesarean section can be performed safely and cost-effectively because it avoids the possibility of repeat laparotomy for fibroid removal in the future. Myomectomy cesarean section may be performed if fibroids are found that make it difficult to suture the uterine incision. A myomectomy is required to ease delivery when fibroids are more than six centimeters in diameter or subserosal fibroids are visible. If an enlarged myoma is found, a myoma with a size >5 cm in the area around the lower uterine segment, or torsion of a pedunculated myoma occurs, an antenatal myomectomy may be necessary.[20]

The indication for myomectomy cesarean section, according to SOGC, is if there are complications related to the myoma in a previous pregnancy. The incision in the uterus required for cesarean section myomectomy is commonly more minor than that required for interval myomectomy because the uterus raises more rapidly than myomas in pregnancy. Due to puerperal contraction and involution, the uterus is more equipped to regulate bleeding after delivery. In addition, suture placement is easier in the gravid uterus because it increases elasticity and reduces fragility. Uterine muscle fibers become hypertrophic in the gravid uterus and contract more forcefully against the blood vasculatures. The administration of uterotonics in the case of myomectomy cesarean section can further enhance these contractions. The potential long-term benefits of cesarean section myomectomy are symptom and quality-of-life enhancement, removal of the risks and costs of repeat surgery and anesthesia. Furthermore, myomectomy cesarean section procedures prevent patients from complications due to myoma during puerperium and future pregnancies.[7,17]

According to previous research, myomectomy during cesarean section is a safe and practical surgery in nearly all situations. This procedure was reported to be successful in all cases in this study. There were no statistically significant differences between the groups in preoperative hemoglobin, postoperative hemoglobin, mean hemoglobin, or length of hospital stay. Both myomectomy groups had significantly longer operation times. Only two (15.38%) patients in the group with myomectomy greater than 5 cm required a blood transfusion. Cesarean myomectomy surgery, when performed by qualified surgeons, has no harmful effects other than increasing the duration of the procedure and can be conducted safely.[21]

Ramya et al. reported cesarean myomectomy to be a safe and practical technique in expert hands. It has the advantage of avoiding a second surgery in certain people. The majority of patients were discharged on the fifth day of surgery. There were no cases of postpartum pyrexia or surgical site infections.[11] The cesarean myomectomy procedure is also reported to be safe and effective under an expert physician and in the tertiary healthcare centers of the selected patients. The myomectomy procedure only added fifteen minutes to the surgery time and one day to the length of hospital stay, but there was no significant postoperative morbidity. Cesarean myomectomy was also proven to be a safe and successful surgery in patients with big myomas, with the researchers concluding that the size of the myoma had no more impact on the higher risks of complications.[22]

Another study showed that myomectomy cesarean section did not increase complications or transfusion rates, indicating safe management. Between the patients who underwent cesarean section with myomectomy and without myomectomy, the reduction in hemoglobin level, rate of complications, and several transfusions

were similar. The duration of the procedure, however, was greater in the group that had a cesarean myomectomy.[23] Other studies also reported a similar result that myomectomy during cesarean section is safe and does not enhance peripartum maternal morbidities. It has been discovered that although it may lengthen the operational time and postoperative hospital stay period, it may have several benefits, such as the avoidance of further operation for fibroid removal. There is no substantial variance between the myomectomy group and the control in the amount of blood transfusion and postoperative hemoglobin level in this study.[24]

In the systematic review and meta-analysis studies in 2020, it was stated that a total of 6545 women who underwent cesarean section myomectomy and classified into 4702 (71.85%) women in the myomectomy cesarean section group and 1843 (28.15%) women in the cesarean section group. This study found that myomectomy cesarean section was insignificant in increasing operating time, bleeding volume, and hospitalization, specifically with large and multiple myomas. Myomectomy cesarean section can be an option compared to cesarean section without myomectomy, especially if it is performed by experienced surgeons with proper hemostatic techniques and performed in tertiary-level health facilities.[25]

Cesarean myomectomy has several benefits, such as a smaller incision on the serosal surface, ease of performance during cesarean delivery, simple suture insertion, and two surgeries in one. In addition, cesarean myomectomy improved the patient's quality of life. However, they found that cesarean myomectomy's benefit and risk ratio should be reconsidered, and more study is required.[26] There are also absolute contraindications for myomectomy cesarean section procedures. Those are multiple myomas, cornual myomas, posterior myomas, asymptomatic myomas and other conditions that can cause bleeding in the future.[20] In the future, it is necessary to conduct a larger study of the safety and benefits of this procedure. In addition, it is also necessary to standardize the implementation of this procedure.

CONCLUSION

From the studies reviewed, myomectomy during cesarean delivery is considered a safe and recommended management. This procedure benefits the patient because it avoids second operation and anesthesia complications and is cost-saving. However, myomectomy cesarean section should be avoided in some cases, and the successful outcome depends on the patient selection, pre-operative planning, and postoperative care. In the future, it is necessary to standardize the implementation of myomectomy during the cesarean section procedure, including the appropriate selection criteria, surgical techniques, and hemostatic options to enhance the procedure's overall result.

DISCLOSURES

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Conflict of interest

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Author contribution

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REFERENCES

1. Sparic R, Mirkovic L, Malvasi A, et al. Epidemiology of uterine myomas: A review. Int J Fertil Steril. 2016;9(4):424-35. doi: 10.22074/ijfs.2015.4599. Epub 2015 Dec 23. PMID: 26985330; PMCID: PMC4793163.
2. Sparic R, Terzic M, Malvasi A, Tinelli A. Uterine fibroids - clinical presentation and complications. Acta Chir Iugosl. 2014;61(3):41–8. doi: 10.2298/ACI1403041S.
3. Giuliani E, As-Sanie S, Marsh EE. Epidemiology and management of uterine fibroids. Int J Gynaecol Obstet. 2020;149(1):3-9. doi: 10.1002/ijgo.13102. Epub 2020 Feb 17. PMID: 31960950.
4. Sparic R, Nejkovic L, Mutavdzic D, et al. Conservative surgical treatment of uterine fibroids. Acta Chir Iugosl. 2014;61(4):11–6. doi: 10.2298/ACI1404011S.
5. Sparić R. [Uterine myomas in pregnancy, childbirth and puerperium]. Srp Arh Celok Lek. 2014;142(1-2):118-24. Serbian. doi: 10.2298/sarh1402118s. PMID: 24684044.
6. Malvasi A, Stark M, Tinelli A. Cesarean myomectomy. In: Uterine myoma, myomectomy

and minimally invasive treatments. 1st ed. Berlin: Springer; 2015. p. 237–52.
7. Sakinci M, Turan G, Sanhal CY, et al. Analysis of myomectomy during cesarean section: A tertiary center experience. J Invest Surg. 2022;35(1):23-9. doi: 10.1080/08941939.2020.1810832. Epub 2020 Aug 30. PMID: 32865048.
8. Kumar RR, Patil M, Sa S. The utility of caesarean myomectomy as a safe procedure: a retrospective analysis of 21 cases with review of literature. J Clin Diagn Res. 2014;8(9):OC05-8. doi: 10.7860/JCDR/2014/8630.4795. Epub 2014 Sep 20. PMID: 25386485; PMCID: PMC4225937.
9. Sparić R, Malvasi A, Tinelli A. Analysis of clinical, biological and obstetric factors influencing the decision to perform cesarean myomectomy. Ginekol Pol. 2015;86(1):40-5. doi: 10.17772/gp/1897. PMID: 25775874.
10. Kwon DH, Song JE, Yoon KR, et al. The safety of cesarean myomectomy in women with large myomas. Obstet Gynecol Sci. 2014;57(5):367-72. doi: 10.5468/ogs.2014.57.5.367. Epub 2014 Sep 17. PMID: 25264526; PMCID: PMC4175596.
11. Ramya T, Sabnis SS, Chitra TV, et al. Cesarean myomectomy: An experience from a tertiary care teaching hospital. J Obstet Gynaecol India. 2019; 69(5):426-30. doi: 10.1007/s13224-019-01239-x. Epub 2019 Jun 3. PMID: 31598045; PMCID: PMC6765039.
12. Sparic R, Stamenkovic J, Nejkovic L, et al. When it is oportune to avoid cesarean myomectomy? An analysis of possible factors influencing duration of treatment in the intensive care unit. Acta Chir Iugosl. 2015;62(2):71–6. doi: 10.2298/ACI1502071S.
13. Spariç R. Intraoperative hemorrhage as a complication of cesarean myomectomy: Analysis of risk factors. Vojnosanit Pregl. 2016;73(5):415-21. doi: 10.2298/vsp141105029s. PMID: 27430104.
14. Pattanaik T, Pati B, Samal S. Caesarean myomectomy: a descriptive study of clinical outcome. Int J Reprod Contraception, Obstet Gynecol. 2014;3(1): 172–4. doi: 10.5455/2320-1770.ijrcog20140334
15. Şükür YE, Kankaya D, Ateş C, et al. Clinical and histopathologic predictors of reoperation due to recurrence of leiomyoma after laparotomic myomectomy. Int J Gynaecol Obstet. 2015;129(1):75-8. doi: 10.1016/j.ijgo.2014.10.023. Epub 2014 Dec 17. PMID: 25541504.
16. Huang Y, Ming X, Li Z. Feasibility and safety of performing cesarean myomectomy: a systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2022;35(13):2619-27. doi: 10.1080/14767058.2020.1791816. Epub 2020 Jul 16. PMID: 32674632.
17. Society of Obstetricians and Gynaecologists of Canada. The Society of Obstetricians and Gynaecologists of Canada. 2022.
18. Milazzo GN, Catalano A, Badia V, et al. Myoma and myomectomy: Poor evidence concern in pregnancy. J Obstet Gynaecol Res. 2017;43(12): 1789-1804. doi: 10.1111/jog.13437. Epub 2017 Sep 11. PMID: 28892210.
19. Sarais V, Cermisoni GC, Schimberni M, et al. Human chorionic gonadotrophin as a possible mediator of leiomyoma growth during pregnancy: Molecular mechanisms. Int J Mol Sci. 2017; 18(9):2014. doi: 10.3390/ijms18092014. PMID: 28930160; PMCID: PMC5618662.
20. Tokgöz C, Hatirnaz Ş, Güler O. Pros and cons of myomectomy during cesarean section [Internet]. Caesarean Section. InTech; 2018. Available from: http://dx.doi.org/10.5772/intechopen.75365.
21. Guler AE, Guler ZÇD, Kinci MF, Mungan MT. Myomectomy During Cesarean Section: Why Do We Abstain From? J Obstet Gynecol India [Internet]. 2020;70(2):133–7. Available from: https://doi.org/10.1007/s13224-019-01303-6.
22. Eyong E, Okon OA. Large uterine fibroids in pregnancy with successful caesarean myomectomy. Case Rep Obstet Gynecol. 2020;2020:8880296. doi: 10.1155/2020/8880296. PMID: 33224543; PMCID: PMC7671803.
23. Senturk MB, Polat M, Doğan O, et al. Outcome of cesarean myomectomy: Is it a safe procedure? Geburtshilfe Frauenheilkd. 2017;77(11):1200-6. doi: 10.1055/s-0043-120918. Epub 2017 Nov 27. PMID: 29200476; PMCID: PMC5703655.
24. El-Refaie W, Hassan M, Abdelhafez MS. Myomectomy during cesarean section: A retrospective cohort study. J Gynecol Obstet Hum Reprod. 2020:101900. doi: 10.1016/j.jogoh.2020.101900. Epub ahead of print. PMID: 32860969.
25. Goyal M, Dawood AS, Elbohoty SB, et al. Cesarean myomectomy in the last ten years; A true shift from contraindication to indication: A systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2021;256:145-57. doi: 10.1016/j.ejogrb.2020.11.008. Epub 2020 Nov 11. PMID: 33232889.
26. Sparić R, Kadija S, Stefanović A, et al. Cesarean myomectomy in modern obstetrics: More light and fewer shadows. J Obstet Gynaecol Res. 2017;43(5): 798-804. doi: 10.1111/jog.13294. Epub 2017 Feb 7. PMID: 28168805.

REVIEW ARTICLE:

Kartu Skor Poedji Rochyati in the Indonesian Maternal Referral System

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ABSTRACT

Maternal Mortality Rate (MMR) represents fatalities during pregnancy, childbirth, and the postpartum period due to complications, not external factors. Timely detection is crucial for preventing maternal deaths, necessitating integrated planning. The "*Kartu Skor Poedji Rochjati*" (KSPR) emerges as a vital tool for identifying high-risk pregnancies, facilitating urgent referrals to mitigate complications and enhance healthcare. A literature review on maternal mortality, risk assessment tools, and KSPR effectiveness was conducted to address the issues. The findings are expected to highlight KSPR's pivotal role in identifying at-risk pregnant women, enabling prompt referrals, and reducing maternal mortality rates. The case studies and data analysis will enrich our understanding of the tool's impact on maternal healthcare. The apex of public health involves embracing health-conscious lifestyles, reflected in indicators like mortality and morbidity. Proactively identifying high-risk pregnancies using KSPR is a strategic step in averting maternal mortality. Leveraging KSPR allows early intervention, reducing complications and contributing to enhanced maternal health, aligning with the goal of minimizing mortality risks.

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Highlights:

1. This review focuses on maximizing the effectiveness of "*Kartu Skor Poedji Rochyati*" (KSPR) in Indonesia's maternal referral system.
2. It addresses the lack of information about Indonesia's maternal referral system, offering valuable insights.
3. Underlining the high rates of maternal and fetal deaths due to referral errors, the article stresses the urgency of understanding KSPR's function for high-risk pregnant women.

INTRODUCTION

The Maternal Mortality Rate (MMR) refers to the tally of maternal fatalities transpiring during pregnancy, childbirth, and the postpartum phase due to complications arising from these processes or their management, excluding factors like accidents or falls. This figure is typically measured per 100,000 births.[1] Maternal mortality persists as a significant global public health challenge, particularly in regions with limited resources, encompassing approximately 85% of all maternal fatalities. Nevertheless, according to various sources, an

estimated 40% to 50% of these maternal deaths are deemed avoidable through appropriate interventions and healthcare measures.[2,3] As per the World Health Organization (WHO), maternal mortality encompasses the concept of maternal death, indicating a demise transpiring during pregnancy or within 42 days following the conclusion of pregnancy, but not resulting from accidental causes. In Indonesia, the central focus continues to revolve around maternal and child health concerns, constituting a primary agenda aimed at ameliorating healthcare service standards and curbing the prevalence of maternal and child mortality. Despite these efforts, maternal and child mortality rates within Indonesia persist at elevated levels in comparison to fellow ASEAN member nations.[4,5]

Preventing maternal mortality hinges on effective detection and proactive planning, facilitating a comprehensive approach to safeguarding maternal well-being. The integration of these strategies is pivotal in preserving the lives of expectant mothers. To identify high-risk pregnant women, the utilization of tools like the *Kartu Skor Poedji Rochyati* (KSPR) emerges as a valuable resource. This tool assists in pinpointing potential risks, enabling healthcare professionals to take timely and informed actions, thereby contributing to the prevention of maternal deaths.[6,7] the KSPR serves as a versatile tool utilized for the early identification of risk factors during pregnancy that have the potential to negatively impact both expectant mothers and the developing fetus. Its application is broad, encompassing the goal of promptly recognizing these risk factors to enable timely interventions and ensure the well-being of pregnant women and their unborn children. Delivery referral is needed to avoid risks that can occur to the mother or baby. Referrals to higher health facilities are carried out because of obstetric complications such as bleeding, obstructed labor, hypertension or factors that can cause a risky delivery.[8] Referrals are urgently needed so that complications related to pregnancy can be reduced and better health care can be obtained.[7]

Delays from referrals and transportation difficulties are the main barriers to getting quick access to health services. One of the factors that influence delays in obstetric care is when making referrals.[9] The referral factor for the high maternal mortality rate is a cause of health problems in Indonesia. Safe and well-prepared referrals can reduce the maternal mortality rate from 1.89% per 1000 live births to 1.09%. Based on research conducted in South India, 90% of 104 maternal deaths were admitted with an emergency and 59% of them were due to late referral decisions.[8] So referrals can affect the maternal mortality rate.

This article review aims to assess the role of KSPR in the maternal referral system in Indonesia and its impact on maternal morbidity and mortality rates.

The aim of this study

This study has been undertaken with the goal of tackling the identified issues in the article review. The focus is on a set of inquiries concerning maternal referrals in Indonesia and their repercussions on maternal morbidity and mortality rates. Firstly, the study delves into the definition of a high-risk pregnancy. Subsequently, it explores the connection between the *Kartu Skor Poedji Rochyati* (KSPR) and high-risk pregnancies. Additionally, the research investigates whether KSPR plays a role in influencing the number of maternal mortalities and morbidities in Indonesia. Lastly, the study examines whether there exists a significant correlation between KSPR and the overall efficiency of maternal referrals in the Indonesian context.

HIGH RISK PREGNANCY

The reproductive age range for women spans from 20 to 35 years, and within this timeframe lies the safest period for conceiving and giving birth. This age bracket is associated with a reduced risk of pregnancy complications. However, individuals below the age of 20 and those exceeding 35 years are considered to be at higher risk for encountering complications during pregnancy. For those under 20 years old, the uterus might not have attained its full size necessary for a healthy pregnancy, thereby elevating the likelihood of disorders like preeclampsia. On the other hand, individuals over 35 years old experience a degenerative process causing structural and functional alterations in peripheral blood vessels. These changes render them more susceptible to fluctuations in blood pressure, thus increasing the vulnerability to conditions like preeclampsia during pregnancy.[6,9,10]

A high-risk pregnancy refers to a situation during pregnancy wherein there exists either an existing or potential risk to the health and well-being of either the mother or the fetus. Such pregnancies involve circumstances where the life and health of either the mother or the baby could potentially be compromised.[11] Indeed, any unexpected or pregnancy-related medical or obstetric condition that possesses the capacity to jeopardize the health or overall well-being of either the mother or the fetus qualifies as a high-risk pregnancy. These conditions warrant increased medical attention and monitoring to ensure the best possible outcome for both the mother and the baby.[12,13]

Very high-risk pregnancies are the risk group for pregnant women with the highest number of maternal deaths followed by high risk pregnancies and low risk pregnancies. This condition is normal, because death is a condition that is always preceded by a very severe disease with very high-risk factors. However, if deaths are still found in pregnant women with low risk, then this proves that there is no riskless pregnancy. In accordance with the scoring system at KSPR, that a total score of 2 is the minimum score for each pregnancy.[6]

Women with high-risk pregnancies are confronted with a heightened likelihood of encountering complications, with a one in four chance, in contrast to women with low-risk pregnancies whose chance of experiencing complications stands at nearly one in ten. Various risk factors during pregnancy contribute to this disparity. These factors encompass the mother's height being below 145 cm, her age being either below 20 years or exceeding 35 years, having given birth to more than four children, maintaining a gap of less than two years between pregnancies, possessing a history of problematic deliveries, grappling with concurrent pregnancy-related ailments (like anemia, hypertension, or heart conditions), and undergoing symptoms such as bleeding, severe headaches, and limb swelling. Additionally, anomalies within the fetus (such as a larger size, malposition, or malpresentation) and aberrations in the mother's pelvic structure can also contribute to the classification of a pregnancy as high-risk. These multifaceted risk factors necessitate attentive medical care and monitoring to ensure the safety and well-being of both the mother and the baby.[6]

Based on when they were found, how they were recognized, and the characteristic of the risk, risk factors are grouped into 3 groups:[14] 1. Risk Factor Group I: There is potential for Obstetric Emergency with 7 Too and 3 Ever. Seven too were young primi, old primi, secondary old primi, age >35 years, grand multi, youngest child aged <2 years, low height <145 cm) and 3 had bad obstetric history, gave birth and experienced postpartum hemorrhage with infusion, transfusion, placental manual, vaginal surgery, former cesarean section. 2. Risk Factor Group II: There is an Obstetric Emergency, women with mild preeclampsia, twin pregnancies, hydramnios, serotinous pregnancies, IUFD, breech position, and transverse position. 3. Risk Factor Group III: Present-Emergency-Obstetrics: antepartum hemorrhage and preeclampsia severe eclampsia. AGDO mothers in conditions that can directly threaten the life of the mother/fetus, must be immediately referred on time (RTW) to the hospital to save the mother/newborn.

KARTU SKOR POEDJI ROCHYATI (KSPR)

In modern obstetrics, a fundamental recognition exists regarding the presence of potential risks inherent to both pregnancy and childbirth. This acknowledgment encompasses the understanding that these processes inherently carry a level of risk, introducing the potential for hazards or complications to arise. The range of possible complications spans from mild to severe, encompassing outcomes that can encompass mortality, morbidity, and even disabilities for either the mother or the infant. The extent and severity of these complications are intricately tied to various levels of risk factors. Essentially, the greater the number of risk factors a pregnant woman possesses, the higher the likelihood that she might encounter complications. This relationship underscores the significance of considering an individual's unique risk profile, with the understanding that tailored medical interventions and vigilance are crucial to mitigating potential complications and ensuring the health and safety of both the mother and the baby.[7] The primary emphasis of maternal and child care programs centers on identifying pregnancies that are at a higher risk of complications, aiming to avert obstetric challenges during childbirth. Within this framework, risk assessment plays a pivotal role in the realm of antenatal care (ANC) and has demonstrated its value in enhancing outcomes for both mothers and infants. By meticulously assessing the potential risks associated with a pregnancy, healthcare professionals can proactively address and manage those factors that might otherwise lead to complications during childbirth. This strategic approach not only contributes to the well-being of expectant mothers but also leads to improved perinatal outcomes, ultimately creating a positive impact on the health of both mothers and babies.[2]

In Indonesia, various risk factor approaches have been developed to address and mitigate the risk of maternal mortality. Among these approaches, the concepts of "Four Too" and "Three Delays" have been recognized for a considerable period. Additionally, the Poedji Rochjati Score Card (KSPR) is widely utilized to identify early risk factors during pregnancy that have the potential to negatively impact both pregnant women and their developing fetuses. The "Four Too" concept refers to identifying four specific factors that contribute to maternal deaths: Too late to seek care, Too far to reach care, Too little care, and Too late to receive adequate care. These factors emphasize the significance of timely and accessible healthcare in preventing maternal mortality. The "Three Delays" concept involves recognizing three types of delays that can lead to adverse maternal outcomes: Delay in decision-making to seek care, delay in reaching appropriate

medical facilities, and delay in receiving adequate and appropriate care once at the facility. This approach underscores the importance of swift decision-making, accessibility, and effective care provision in averting maternal deaths.[8]

The KSPR, or Poedji Rochjati Score Card, is utilized for early detection of risk factors in pregnancy. It aids in identifying potential complications that could impact both pregnant women and their fetuses. This tool helps healthcare professionals take timely interventions and actions to ensure the health and safety of both mother and baby. Within the KSPR framework, the concept of "Factor Four" is included, further emphasizing the importance of addressing risks and complications early in pregnancy.[8] The purpose of screening with KSPR is to classify pregnant women with Low Risk Pregnancy (LRP), High Risk Pregnancy (HRP), Very High Risk Pregnancy (VHRP), so that the behavior of the need for a place and delivery assistance is developed according to the conditions of the pregnant woman and empowering the mother. pregnant women, husbands, families, and communities to care and provide support and assistance with mental readiness, costs, and transportation to carry out planned referrals.[6]

KSPR has 6 functions as follows:[15] 1. Antenatal screening/early detection of risk factors in high-risk pregnant women. 2. Monitoring and control of pregnant women during pregnancy. 3. Recording and reporting of the condition of the mother during pregnancy, child-birth, postpartum, regarding mothers and newborns. 4. Guidelines for giving counseling and education. 5. Data validation of pregnancy, postpartum and family planning. 6. MPA (Maternal Perinatal Audit). The higher the score of pregnant women can increase the risk of the mother during pregnancy and childbirth can even be at risk to the baby. Assistance during pregnancy and comprehensive treatment is needed so that maternal risk factors can be minimized and handled properly.[7]

EFFECTIVENESS OF KSPR FOR DETECTION OF HIGH RISK IN PREGNANT WOMEN

The application of the Poedji Rochjati Score Card (KSPR) serves a dual purpose: detecting pregnancy and categorizing pregnancies as high-risk or low-risk. This facilitates the early formulation of comprehensive midwifery care plans. Within the KSPR framework, pregnant women with a score of 2, indicating a low-risk pregnancy, generally experience minimal complications throughout pregnancy and childbirth. However, instances have arisen where women consistently scored 2 throughout their pregnancy yet encountered complications during delivery. This highlights a vital consideration: the need for comprehensive care planning extends beyond just high or very high-risk pregnancies. Even women initially deemed low risk can face unexpected complications during both pregnancy and childbirth, necessitating diligent care and attention to ensure optimal outcomes.[7,16]

INDONESIAN MATERNAL REFERRAL SYSTEM

The significant maternal mortality rate in Indonesia underscores the inadequacies in health services, particularly concerning maternal health. As a pivotal step toward mitigating this issue, the establishment of an efficient referral system becomes imperative, particularly for cases involving complications. An integral facet of robust primary healthcare lies in maintaining a seamless connection with higher levels of care. This connection is manifested as an effective referral system, facilitating swift and coordinated response to maternal health challenges and ultimately contributing to the reduction of maternal mortality.[4,17,18]

The Ministry of Health of the Republic of Indonesia through the Director of Maternal Health Development has established a National Action Plan to Accelerate the Reduction of Maternal Mortality Rate for 2013–2015, in which the fourth main program is the implementation of effective referrals for cases of maternal complications. This is based on the fact that one of the main obstacles to the slow decline in MMR in Indonesia is barriers to providing and accessing emergency obstetric services. The ability to handle complicated cases at this time still relies on advanced health care facilities in hospitals, while the handling of complicated cases at the health center level has not gone well. Therefore, it is necessary to have a level division of tasks among various health service units through a referral system arrangement.[17]

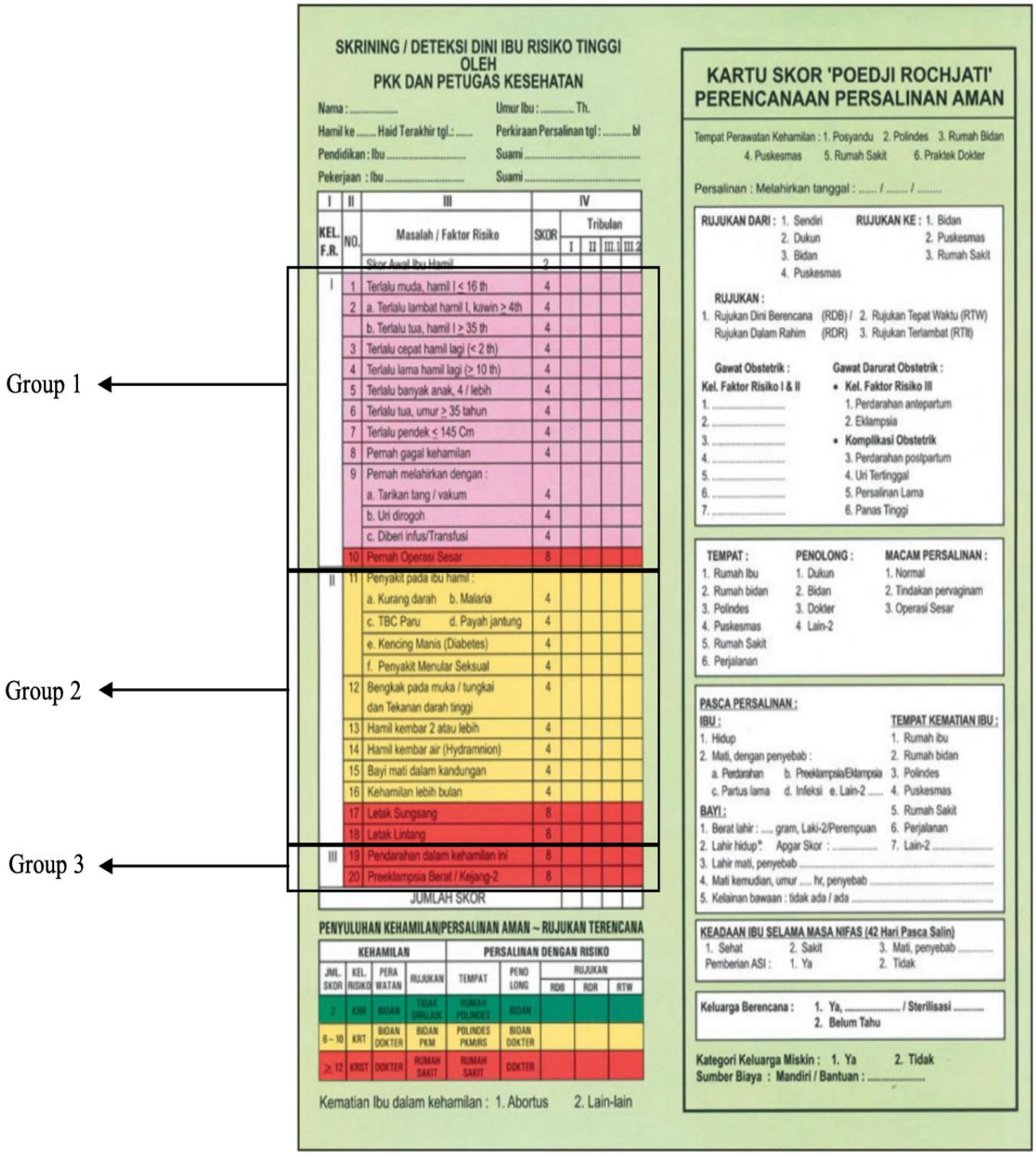

Figure 1. *Kartu Skor Poedji Rochyati* (KSPR)[15]

KSPR is divided into 3 groups: Group 1 (1-10): there is a potential obstetric emergency, with 7 being too much and 3 having occurred previously; Group 2 (11-18): there is an obstetric emergency; Group 3: there is an obstetric emergency.

In 2014, the Decree of the Minister of Health of the Republic of Indonesia No.HK.02.02/MENKES/390/ 2014 regarding Guidelines for Designating National Referral Hospitals. This guideline discusses the existence of national referral hospitals, provincial referrals, and regional referrals. The strategy for implementing referral hospitals in 2017 is by mapping national, provincial, and regional referral hospitals by strengthening the telematics system. In 2019 it appears that the development of the referral system still needs strengthening. Various obstacles occurred including the unclear relationship with BPJS Health in terms of setting up the referral system, the occurrence of differences of opinion on tiered referrals or competency-based referrals, as well as attention to the development of a referral system in areas where there is still a lack of strength. Regarding the current Referral System, in 2020 the Indonesian Ministry of Health issued Permenkes No. 3/2020 which regulates Hospital Classification and Licensing. The existence of Permenkes/PMK 3/2020 certainly affects the referral system. Conceptually, PMK No. 3/2020 strengthens the mapping of competency-based referral ladders. Competency-based tiered referral systems are determined based on the medical needs of a disease and the competence of health service facilities (hospitals), not hospital grade levels. This system requires the ability of the Provincial Health Office to prepare competency maps and a referral system to be built. Each province will have a different map.[18,19]

Referral is the transfer of responsibility from one health service to another. The referral system is a network of health services that allows for reciprocal delegation of responsibility for the emergence of problems from a case or public health problems both vertically and horizontally to those who are more competent, affordable, and carried out rationally. Referral system for quality health services, so that service objectives are achieved without having to use high costs. Referral is a system where coordination is the main element that is multi-sectoral and there must be support from various professions that are multi-disciplinary and multi-professional to carry out and organize a form of integrated service for emergency patients both in daily situations and in disasters and incidents. Extraordinary. Effective referrals require communication between facilities, the goal is that the referred facility knows the patient's condition and can prepare early the treatment needed by the patient as soon as the patient arrives at the hospital.[18,20]

The aim of referral is to produce equal distribution of health efforts in the context of solving health problems in an efficient and effective manner. The aim of the referral system is to improve the quality, coverage, and efficiency of health services in an integrated manner. Strengthening the referral system is one of the ways to accelerate the reduction of the Maternal Mortality Rate (MMR) as well as problems and challenges facing the health center in supporting the maternal referral system to the Regional General Hospital can be overcome. The referral must obtain the consent of the patient and/or family, as well as the authorized health worker must provide an explanation to the patient regarding the diagnosis and therapy or medical action required by the patient, the reason and purpose for the referral, the risks that may arise if the referral is not made, referral transportation, and the risks or complications that may arise during referral mobilitation.[18]

A safety referral system is a network system for health care facilities that allows for reciprocal delegation of responsibility for problems that arise both vertically (communication between equal units) and horizontally (higher core communication to lower units) to service facilities. more competent, rationally affordable, and not limited by administrative area. The referral system according to the 2009 Indonesian Ministry of Health National Health System is a health service delivery system that carries out reciprocal delegation of responsibility for one/more cases of disease or health problems vertically from units with less ability to units that are more capable or horizontally between units that are level of ability in the field of maternal and perinatal health.[18]

As outlined in Article 7 of the Minister of Health Regulation No. 001 of 2012 regarding the Referral System for Individual Health Services, the referral process can occur both vertically and horizontally. Vertical referrals encompass transfers between varying levels of healthcare services, primarily undertaken when a patient necessitates specialized or sub-specialized medical attention. These referrals also occur if the referring facility lacks the resources, equipment, or personnel required to cater to the patient's needs adequately. On the other hand, horizontal referrals pertain to transfers between healthcare services at the same level. Such referrals are made when the referring facility confronts limitations, be they temporary or permanent, in terms of facilities, equipment, or staff, and therefore cannot fulfill the patient's healthcare requirements effectively.[17]

The referral system is divided into:[14] 1. Planned referrals, which are referrals to the hospital from the start of pregnancy for women with high-risk pregnancies. Referral types are categorized into 2: a) Intrauterine early referral planning: Mothers at high risk who have not experienced maternal complications and have not yet been in partum. Mother was escorted by

the family independently to the hospital; b) Intrauterine referrals: Fetuses with special conditions or problems with healthy fetuses, or high-risk fetuses, such as fetuses with mothers with poor obstetric history. 2. Timely referral, is a referral to the hospital when obstetric problems occur for women with risk factor III or mothers with early complications.

RELATIONSHIP BETWEEN KSPR AND REFERRAL SYSTEM IN INDONESIA

Timely identification of high-risk pregnancies holds paramount importance in averting delays in intervention and referral processes. Among the factors contributing to elevated maternal and infant mortality, the occurrence of the four delays—namely, late detection of danger signs, delayed decision-making for referral, tardiness in reaching the designated referral facility, and being unable to access assistance promptly at the referral site—stands out. To counter the delay in detecting issues, education is a vital tool for pregnant women and their families, enabling them to recognize signs of potential danger. Addressing delays in decision-making involves transforming decision-making practices. Furthermore, enhancements to the transportation system are pivotal, facilitating swifter and easier access to healthcare centers and eliminating hindrances that could lead to delays in reaching referral points.[6]

Figure 2 shows how the risk factor screening pattern is implemented in referral health facilities. With the existence of a referral system, it is hoped that it can improve health services with a higher quality. One of the weaknesses of health services is the inaccurate and fast referral implementation. Deaths of mothers and babies are caused because services at health facilities are not optimal or there is a delay in referral services for mothers and babies which results in very late arrival of patients at referral service facilities.[18,19]

In Indonesia, the concept of the "3 delays" is widely recognized as a prominent contributor to maternal and infant mortality. These delays encompass delayed decision-making within families, delayed access to healthcare facilities, and delays in receiving adequate assistance at the healthcare facility level. Decision-making delays often arise due to preferences for home births, financial constraints, transportation limitations, and challenges in accessing remote healthcare facilities. Delays in reaching healthcare facilities result from transportation difficulties, the lack of a well-established referral network between village midwives and hospitals, and the absence of a standardized referral protocol. Delays in obtaining appropriate assistance at healthcare facilities are linked to suboptimal quality of obstetric and neonatal care across different facilities, limited recognition of services for social insurance beneficiaries such as BPJS, and unconventional return referrals.[21] An exploration of the underlying factors within these three delays reveals issues within the referral system. Consequently, there arises a critical need to enhance the existing referral system to establish an effective and efficient framework. Such improvements are vital for addressing the challenges posed by the "3 delays" and ultimately improving maternal and infant health outcomes in Indonesia.[18,19]

According to the study conducted by Widarta and colleagues, KSPR remains applicable for the early identification of risk factors in expectant mothers. Effectively addressing the four delayed factors is pivotal in reducing maternal mortality rates. The research revealed that all instances of maternal mortality exhibited elements of risk factors as outlined in KSPR and the four delayed factors. KRST emerged as the most prevalent risk factor group, accounting for 55.2%, followed by KRT at 39.7%, and KRR at 5.2%. Late factors, including delayed detection of warning signs (82.8%), delayed decision-making for referrals (56.9%), and delayed arrival at the referral facility (15.5%), were identified. Notably, the delayed factor of receiving assistance at the final referral facility was not observed in this study.[8]

As per the investigation by Susanti and colleagues, the objective of employing the KSPR for screening is to categorize expectant mothers into groups based on the level of pregnancy risk. This categorization facilitates the development of tailored behaviors related to the choice of delivery location and birth attendants, aligning with the specific conditions of pregnant women. Moreover, the goal is to empower pregnant women, their spouses, families, and the community to exhibit concern and extend support, encompassing assistance in mental preparedness, financial considerations, and transportation for planned referrals.[6]

In another study conducted by Nur Jannah at dr. Soebandi Hospital, Jember, Indonesia, the research results suggest a correlation between the pregnancy risk approach as indicated by KSPR and referral patterns. This correlation strengthens the significance of KSPR in the maternal referral system in Indonesia, consequently contributing to the decline in maternal morbidity and mortality rates in the country.[22]

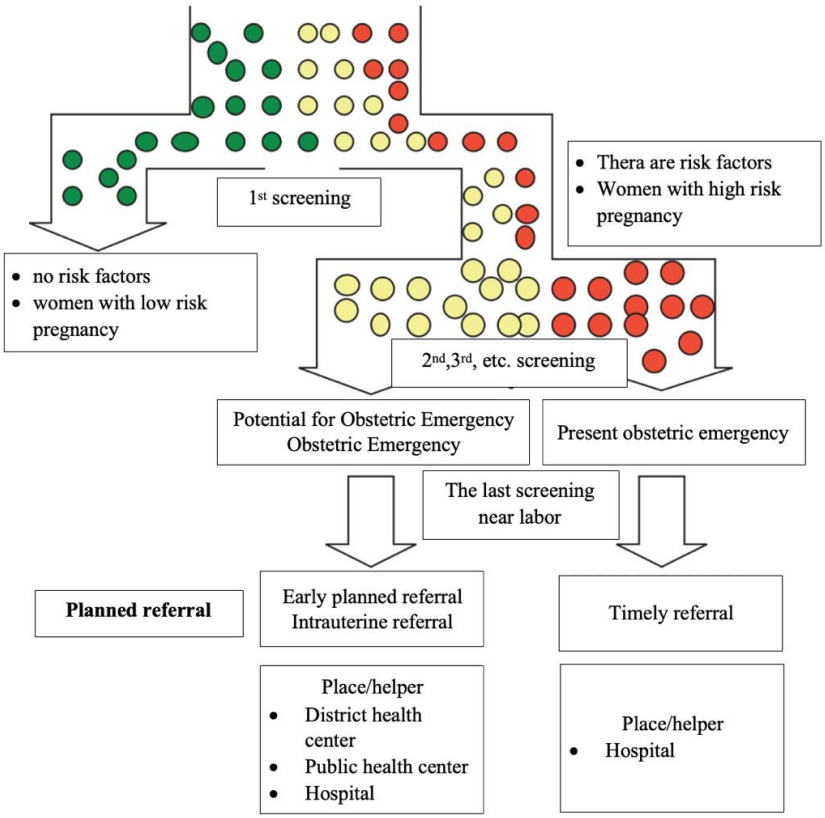

Figure 2. Screening implementation diagram

The primary drawback associated with crafting this review article lies in the less of original research studies centered around KSPR (*Kartu Skor Poedji Rochyati*) as the central research subject. This absence hinders the feasibility of conducting a comprehensive systematic review. However, as research efforts related to the article's title gain momentum, the potential for a more robust systematic review in the future becomes increasingly promising.

CONCLUSION

At the apex of public health achievement lies the trajectory of health development characterized by heightened awareness, willingness, and capacity to embrace a health-conscious lifestyle. The yardsticks defining the status of public health encompass crucial indicators such as mortality, morbidity, and nutritional well-being. A pivotal strategy in the pursuit of averting maternal and infant mortality involves the proactive identification of high-risk pregnancies through the application of the KSPR. Leveraging the KSPR for the early recognition of risk factors among pregnant women stands as a preventive measure aimed at curtailing maternal mortality rates. By harnessing the power of KSPR, the aim is to intervene proactively, minimizing potential complications and thereby contributing to the overarching goal of enhancing maternal health and reducing mortality risks.

DISCLOSURES

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Conflict of interest

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Author contribution

Initiated by the first author, the concept of crafting an article review took shape. The collaborative efforts of

the two authors converged as they jointly scoured for relevant articles, subsequently melding them into a seamless, continuous review.

REFERENCES

1. Usman H, Maeneny A, Kuswanti F. Peningkatan Keterampilan Kader dalam Deteksi Dini Risiko Tinggi Kehamilan (Kaderink) [Improvement of cadre skills in early detection of high risk of pregnancy]. Jurnal Pengabdian Masyarakat. 2022; 3(1):19–26. doi: 10.33860/pjpm.v3i1.405.
2. Rajbanshi S, Norhayati MN, Nik Hazlina NH. High-risk pregnancies and their association with severe maternal morbidity in Nepal: A prospective cohort study. PLoS One. 2020;15(12):e0244072. doi: 10.1371/journal.pone.0244072. PMID: 3337 0361; PMCID: PMC7769286.
3. Prajapati AK, Kumar V, Soni K, et al. Prevalence of high-risk pregnancy among pregnant women enrolled under Pradhan Mantri Surakshit Matritva Abhiyan in government health facilities of district Etawah, Uttar Pradesh: A cross-sectional study. J Family Med Prim Care. 2022;11(5):1876-82. doi: 10.4103/jfmpc.jfmpc_1636_21. Epub 2022 May 14. PMID: 35800511; PMCID: PMC9254766.
4. WHO. Trends in maternal mortality 2000 to 2017. World Health Organization, 2019. Available from: https://apps.who.int/iris/handle/10665/327595.
5. Wagner AL, Xia L, Ghosh A, et al. Using community health workers to refer pregnant women and young children to health care facilities in rural West Bengal, India: A prospective cohort study. PLoS One. 2018;13(6):e0199607. doi: 10.1371/ journal. pone.0199607. PMID: 29928057; PMCID: PMC6013192.
6. Susanti E, Zainiyah Z, Amimastura, et al. Kartu Skor Puji Rochyati (KSPR) dalam upaya screening kehamilan ibu resiko tinggi [Pudji Rochyati Score Card for high-risk pregnancy screening]. Jurnal Paradigma. 2020;2(2):1–9. Available from: https:// stikes-nhm.e-journal.id/PGM/article/view/ 514.
7. Saraswati DE, Hariastuti FP. Efektivitas Kartu Skor Poedji Rochjati (KSPR) untuk deteksi resiko tinggi pada ibu hamil di Puskesmas Ngumpak Dalem Kabupaten Bojonegoro [KSPR effectiveness for detecting high-risk pregnancy in the health center of Ngumpak Dalem, Bojonegoro]. Jurnal Ilmu Kesehatan MAKIA. 2017;5(1):28-33. Available from: https://jurnal.istekicsadabjn.ac.id/index.php/ jmakia/article/view/52.
8. Widarta GD, Laksana MAC, Sulistyono A, et al. Deteksi dini risiko ibu hamil dengan Kartu Skor Poedji Rochjati dan pencegahan faktor Empat Terlambat [Early detection of pregnancy risk using Poedji Rochjati Score Card and preventing the Four Lates factors]. Majalah Obstetri & Ginekologi. 2015;23(1):28–32. doi: 10.20473/ mog.V23I12015. 28-32.
9. Sinaci S, Ozden Tokalioglu E, Ocal D, et al. Does having a high-risk pregnancy influence anxiety level during the COVID-19 pandemic? Eur J Obstet Gynecol Reprod Biol. 2020;255:190-6. doi: 10.1016/j.ejogrb.2020.10.055. Epub 2020 Oct 24. PMID: 33147531; PMCID: PMC7585497.
10. Chate SU, Metgud CS. Pregnancy outcome among high-risk pregnant women in the rural area of Belagavi. J Family Med Prim Care. 2022;11(8) :4440-6. doi: 10.4103/jfmpc.jfmpc_10_22. Epub 2022 Aug 30. PMID: 36353024; PMCID: PMC963 8629.
11. Mochtar R. Sinopsis Obstetri: Obstetri Fisiologi, Obstetri Patologi [Obstetric synopsis: Obstetric physiology. Obstetric pathology]. 3hd edition. Jakarta: EGC; 2012.
12. Holness N. High-Risk Pregnancy. Nurs Clin North Am. 2018;53(2):241-51. doi: 10.1016/j.cnur.2018. 01.010. Epub 2018 Apr 7. PMID: 29779516.
13. Isaacs NZ, Andipatin MG. A systematic review regarding women's emotional and psychological experiences of high-risk pregnancies. BMC Psychol. 2020;8(1):45. doi: 10.1186/s40359-020- 00410-8. PMID: 32362285; PMCID: PMC7197 168.
14. Prawirohardjo S. Ilmu kebidanan [Midwifery science]. Jakarta: PT. Bina Pustaka Sarwono Prawirohardjo; 2016.
15. Rochjati P. Skrining antenatal pada ibu hamil. Pengenalan faktor risiko deteksi dini ibu hamil risiko tinggi [Antenatal screening for pregnancy. Recognizing high-risk pregnancy with risk factors early detection]. 2nd edition.. Surabaya: Pusat Penerbitan dan Percetakan Unair; 2011.
16. Noftalina E, Safitri Y, Feronika L. Pelatihan mengisi Kartu Skor Poedji Rochyati untuk meningkatkan pengetahuan dan sikap kader dalam mendeteksi dini risiko kehamilan [Training to fill Poedji Rochyati Score Card to improve knowledge and attitude in early detection of pregnancy risk. Jurnal Pengabdi. 2021;4(2):177-82. doi: 10.26418/jplp 2km.v4i2.47191.
17. Rukmini, Ristrini. Pelaksanaan sistem rujukan maternal di Puskesmas Tambakrejo dan Tanah Kali Kedinding Kota Surabaya [Implementation of maternal reference system at Tambakrejo and Tanah Kali Kedinding Health Centres in Surabaya City]. Buletin Penelitian Sistem Kesehatan. 2015;18(4):365-75. doi:10.22435/bpsk.v18i4.4570.
18. Susiloningtyas L. Sistem rujukan dalam sistem pelayanan kesehatan maternal perinatal di Indonesia [Refferal system in maternal perinatal

health services in Indonesia]. Jurnal Ilmiah Pamenang. 2020;2(1).6-16. doi: 10.53599/jip.v2i1.57.

19. Tirtaningrum DA, Sriatmi A, Suryoputro A. Analisis response time penatalaksanaan rujukan kegawatdaruratan obstetri ibu hamil [Response time analysis of management obstetric maternal emergency referral]. Jurnal MKMI. 2018;14(2): 139-46. doi: 10.30597/mkmi.v14i2.2866.
20. Ratnasari D. Analisis pelaksanaan sistem rujukan berjenjang bagi peserta JKN di Puskesmas X Kota Surabaya [Analysis of the implementation of tiered referral system for participant of National Health Security at Primary Health Center X of Surabaya]. Jurnal Administrasi Kesehatan Indonesia. 2017;5(2) :145-54. doi: jaki.v5i2.2017.145-154.
21. Lestary H, Sugiharti, Mujiati. Sistem rujukan maternal dan neonatal di daerah kepulauan (Studi kasus di Provinsi Papua dan Maluku) [Maternal and neonatal referral system in Papua and Maluku Province]. Media Litbangkes. 2018;28(2):83–94. doi: 10.22435/mpk.v28i2.177.
22. Nur Jannah A. Pendekatan resiko kehamilan Kartu Skor Poedji Rochjati (KSPR) dengan pola rujukan di RSUD Dr. Soebandi Jember [Approach to pregnancy risk using Poedji Rochjati Score Card with referral patterns at Dr. Soebandi Hospital Jember]. Jurnal Kesehatan Dr. Soebandi. 2014;2(1): 99-105. Available from: https://journal.uds.ac.id/jkds/article/view/24.

CASE REPORT

A case of vaginal varicosities without rupture after vaginal delivery

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ABSTRACT

Objective: Vaginal varicose is a rare condition characterized by dilated veins in the labia majora, labia minora, and vagina. This case report reported a woman with vaginal varicose who experienced labor without any delivery complications.

Case Report: The patient, a 29-year-old woman, gravida 3, para 2, presented with discomfort and swelling in the vagina at 32 weeks of gestational age. Despite reaching 39 weeks of gestation, the vaginal varicosities remained stable and painless. She had no prior history of varicose veins, hypertension, blood abnormalities, malignancy, or contraception usage. Physical examination revealed mild varicosities in the labium and significantly swollen varicosities protruding toward the vaginal introitus. Interestingly, a small varicose vein was also noted on her right leg, previously unnoticed by the patient. At 39 weeks pregnant, she experienced spontaneous vaginal delivery without complications. During the third stage of labor, the vaginal varicosities decreased in size, and no rupture occurred. The newborn, a healthy baby boy weighing 2961 grams and measuring 48 cm, was delivered vaginally. Despite a second-degree perineal tear, blood loss was minimal, and no complications nor rupture arose from the varicose veins.

Conclusion: Vaginal varicosities are rare, primarily occurring in multigravida pregnant women between 12 and 26 weeks of gestation. This case highlights that cesarean section is not necessarily indicated in pregnant women with vaginal varicosities. The successful vaginal delivery in this instance resulted in no varicose vein rupture, controlled bleeding, and regression of vaginal varicosities postpartum.

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Highlights:

1. Vaginal varicosities are prone to happen in pregnant women with unspecific causes and multifactorial.
2. The mode of delivery in a pregnant woman with vaginal varicosities is still unknown, but it is not an indication of cesarean section.

INTRODUCTION

Vulvovaginal varicosities refer to the enlargement of veins in the labia majora, labia minora, and vagina. The prevalence of this condition is believed to be between 18% and 22% among pregnant women. Typically, vulvovaginal varicose veins naturally decrease in size and disappear within 6 weeks after childbirth, with only 4-8% of instances persisting or becoming larger.[1,2] Pregnant women are susceptible to developing vulvo-vaginal varicosities due to the compression of veins by enlarged uterus, resulting in mechanical obstruction in the veins' pathways. Additionally, pregnancy can be attributed to hormonal fluctuations, as well as an augmentation in plasma volume and blood circulation.[2,3]

There is currently no established theory for determining the method of delivery in cases of pregnancy involving vaginal varicosities. This case is usually not indicating delivery through cesarean section. However, in certain instances, there may be a significant hemorrhage when the rupture occurs during vaginal birth. To choose the appropriate method of delivery, it is crucial to understand the root cause of the development of vaginal varicosities during pregnancy.[2,4]

This article presents a case of vaginal varicosities during pregnancy that resulted in a vaginal delivery without significant bleeding. This case report demonstrates that vulval varicosities are not be considered a contra-indication for vaginal delivery.

CASE REPORT

A 29-year-old woman who has been pregnant three times and has given birth twice reported experiencing swelling and discomfort in the vagina during 32 weeks of gestation. The patient exhibited no signs of bleeding or pain and this was her initial encounter with these symptoms. There was no record of varicose veins in her pregnancy. The patient had no prior medical history of hypertension, hematological problems, or cancer, and had never utilized contraception previously. On examination, it was discovered that the patient had a minor varicose vein in her right leg that had gone unnoticed and had not been previously evaluated. Figure 1 shows the presence of mild vaginal varicosities in the labium. Figure 2 shows significantly enlarged varico-sities of the vagina protruding towards the vaginal introitus.

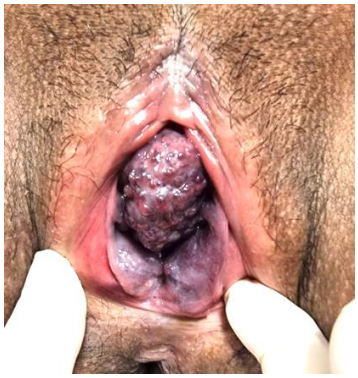

Figure 1. Mild vaginal varicosities.

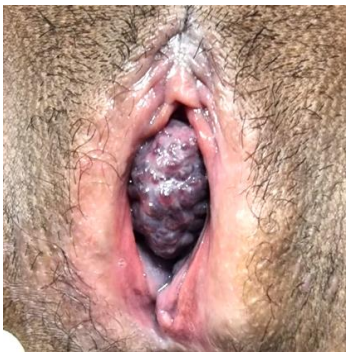

Figure 2. Extensively swollen varicosities of the vagina protrude toward the vaginal introitus.

The hemodynamics of the patient were stable. Throughout the 39 weeks of gestation, the vaginal varicosities were quite stable and did not result in any discomfort. The patient was informed about the condition and the risk of vaginal delivery, specifically the possibility of rupture. However, the patient agreed proceed with the vaginal delivery. The obstetric examination revealed a fundal height of 36 cm, indicating a cephalic presentation. The fetal heart rate was normal, and the contractions occurred every 3 minutes and lasted for 30 seconds. The patient experienced the onset of childbirth at 39 weeks gestation. During the second stage of labor, the vaginal varicosities decreased in size (as shown in Figure 3) and further reduced in the third stage of labor (as seen in Figure 4). A healthy male infant was delivered by spontaneous vaginal delivery, weighing 2961 grams and measuring 48 cm in length. The total blood loss was 250 cc, accompanied by a second-degree perineal tear, and no occurrence of complications or varicose vein rupture.

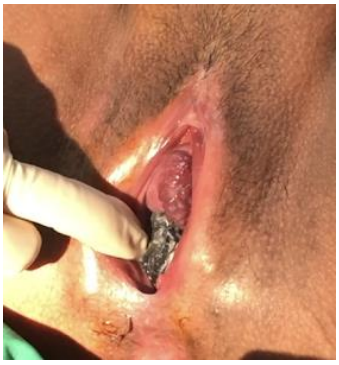

Figure 3. Vaginal varicosities shrank in the second stage of labor.

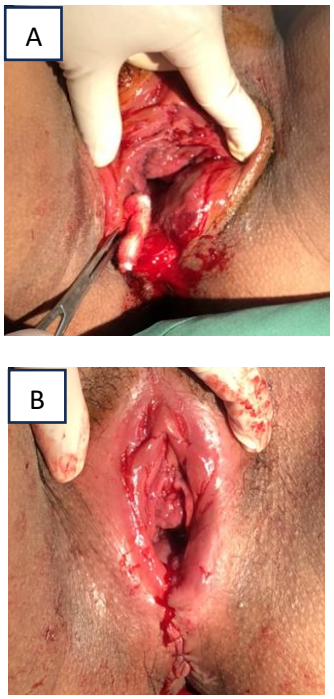

Figure 4. Vaginal varicosities diminished in the third stage of labor (a) before perineal tear repair; (b) after perineal tear repair.

DISCUSSION

Vaginal varicosities, also known as varicose veins of the vulva, refer to the enlargement of veins in the labia majora, labia minora, and vagina. Vaginal varicosities are a rare condition, occurring in only approximately 4% of women. However, they are even less prevalent than other types of varicosities. Vulvovaginal varicose veins are infrequently observed in non-pregnant individuals and typically occur in 18-22% of pregnancies. Vaginal varicosities typically occur during pregnancies that are at least 13 weeks gestation, and are more common in second or subsequent pregnancies. More precisely, throughout the period of 12-26 weeks of gestation, it had a prevalence of approximately 19.5%, which increased to over 32% after 27 weeks.[1,5,6] Studies indicate that the probability of developing vaginal varicosities rises with each pregnancy, and 72% of cases occur in women who have had six or more pregnancies. The prevalence of pelvic congestion syndrome (PCS) in women between the ages of 20 and 45 also shows an increase of 22-40%. When it occurs outside of pregnancy, it is most likely to happen around the second or third decade of life and is typically caused by portal hypertension or Klippel-Trenaunay Syndrome. Vaginal varicosities typically resolve spontaneously shortly after childbirth, or during the sixth week after giving birth.[3,5,7,8]

The etiology of vaginal varicosities is not well understood, although it is thought to arise from both proximal venous obstruction and valvular ineffectiveness. This leads to higher pressure in the veins and causes them to expand. The external pudendal veins serve as the means by which blood is drained from the vulvar area. It flows towards the saphenous opening. The internal pudendal veins serve as the means by which blood is drained from the labia and clitoris. The round ligament serves as an additional route for the drainage of the ovarian vein. The absence of valves in these perineal veins renders them more susceptible to developing varicose veins. Varicose veins can vary in size, typically have numerous connections between blood vessels, and can affect the vulva and the back and inner side of the leg. The etiology of the condition is not well comprehended due to the blood flow in the pelvic region.[9,10]

In pregnancies, there are several physiological changes in the body, especially in the blood vessels. Contraction on the blood vessels happens with the help of angiotensin II (AT II), meanwhile, prostacyclin (PGI-2) which functions to inhibit AT II in pregnancy, increases with gestational age. The pressure in the femoral vein increased from 8 mmHg (first trimester) to 24 mmHg in the term pregnancy. However, the antecubital vein pressure does not change and is suspected caused by inferior vena cava compression by the fetus. The combination of the decreasing blood flow in the pelvic vein, occlusion on the inferior vena cava by the enlarged uterus, the resistance of AT II, and increased vein pressure caused by fetal growth lead to the occurrence of varicosities. The varicose will enlarge as the gestational age increase and can expand from the vulvar to the vaginal.[3,11]

In most of the cases following the vaginal varicosities, diagnosis can be made through history taking and physical examination, especially in the external genitalia. Vaginal varicosities can be asymptomatic, but the common symptoms are swelling in the major and/or minor labia, vulvodynia, pain in the labium, swelling in the perineal area, discomfort in the hypogastric region, dyspareunia, dysuria, dysmenorrhea, and itch in the genital area. In the physical examination, we can also see the bluish or purplish color of the vein underneath the skin that bulges and may look swollen, twisted, or bunched into a cluster. These dilated veins may not only be seen in the vulvovaginal area but also in the upper thighs, buttocks, or calves. It is sometimes called a bag of worms. Inspection needed to be done while standing to see when the veins are not compressed and sitting to see when the veins are compressed. There are several modalities that can help diagnose vulvar varicosities, such as Doppler ultrasonography, CT scan, MRA, venography, and diagnostic laparoscopy. These modalities can also be used to determine the mode of surgery in vaginal varicosities.[3,9,12,13]

The management of this condition varies between pregnant and non-pregnant women. During pregnancy, the treatment typically focuses on managing symptoms as regression often happens after delivery. The recommended therapies include elevating the legs, utilizing a pelvic supporter that applies pressure and provides support to the vulvar area, engaging in physical exercise, avoiding prolonged periods of standing or sitting, applying compression with a support hose, and sleeping on the left side.[9,14] Surgical intervention during pregnancy is reserved for cases where complications such as thrombosis, hemorrhage, or ineffective conservative therapy arise. The methods include sclerotherapy, endovascular transcatheter embolization, and local excision. After pregnancy, varicose veins frequently resolve, leaving a visible minor residual varicose vein. Vaginal varicosities may rupture, leading to bleeding. Severe blood loss may occur due to large size of the varicose. However, the majority of the bleeding in varicosities is minor and not life-threatening. The treatment involves the ligation of blood vessels, the use of cautery, and the application of laser therapy.[15,16,17]

The precise theory on the method of delivery in cases of vaginal varicosities during pregnancy remains uncertain. Cesarean section is contraindicated in pregnancies with vaginal varicosities, although spontaneous vaginal delivery is permissible. This is because during labor, the descent of the baby's head exerts pressure on the veins, which helps alleviate the varicosities. Nevertheless, there is a lack of evidence to support the notion that either vaginal delivery or cesarean section provides any benefits in cases of significant vaginal varicosities. Furthermore, there is no current data to quantify the risk of varicose veins rupturing during vaginal delivery.[2,18] Spontaneous vaginal delivery typically does not result in complications, as stated in several literatures. However, it is crucial to do a comprehensive evaluation and analysis of the risks and advantages when deciding on the method of delivery in order to avoid the issues associated with vaginal varicosities. The complications include thrombosis, pulmonary embolism, and severe bleeding resulting from the rupture of the veins in the extensive vaginal varicosities (Table 1).[19,20]

We reported a successful spontaneous vaginal delivery of a 39-week pregnant woman who presented with vaginal varicosities. The patient was eligible for a vaginal delivery as there were no indications for a cesarean section and no contraindications for a vaginal delivery. The delivery did not result in rupture to the varicose and other veins. The bleeding was managed effectively, and the vaginal varicosities regressed the baby was delivered.

Table 1. Complications on mode of delivery in vaginal varicosities.[1,2,18,21]

Mode of delivery	Complications	Treatments	Prevention
Vaginal delivery	Rupture	● External pressure ● Antifibrinolytic	● Apply ice or cold pack onto the vulva area ● Antifibrinolytic
	Vulvar hematoma	● Incision and drainage of the hematoma	
	Hemorrhage	● Antifibrinolytic	
Cesarean section	Venous Thromboemboli (VTE) Lung embolism	● Anticoagulants ● Embolectomy ● Vena cava filter ● Vein ligation ● Phlebectomy	● Avoid staying in one position for long, change position from time to time ● Get a support garment specifically for vaginal varicosities ● Elevate legs to help promote circulations ● Antifibrinolytic*

*Post-delivery

CONCLUSION

Vaginal varicosities are a rare condition primarily affecting pregnant women with multigravida and occurring during the 12-26 weeks of gestation. Diagnosis is based on anamnesis, physical examination, and radiologic tests. The consensus on diagnosis, treatment, and delivery mode is still undefined. Conservative, symptomatic, and prophylactic treatment is the only choice. Surgery may be necessary in some cases, but cesarean section is not recommended. Most cases can regress spontaneously within 6 weeks postpartum. In this case, spontaneous vaginal delivery was chosen and the vaginal varicosities regressed spontaneously as the baby was delivered and caused no complications at all.

DISCLOSURE

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Conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Patient consent for publication

Written informed consent for the case to be published (including images, case history, and data) was obtained from the patient for publication of this case report.

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Author contribution

All authors have contributed to all processes in this research, including preparation, data gathering, analysis, drafting, and approval for publication of this manuscript.

REFERENCES

1. Gavrilov SG. Vulvar varicosities: diagnosis, treatment, and prevention. Int J Womens Health. 2017;9:463-75. doi: 10.2147/IJWH.S126165. PMID: 28721102; PMCID: PMC5500487.
2. Furuta N, Kondoh E, Yamada S, et al. Vaginal delivery in the presence of huge vulvar varicosities: a case report with MRI evaluation. Eur J Obstet Gynecol Reprod Biol. 2013;167(2):127-31. doi: 10.1016/j.ejogrb.2012.11.024. Epub 2012 Dec 31. PMID: 23287636.
3. Kim AS, Greyling LA, Davis LS. Vulvar varicosities: A review. Dermatol Surg. 2017;43(3):351-6. doi: 10.1097/DSS.0000000000001008. PMID: 28005626.
4. Giannella L, Montanari M, Delli Carpini G, et al. Huge vulvar varicosities in pregnancy: case report and systematic review. J Int Med Res. 2022;50(5):3000605221097764. doi: 10.1177/03000605221097764. PMID: 35635336; PMCID: PMC9158414.
5. Soule HM, Conte AB, Jayi S, et al. Vulvar varicose veins and pregnancy: childbirth management. PAMJ Clin Med. 2020;3(157). doi: 10.11604/pamj-cm.2020.3.157.24156.
6. Jindal S, Dedhia A, Tambe S, et al. Vulvovaginal varicosities: An uncommon sight in a dermatology clinic. Indian J Dermatol. 2014;59(2):210. doi: 10.4103/0019-5154.127757. PMID: 24700962; PMCID: PMC3969704.
7. Sueyoshi M, Clevenger S, Hart E. Large vaginal varicosities in the setting of pregnancy without known hepatic or vascular risks: A case report and review of the literature. Case Rep Obstet Gynecol. 2018;2018:2394695. doi: 10.1155/2018/2394695. PMID: 29607234; PMCID: PMC5827883.
8. Sun J, Guo Y, Ma L, et al. An unusual cause of postmenopausal vaginal haemorrhage: A case report. BMC Womens Health. 2019;19(1):31. doi: 10.1186/s12905-019-0731-4. PMID: 30732650; PMCID: PMC6367833.
9. Vulvovaginal varicosities and pelvic congestion syndrome - UpToDate [Internet]. [cited 2023 Aug 17]. Available from: https://www.uptodate.com/contents/vulvovaginal-varicosities-and-pelvic-congestion-syndrome#H2

10. Giannouli A, Tsinopoulou VR, Tsitsika A, et al. Vulvar varicosities in an adolescent girl with morbid obesity: A case report. Children (Basel). 2021;8(3):202. doi: 10.3390/children8030202. PMID: 33800092; PMCID: PMC7998964.
11. Cunningham FG, editor. Williams obstetrics. 25th edition. New York: McGraw-Hill; 2018.
12. Hoffman BL, editor. Williams gynecology. Third edition. New York: McGraw-Hill Education; 2016. p. 1270.
13. Laghzaoui O. Pseudo tumour appearance of vulvar varicose veins. BMJ Case Rep. 2016;2016:bcr2016 214819. doi: 10.1136/bcr-2016-214819. PMID: 270 30463; PMCID: PMC4823563.
14. Slagsvold CE, Stranden E. Venøse leggsår [Venous leg ulcers]. Tidsskr Nor Laegeforen. 2005; 125(7):891-4. Norwegian. PMID: 15815737.
15. Dascanio JJ. Treatment of vaginal varicosities. In: Dascanio JJ, McCue PM, editors. Equine reproductive procedures [Internet]. Hoboken, NJ, USA: John Wiley & Sons, Inc; 2014 [cited 2023 Aug 18]. p. 240–2. Available from: https://onlinelibrary.wiley.com/doi/10.1002/9781118904398.ch72
16. Al Wahbi AM. Isolated large vulvar varicose veins in a non-pregnant woman. SAGE Open Med Case Rep. 2016;4:2050313X16672103. doi: 10.1177/2050313X16672103. PMID: 27757232; PMCID: PMC5051671.
17. Susetiati DA, Satria B. Vulvovaginal varicosities on pregnant woman in conjunction with condyloma acuminata. Asian Jr. of Microbiol. Biotech. Env. Sc. 2020; 22(2):303-8. Available from: http://www.envirobiotechjournals.com/article_abstract.php?aid=10573&iid=304&jid=1
18. Fukaya E, Flores AM, et al. Clinical and Genetic Determinants of Varicose Veins. Circulation. 2018;138(25):2869-80. doi: 10.1161/CIRCULATIONAHA.118.035584. PMID: 30566020; PMCID: PMC6400474.
19. Furuta N, Kondoh E, Yamada S, et al. Vaginal delivery in the presence of huge vulvar varicosities: a case report with MRI evaluation. Eur J Obstet Gynecol Reprod Biol. 2013;167(2):127-31. doi: 10.1016/j.ejogrb.2012.11.024. Epub 2012 Dec 31. PMID: 23287636.
20. Kikuchi N, Ohira S, Asaka R., et al. A Case of Vaginal Varices that Caused Massive Bleeding after Vaginal Delivery. Shinshu Med J. 2016; 64(1):35-9. doi: 10.11441/shinshumedj.64.35.
21. Theodorou G, Khomsi F, Bouzerda-Brahami K, et al. Surgical management of a large postoperative vulvar haematoma following vulvar phlebectomy and ovarian vein embolization for vulvar varicose veins: A case report. Case Rep Womens Health. 2020;27:e00225. doi: 10.1016/j.crwh.2020.e00225. PMID: 32489909; PMCID: PMC7262542.

CASE REPORT

Early diagnosis and appropriate management of vaginal leiomyoma in rural areas

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ABSTRACT

Objective: To describe the challenges of early diagnosis and appropriate management of vaginal leiomyoma in rural areas.

Case Report: A 26-year-old woman, P1A0, was referred from a rural hospital and presented a chief complaint of vaginal mass. The patient was admitted to the tertiary hospital with suspected malignant vaginal tumor and underwent a biopsy, which revealed leiomyoma on pathological examination. Despite conservative treatment, the mass continued to grow, unaffected by the menstrual cycle, causing discomfort. Following a second hospital admission, the patient underwent surgical management of extirpation and vaginal reconstruction. The microscopic finding of the tumor showed myositis cell proliferation with hyperplastic growth, monotonous nuclei, and variable cell shapes, supporting the diagnosis of vaginal leiomyoma. During postoperative monitoring, there was no vaginal bleeding. Thereafter, on the day following surgery, it was found that the right labium major was swollen. This was treated with anticoagulants, topical NSAIDs, and a sitz bath. The patient was discharged from the hospital in good condition and had an uneventful postoperative recovery.

Conclusion: Although the incidence of vaginal leiomyoma is uncommon, precise early diagnosis and appropriate management might improve outcomes, particularly in rural areas.

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Highlights:

1. Extrauterine leiomyoma, including vaginal leiomyoma, is an exceedingly rare condition with complex pathogenesis and management.
2. Clinical evaluation and high-quality imaging are required to confirm the diagnosis of vaginal tumor. If there are insufficient facilities, referrals must be made.
3. Operative management using vaginal approach was described for treating vaginal leiomyoma.

INTRODUCTION

Leiomyoma is a benign mesenchymal tumor originating from the clonal proliferation of uterine smooth muscle cells. The uterus is the most typical site. However, it can manifest in any part of the female reproductive system. This tumor is the most common benign gynecological tumor and affects around 30% of women by age 30. Extrauterine leiomyoma is a very uncommon condition characterized by complex pathogenesis and management.[1]

Diagnosing extrauterine leiomyoma can be somewhat difficult due to its histological characteristics as a benign tumor that originates from smooth muscle cells. It often develops in the genitourinary tract, including the vulva, ovaries, urethra, and vagina. Alternatively, it may also arise in close proximity to other anatomical structures within the genitourinary system. Unusual growth patterns of leiomyoma beyond the uterus include the benign leiomyoma metastasis, peritoneal leiomyomatosis, intravenous leiomyomatosis, parasitic leiomyoma, and retroperitoneal growth.[1,2]

Vaginal leiomyoma is an exceptionally uncommon neoplasm. Vaginal leiomyoma commonly affects individuals between the ages of 19 and 70, with tumor sizes ranging from 0.5 to 15 cm in diameter. Vaginal leiomyoma typically occurs on top the anterior midvaginal wall and is generally smaller than 6 cm in size. The recommended treatment option is surgical excision of the mass through the vagina, which has a low chance of recurrence.[3-5] This case report outlines a successful surgical treatment of a vaginal leiomyoma by removing the tumor with excision and enucleation using a vaginal approach.

CASE REPORT

A 26-year-old woman, P1A0, was referred from a rural hospital in Central Kalimantan with a diagnosis of vaginal wall solid tumor. The patient complained of a solid mass in the right vaginal canal for the past month, rapidly increasing in size, accompanied by vaginal discharge. The patient also reported discomfort, especially when sitting or standing. The patient confirmed the ability to have sexual intercourse, and there was no pain during intercourse. On gynecological examination, a solid mass was found on the right lateral vaginal wall, measuring approximately 4 cm, fixed to the surrounding area. The mass had a smooth surface and no tenderness upon palpation. Initially the gynecologist suspected this as a malignancy due to the mass being fixated to the lateral vaginal wall, although standard equipment for gynecologic examination, such as speculum, and pelvic examination table, were present at the time in the referring hospital, malignancy still needed to be excluded. Lack of urogynecologists and gyneco-oncologists posed a challenge in diagnosing this type of vaginal mass. Upon consideration of facility and the need for further investigation by consultants, the patient was decided to be referred to a tertiary hospital. Availability of MRI and definitive surgery by urogynecologist were the main reason for the referral.

The patient was admitted to a tertiary hospital and underwent a biopsy of the vaginal solid mass, suspected of malignancy, by a gyneco-oncologist which revealed leiomyoma in the vaginal region (Figure 1). The patient was then referred to an urogynecologist. Upon re-evaluation, the mass had enlarged to 6 cm and was accompanied by pain in the mass area, with a VAS of 3-4. Subsequently, a pelvic MRI was performed.

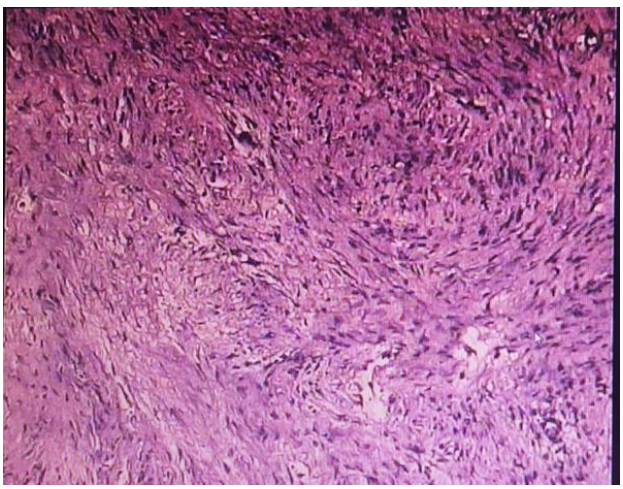

Figure 1. Biopsy histopathological finding consistent with a leiomyoma.

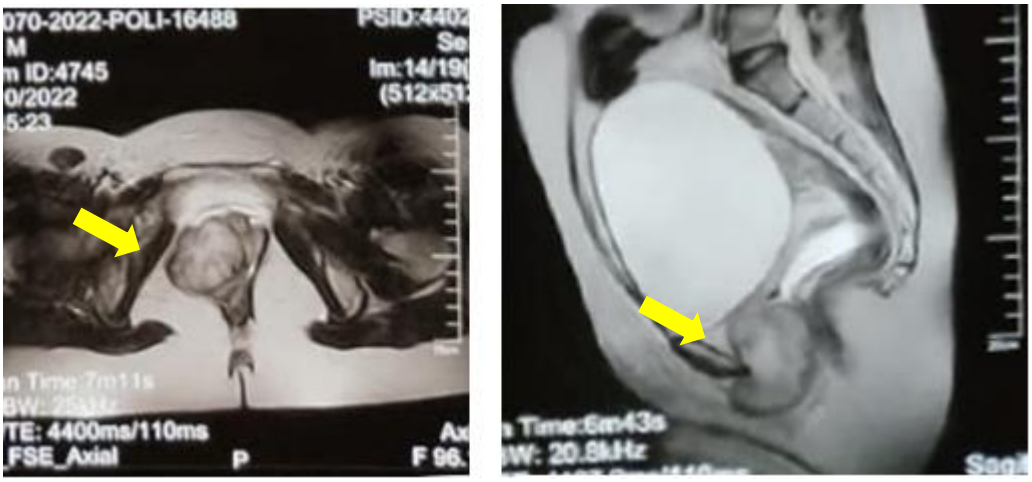

Figure 2. Pelvic MRI results (see yellow arrows).

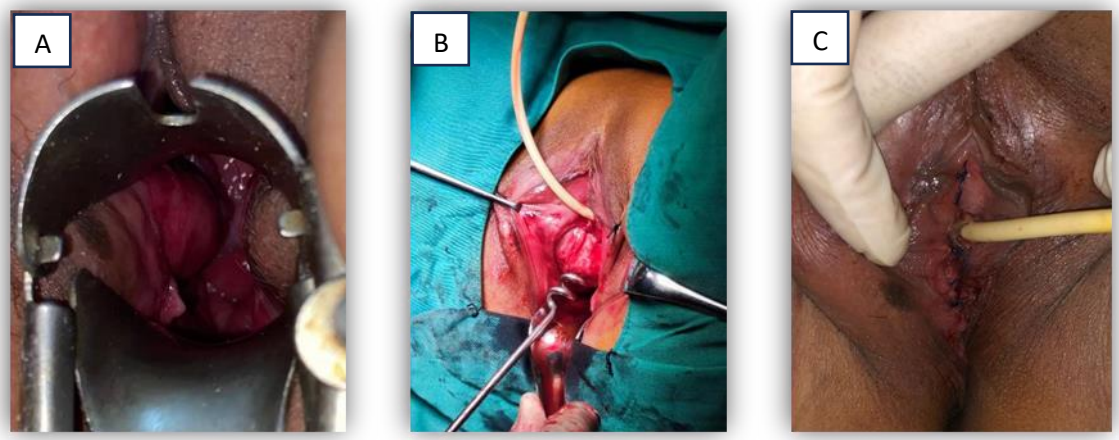

Figure 3A-C. Clinical pictures during preoperative (A), intraoperative (B), and postoperative (C) phases.

The MRI results concluded that there was a solid mass in the anterolateral right vaginal wall, suggestive of either a Bartholin gland mass, vaginal fibromyolipoma, or chronic abscess. The solid mass appeared to be unrelated to the surrounding bones (Figure 2).

The surgery was conducted four months after the biopsy (Figure 3A-C). During the intraoperative evaluation, a solid mass with a smooth surface was found on the upper lateral wall of the vagina, measuring 10 x 6 x 5 cm, attached to the M. bulbocavernosus, extending inferiorly to the pubic bone (right side), with its peak surpassing the posterior part of the pubic symphysis (Figure 4A). The medial part of the mass was adherent to the urethral wall (right side) up to the bladder neck, while the lower part was free. Subsequently, the leiomyoma was excised (Figure 4B), and lateral vaginal wall reconstruction was performed. The excised mass was sent for histopathological examination. The results revealed a mass measuring 12 x 10 x 8 cm, consisting of myositis cell proliferation with hyperplastic growth, monotonous nuclei, and variable cell shapes, supporting the diagnosis of vaginal leiomyoma (Figure 5).

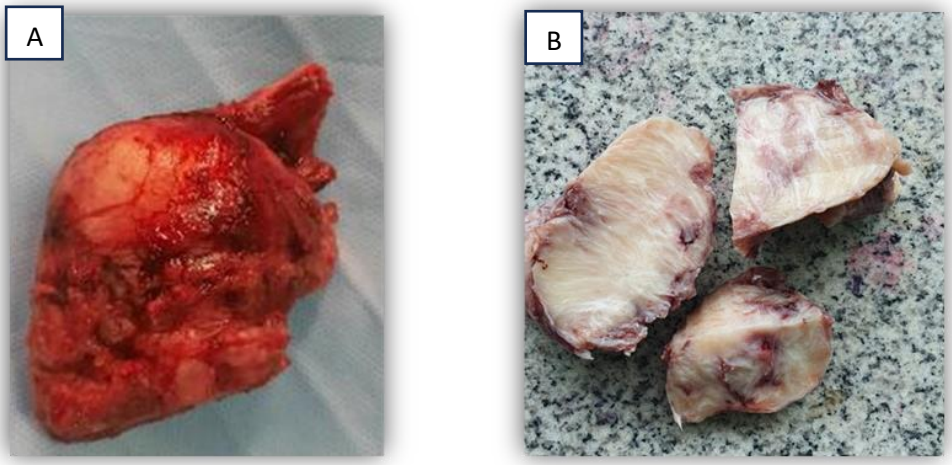

Figure 4A and B. Specimen of the mass.

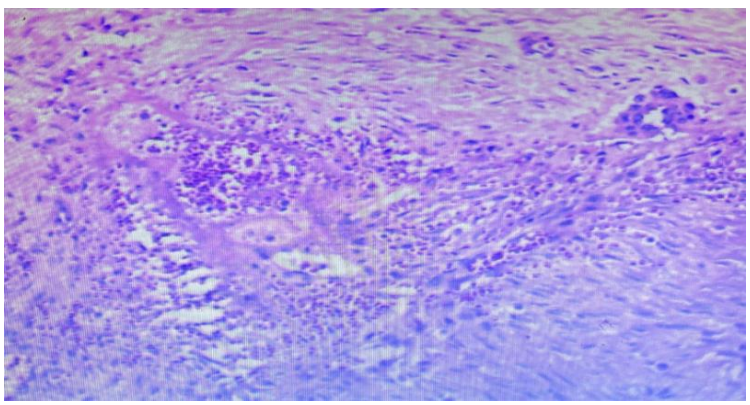

Figure 5. Mass histopathological result supporting a vaginal leiomyoma.

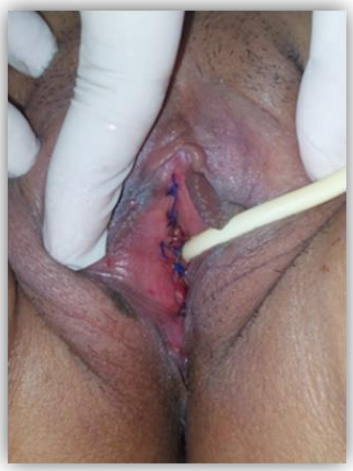

Figure 6. Postoperative day 7, no vaginal bleeding and good wound healing.

Following surgery, the patient spent four days in postoperative care, receiving antibiotics, analgesics, anti-inflammatories, and a one-time 24-hour vaginal tampon insertion. No vaginal bleeding was seen (Figure 6). Right labia majora swelling, however, occurred on the first day following surgery and was treated with topical anticoagulants, NSAIDs, and sitz baths. The patient was able to urinate on her own after the foley catheter was removed after three days of indwelling. The swelling of the right labia majora gradually diminished, and the patient was discharged.

DISCUSSION

Vaginal leiomyoma is a rare condition, with a total of approximately 330 cases reported since its initial discovery in 1733 by Denys de Leyden. Vaginal leiomyoma primarily affects women between the ages of 35 and 50 and is more prevalent among individuals of Caucasian ethnicity. Vaginal mesenchymal tumors are highly prevalent. Vaginal leiomyoma commonly develops on the front part of the middle vaginal wall and infrequently on posterior vaginal wall. Typically, it manifests as a solitary, clearly delineated mass. Leiomyomas are frequently found in the female reproductive system, mostly in the uterus, to a lesser extent in the cervix, and also in the round ligament, utero-sacral ligament, ovary, and inguinal canal.[6-8]

The exact pathogenesis of vaginal leiomyoma development is yet unknown. However, it is believed to be controlled by hormones, which means that it may regress during menopause. Vaginal leiomyoma exhibits the same macroscopic and microscopic characteristics to uterine leiomyoma. Most published reports suggest that vaginal leiomyoma is not thought to come from myometrial cells. Instead, it is believed to develop from several sources such as vaginal smooth muscle, rectum, bladder, urethra, smooth muscle blood vessels, or embryonic remains within the vagina. Vaginal leiomyoma can manifest either as a component of other leiomyomas or as an independent occurrence.[5,7].

A retrospective study investigated twenty-six patients with vaginal leiomyoma.[9] Smooth muscle actin (SMA), S-100 protein (calcium-binding protein), CD34 (cluster of differentiation 34), ER (estrogen receptor), and EGFR (epidermal growth factor receptor) were detected using S-P immunohistochemistry. Immunohistochemical staining revealed a high positive expression of SMA and a negative expression of S-100 protein and CD 34 in all cases. The expression of ER and EGFR was positive in 38.5% (10 out of 26 cases) and 34.6% (9 out of 26 cases) respectively. A strong association was seen between the expression of ER and EGFR. The study determined that estrogen hormone and EGF (epidermal growth factor) likely have a crucial function in the development and growth of vaginal leiomyoma.

The clinical manifestations of vaginal leiomyoma differ according on the size and location of the tumor. The most common complaint is the presence of a mass protruding from the vagina. Additional symptoms may include abdominal discomfort, vaginal discharge, dyspareunia (pain during sexual intercourse), infertility, frequent urination, inability to completely empty the bladder, urinary tract infections (UTIs), dysmenorrhea (painful menstruation), abnormal uterine bleeding, and pain in the right iliac fossa. Vaginal tumors can vary in size, ranging from 2 cm to as large as the umbilicus. These tumors have the potential to cause infection, necrosis, or rapid growth that resembles malignancy.[10] In our case, the main complaint was a rapidly enlarging mass in the vaginal canal with associated pain, no dyspareunia, and no urinary disturbances.

In the evaluation, it is important to differentiate between vaginal leiomyoma and malignancy. Establishing a diagnosis can be challenging due to the various clinical symptoms and diverse clinical manifestations of the tumor. Therefore, evaluation is necessary to distinguish vaginal leiomyoma from malignancy. A solid vaginal tumor can be identified through a physical examination, and it is important to differentiate it from other solid tumors in the vagina, such as fibroepithelial polyp, condyloma acuminatum, urethral leiomyoma, skene duct abscess, or, in rare cases, vaginal malignancy. The precise location of a solid mass can help to exclude differential diagnosis. When there is a solid mass positioned in half of the vagina, an examination is necessary to determine between vaginal leiomyoma, vaginal cyst, or uterine prolapse.[11-13]

Several diagnostic procedures such as transabdominal ultrasound (US), transvaginal US, translabial US, and MRI can be used to distinguish between vaginal leiomyoma and cancer. Magnetic Resonance Imaging (MRI) is advantageous for quickly proliferating leiomyomas that are difficult to visualize with ultrasonography (US) and when there is a suspicion of malignancy. MRI is a highly reliable method for identifying leiomyoma, with a sensitivity ranging from 88% to 93% and a specificity ranging from 66% to 91%. MRI is a useful tool for identifying the location of a mass, determining the size of the mass, and distinguishing the composition of the mass. Magnetic resonance imaging (MRI) usually reveals a clearly defined, solid mass with signal intensity that falls between T1 and T2, and exhibits uniform enhancement

when contrast is applied. On the other hand, leiomyosarcomas and other types of vaginal cancers typically show an intense signal on T2 imaging, have irregular margins, and heterogeneous contrast enhancement in areas of necrosis or hemorrhage. Leiomyomas that are undergoing degeneration may exhibit regions with a high T2 signal intensity, suggesting a combination of swollen, deprived of blood myoma cells, cystic alterations, or myxoid degeneration.[3,6,7,14]

Several studies have indicated increased levels of tumor markers, including Ca125, Ca19-9, and Ca15.3, in respectively 19.7%, 6.6%, and 5.1% of women diagnosed with vaginal leiomyoma, as observed in laboratory tests. Additional studies have shown that increased LDH levels are significant in the preoperative diagnosis of sarcoma. In our case, however, laboratory studies for tumor markers were not performed.[3]

Biopsy or fine-needle aspiration biopsy (FNAB) can be performed preoperatively for diagnostic confirmation. Histopathological confirmation is the gold standard for diagnosis with an ability to rule out any potential focus of malignancy. Vaginal leiomyoma consists of spindle-shaped cells with elongated and oval nuclei with minimal mitotic activity. The presence of atypical cells, hypercellularity, and numerous mitoses indicates malignancy on histopathological examination.[6,7,15]

In our case, the MRI results showed a mass with an isointense signal on T1W1 and T2W1 with relatively well-defined borders, seemingly surrounded by fat, no connection to the surrounding bones, and a size of 5.85 x 6.03 x 4.04 cm, located in the right anterolateral wall of the vagina. This mass exhibited mild inhomogeneous enhancement on T1 with contrast. Vaginal leiomyoma can be diagnosed precisely when MRI shows low signal intensity on T1 and T2 weighted images. However, the pathognomonic findings in MRI will change depending on histological changes. Preoperative biopsy results indicated a tumor mass composed of round, oval, and spindle-shaped cells grouped in fascicles, with cell nuclei within normal limits and no malignant cells, supporting the diagnosis of vaginal leiomyoma.[16,17]

The management of this tumor typically involves vaginal enucleation in most cases, but sometimes an abdominopelvic approach may be required depending on the size and location of the mass. An abdominal approach is also performed in cases where the tumor is located proximally in the vagina and the upper part of the tumor cannot be reached via the vaginal route. If vaginal leiomyoma is diagnosed before surgery, GnRH analogs or selective progesterone receptor modulators (SPRMs) may be administered to shrink the mass, and an embolization before surgery has also been reported to reduce mass vascularity, thereby reducing intraoperative bleeding. The operator should consider the risk of urethral or bladder injury during vaginal surgery. A urethral catheter insertion during tumor removal surgery via vaginal approach is preferred to prevent urethral injury.[3,4,6,7,18]

Hemostatic suturing and proper closure are necessary following effective mass removal to avoid dead spaces. In this case, mass enucleation was performed by making a vertical incision parallel to the labia on the distal vaginal wall, 5 cm above the tumor mass, until the myoma capsule was visible. A myoma screw was placed to pull the mass. Subsequently, sharp and blunt extirpation of the myoma tissue was carried out until the mass was detached from the surrounding tissue. A foley catheter was placed as a marker before freeing the mass attached to the right urethral wall. Sutures were used to provide hemostatic care after the mass was removed. An absorbable hemostatic gelatin sponge was applied, and then the reconstruction of the lateral vaginal wall was performed with layered sutures using PGA 2.0. Histopathological examination for diagnosis confirmation is crucial to rule out malignancy. After surgery, it is recommended for an indwelling 24 hours foley catheter to be inserted for overseeing visceral injuries. Vaginal packing placement could also be implemented for hemostasis.[6,19]

Routine postoperative monitoring is required to evaluate recurrences. Furthermore, several studies have reported sexual intercourse disturbances following the diagnosis and management of vaginal tumors. Therefore, psychological support is essential to improve sexual function and quality of life.[20]

Rural areas refer to regions that are distinct from urban areas. These locations typically consist of habitats surrounded by trees in forests, accessible via footpaths or, at most, unpaved or previously paved roads. The residents are primarily composed of peasant farmers, low-grade artisans, and other individuals with modest incomes.[21] The obstetric and gynecologist in rural areas is involved in general obstetric and gynecologic surgery. Due to the unique setting, they may also perform procedures in urogynecology, oncology, reproductive-endocrinology-infertility, and maternal-fetal medicine.

Patients may undergo incomplete investigations due to a lack of facilities, necessitating outsourcing with added inconvenience and higher costs for the patient. To address this issue, it is essential to have trained consultants working in rural areas, either on a full-time or part-time basis. This approach aims to minimize the time lost in referring patients to distant tertiary hospitals

and enhance the overall quality of service. As for our patient, she needed further investigation not only by general obstetrician and gynecologist but also urogynecologist and gyneco-oncologist. She was referred to the tertiary hospital which took hours by road in consideration to seek urogynecology consult and biopsy. Further management was also done in the same tertiary hospital. Challenges such as transportation, funds, and time from referral until obtaining complete case management remain a problem especially during the Indonesian universal health coverage program as referral needed multiple sequence starting from primary health care facility until it reaches the tertiary care facility.

This is the first case report for vaginal leiomyoma in Indonesia. We tried to provide insights on how to diagnose and manage vaginal leiomyoma case, especially in a resource-limited area. The limitation of this study was that tumor markers such as Ca 125, Ca19-9, Ca15.3, and LDH were not examined to rule out the diagnosis of malignancy.

DISCLOSURES

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Conflict of interest

The authors report no conflicts of interest in this work.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Author contribution

All authors have contributed to all process in this research, including preparation, data gathering, drafting and approval for publication of this manuscript.

REFERENCES

1. Tang Y, Nadarajah R. Challenges in the diagnosis and treatment of extrauterine leiomyomas: case series. Int J Reprod Contracept Obstet Gynecol. 2021;11(1):232-6. doi: 10.18203/2320-1770.ijrcog20215109.
2. Chen M, Li Y, Chi Y, et al. Diagnosis and management of vaginal leiomyoma: a case report and literature review. Ginekol Pol. 2023;94(10): 858-61. doi: 10.5603/GP.a2022.0145. Epub 2023 Jan 4. PMID: 36597753.
3. Egbe TO, Kobenge FM, Metogo JAM, et al. Vaginal leiomyoma: medical imaging and diagnosis in a resource low tertiary hospital: case report. BMC Womens Health. 2020;20(1):12. doi: 10.1186/s12905-020-0883-2. PMID: 31964370; PMC ID: PMC6975035.
4. Costa C, Barba M, Cola A, et al. Transvaginal excision of vaginal paraurethral leiomyoma: A video case report. Eur J Obstet Gynecol Reprod Biol. 2023;290:11-3. doi: 10.1016/j.ejogrb.2023.09.008. Epub 2023 Sep 11. PMID: 37708657.
5. Dunphy L, Wood F, Siraj M, et al. Leiomyoma presenting as an anterior vaginal mass. BMJ Case Rep. 2023;16(3):e253081. doi: 10.1136/bcr-2022-253081. PMID: 36863759; PMCID: PMC9990660.
6. Wethmar EI, D Mouton A, Dreyer G. Vaginal leiomyoma presenting as a lateral vaginal wall mass. Southern African Journal of Gynaecological Oncology. 2017;9(1):16–8. doi: 10.1080/20742835.2017.1314630
7. Harada K, Ishikawa Y, Fujiwara H, et al. Female paraurethral leiomyoma successfully excised through a vaginal approach: A case report. J Obstet Gynaecol Res. 2018;44(6):1174-6. doi: 10.1111/jog.13641. Epub 2018 Apr 2. PMID: 29607582.
8. Kant RH, Mir N, Sharma P, Najeeb R. Vaginal Wall Leiomyoma: A Rare Entity-Case Report Case Report. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2015;14(5):60–1. doi: 10.9790/0853-14556061.
9. Asnani M, Srivastava K, Gupta HP, et al. A rare case of giant vaginal fibromyoma. Intractable Rare Dis Res. 2016;5(1):44-6. doi: 10.5582/irdr.2015.01037. PMID: 26989649; PMCID: PMC4761584.
10. Patil RR, Vijay NR, Joshi S. An unusual presentation of vaginal leiomyoma. J Midlife Health. 2019;10(4):204-5. doi: 10.4103/jmh.JMH_40_19. PMID: 31942157; PMCID: PMC6947721.
11. Woo J, Choi SY, Kim HK, et al. Extremely Rare CT and MRI Findings of Peritoneal Leiomyoma Mimicking Hepatic Mass: A Case Report. J Korean Soc Radiol. 2023;84(4):946-51. doi: 10.3348/jksr.2022.0032. Epub 2023 Jul 10. PMID: 37559801; PMCID: PMC10407062.

12. Ashraf Muhammed P, Karim HA, Majeed NG, et al. A rare case of benign vulvovaginal leiomyoma: Case report and literature review. Ann Med Surg (Lond). 2022;77:103720. doi: 10.1016/j.amsu.2022.103720. PMID: 35637979; PMCID: PMC9142705.
13. Singh R, Yadav P, Kaur H. Vaginal leiomyoma: A rare presentation. Journal of SAFOG. 2014;6(2): 112–3. doi: 10.5005/jp-journals-10006-1284.
14. Gupta A, Gupta MM, Manaktala U. Vaginal leiomyoma: MRI features with pathologic correlation. Egyptian Journal of Radiology and Nuclear Medicine. 2015;46(2):507–9. doi: 10.1016/j.ejrnm.2015.01.010.
15. Ning Y, Ling R, Zhang F, et al. Common and uncommon lesions of the vulva and vagina on magnetic resonance imaging: correlations with pathological findings. BJR Open. 2023;5(1): 20230002. doi: 10.1259/bjro.20230002. PMID: 37389007; PMCID: PMC10302693.
16. do Amaral CC, Castro PT, Frota R, et al. Vaginal leiomyoma: Advantages of clinical sonovaginography and ultrasound dynamic evaluation of uterine cervix-related lesions. J Clin Ultrasound. 2023;51(9):1509-11. doi: 10.1002/jcu.23580. Epub 2023 Oct 6. PMID: 37800472.
17. Gao Y, Qin Y, Li J, et al. Vaginal leiomyoma: A case report. Exp Ther Med. 2022;24(5):661. doi: 10.3892/etm.2022.11597. PMID: 36168424; PMCID: PMC9475341.
18. Agarwal S, Trigunait P, Meena M. A rare case of vaginal fibroid presenting as urethrocele. Indian Journal of Basic and Applied Medical Research [Internet]. 2016;(5):824–7. Available from: https://www.ijbamr.com/assets/images/issues/pdf/march%202016%20824-827.pdf.pdf
19. Costa C, Barba M, Cola A, et al. Transvaginal excision of vaginal paraurethral leiomyoma: A video case report. Eur J Obstet Gynecol Reprod Biol. 2023;290:11-3. doi: 10.1016/j.ejogrb.2023.09.008. Epub 2023 Sep 11. PMID: 37708657.
20. Nowosielski K, Pałka A. Couples' sexual health after gynaecological cancer diagnosis - an unexplored area for further research. Contemp Oncol (Pozn). 2023;27(1):47-56. doi: 10.5114/wo.2023.127308. Epub 2023 Apr 27. PMID: 37266338; PMCID: PMC10230241.
21. Umunna J. The scope and challenges of rural surgical practice in Nigeria. Nigerian Journal of Surgery. 2011;17(1):25-8. doi: 10.4314/njs.v17i1.70708.

CASE REPORT

Early diagnosis and management of inseparable conjoint twins. A low-middle-income country experience

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ABSTRACT

Objectives: To discuss the crucial early diagnosis of conjoined twins to determine the type and prognosis.

Case Report: A 27-year-old woman was referred to the type A referral hospital with suspicion of congenital abnormalities at 17 weeks of pregnancy. Ultrasound results showed intrauterine monochorionic monoamniotic twins with babies fused on their heads to the urogenital part. The MRI showed a craniopagus, suspected meningomyelocele, and severe bilateral hydronephrosis in the second baby. Due to non-separable cases and a bad prognosis for the fetus, the pregnancy was terminated using misoprostol induction and inserting a balloon catheter. The fetus was born weighing 400 g and 20 cm in length. Conjoined twins obtained the rostral type: a fused head with two faces, a fused thorax until the lower abdomen with one umbilicus, and two pairs of hands and feet. The diagnosis of conjoint twins becomes a problem in early pregnancy, mostly in developing countries. Early diagnosis of conjoined twins during prenatal examination is critical for ascertaining the prognosis of the fetus, guiding parental counseling over appropriate courses of action, and potentially enabling the termination of the pregnancy to prevent maternal stress and complications.

Conclusion: Conjoined twins should be identified as soon as feasible to establish the best course of management for both mother and fetus. Ultrasonography and MRI are modalities for determining the diagnosis and prognosis of conjoined twins.

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Highlights:

1. Conjoined twins have captivated mankind for centuries due to the rarity of this birth type. Nonetheless, physicians have constantly encountered difficulties in dealing with conjoined twins.
2. Early diagnosis of conjoined twins during prenatal examination is critical for ascertaining the prognosis of the fetus, guiding parental counseling over appropriate courses of action, and potentially enabling the termination of the pregnancy.
3. First-trimester ultrasonography and MRI are complementary modalities in determining the diagnosis and prognosis of conjoined twins in early pregnancy.

INTRODUCTION

Conjoined twins occur due to abnormalities in the process of embryogenesis in monoamniotic monochorionic pregnancies, which are proposed to have resulted from either fission or fusion. Due to the imperfect division of one fertilized ovum, conjoined twins are identical monozygotic twins that do not entirely separate from one another but are still partially linked to one another.[1] The incidence of conjoined twins is 1 in 50,000 to 100,000 births. However, because 60% of them die in the womb or shortly after birth, the actual incidence can reach 1 in 250,000 live births. The ratio of women to men babies is 3:1.[2]

Conjoined twins are classified based on the area of the body and internal organs that are fused: 11% cephalopagus (joined at the head), 19% thoracopagus (joined at the chest with one heart), 18% omphalopagus (lower abdomen), 11% ischiopagus (lower abdomen and thoracic system genitourinary), 28% parapagus (joined on the sides of the body and pelvis), 5% craniopagus (cranium), 2% rachipagus (vertebral column), and 6% pyopagus (sacrum).[3] Based on the prognosis, conjoined twins are classified into 2, survived and non-survived. Survived conjoined twins consist of separable and non-separable twins. Cephalophagus is frequently missed as a singleton pregnancy because of the extreme degree of fusion. The type of conjoined twins, cephalothoraco-abdominopagus itself, is a scarce type of conjoined twins with a poor prognosis. Prenatal diagnosis of conjoined twins is crucial to determine the prognosis so that it can properly manage both the mother and the fetus. The tools that can be used for early detection are ultrasonography and MRI.[4]

Conjoined twins can be challenging to diagnose accurately, especially in the early stages of pregnancy. Sometimes, a diagnosis might be ambiguous, necessitating additional imaging or specialist testing. Referral to a specialized prenatal facility or consultation with a fetal medicine expert may be advised under challenging circumstances. This case report will describe a rare conjoint twin case that could be diagnosed early in pregnancy, and can be appropriately managed in early pregnancy.

CASE REPORT

A 27-year-old woman, gravida 4, para 1, abortion 2, child alive 1, was referred to the type A referral hospital with suspicion of multiple congenital abnormalities with two hearts. The patient received antenatal checks twice at the public health care and once times at an obstetrician during pregnancy. Anamnesis obtained a history of twin pregnancies from the husband's grandmother. General examination was recorded within normal limits. An obstetric examination found fundal height three fingers below the umbilical, a positive fetal heart rate was observed, and an ultrasound examination revealed multiple congenital anomalies. The patient had been taking pregnancy vitamins and folic acid since five weeks of gestation.

Ultrasound results at 17/18 weeks of gestation at Dr. Soetomo Hospital showed conjoined twins fused from head to urogenital part (one thalamus, two cerebellum, two hearts, two lungs, fetal hydrops, and spina bifida abnormalities were seen in one of the fetuses). The MRI confirmation showed a craniopagus, suspected meningomyelocele, and severe bilateral hydronephrosis in the second baby. Based on the ultrasound and MRI results, it showed a bad prognosis because it was categorized as non-separable and non-survived conjoint twins. The multidisciplinary conjoint twin team discussion decided to terminate the pregnancy.

In non-separable cases, if it is discovered early in pregnancy, there is a possibility of terminating the pregnancy or maintaining it until term or the patient goes into labor spontaneously. However, if the decision waits until term, there is a possible risk of having a cesarean section at the time of delivery. If the diagnosis is early, it allows for early termination so that no surgery is required and prevents stress on the mother. The patient was informed of her pregnancy's prognosis and management options. The patient and her family decided to terminate it. The fetus was terminated at 20 weeks of pregnancy by inducing a combination of misoprostol 200 mcg vaginally every 6 hours and the insertion of a balloon catheter. The fetus was born weighing 400 g and has a length of 20 cm. There were rostral conjoined twins, two heads with two faces in opposite positions, each with two eyes, one nose showing nasal proboscis, two ears, and one mouth. The head is fused to the thoracic and lower abdomen, and an omphalocele was obtained in one fetus with one umbilicus and one placenta. Siamese twins have two pairs of arms and legs. However, the patient refused to undergo an autopsy.

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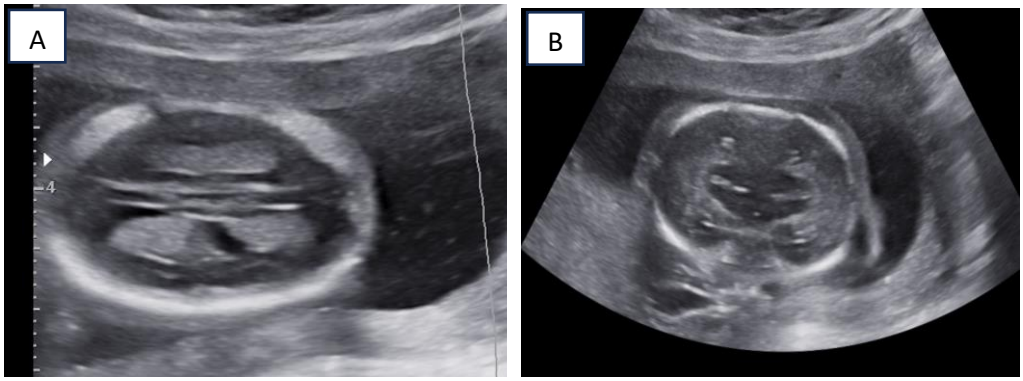

Figure 1. 2D ultrasonography results in a) Arrows indicate two choroid plexuses, b) Two fetal heads fused at the thalamus.

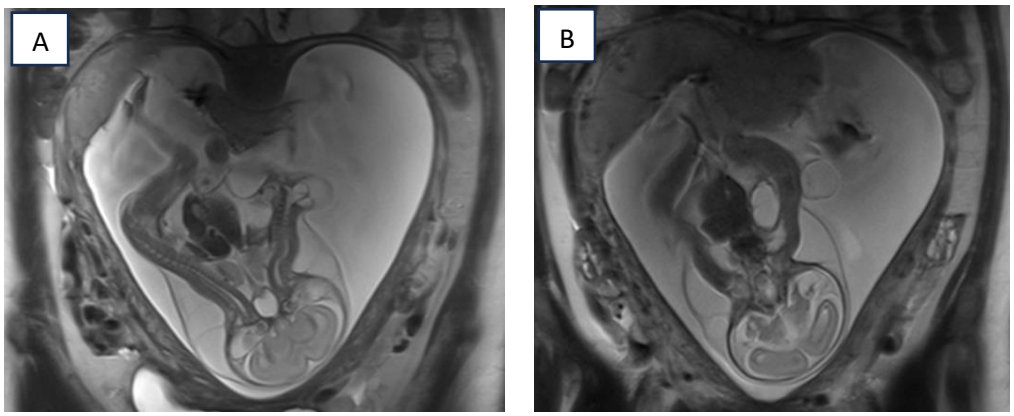

Figure 2. MRI results show two cerebellum lobes, two spines, two hearts, two lungs, and two livers. This organ fused on head to abdomen. Hydronephrosis and meningomyelocele are also seen in this small fetus.

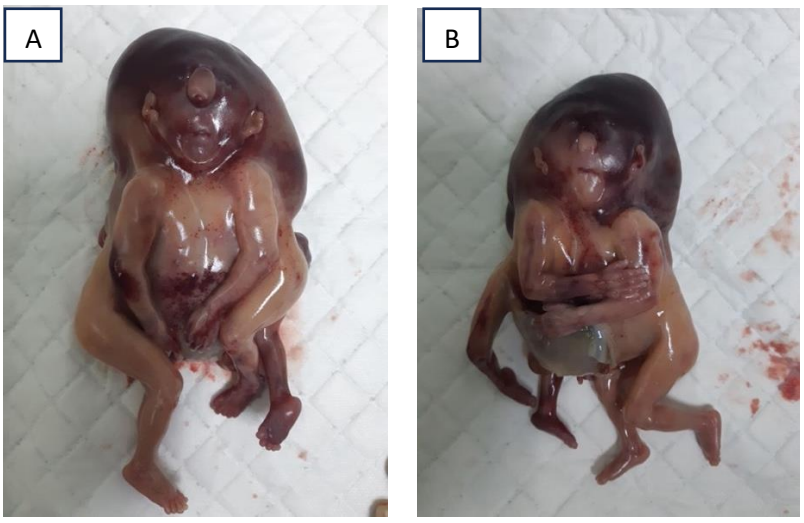

Figure 3. a) anterior part, b) posterior part

DISCUSSION

Conjoined twins have captivated mankind for centuries due to the rarity of this birth type. Nonetheless, physicians have constantly encountered difficulties in dealing with conjoined twins.[5] The embryological process of conjoined twins has yet to be discovered clearly. There are various theories on the formation of conjoined twins: a) Fission theory, which states that conjoined twin results from division in the early stages of embryo formation that comes from the fertilization of one ovum; b) Fusion theory, which suggests that conjoined twins result from two, initially separate monozygotic embryos, which coalesce and become secondarily and homologously fused (cephalo-pagus, thoracopagus, omphalopagus, ischiopagus, and parapagus).[3] Research on conjoined twins finds that union is homologous: head to head, buttocks to buttocks, chest to chest, back to back, sides to sides, but never head to buttocks or chest to back.[6]

Conjoined twins are classified based on the area of the body and the fused internal organs. The most common conjoined twins found are the thoracopagus, omphalopagus, and thoracic-omphalopagus types, with an incidence of around 56% of the total number of conjoined twins.[7] Cephalopagus conjoined twins fused from head to umbilicus are the rarest type. This type has one cranium and two opposite faces, with one face usually rudimentary. Another finding in cases of cephalopagus can be found in the lower abdomen and pelvis, which are separated by two pairs of hands and feet.[8]

Seventy percent of conjoined twins die within twenty-four to forty-eight hours after delivery or have a lethal congenital disease caused by the untimely diagnosis, which delays the implementation of optimal surgical treatment. Thus, early diagnosis and treatment are preferred.[9,10] Prior studies utilized ultrasonography to diagnose conjoined twins between 11 and 13 weeks of gestation.[11] Recent studies have documented the diagnosis of fetal abnormalities in twin pregnancies as early as 8 weeks gestation. Nevertheless, precise assessment of shared anatomical components remains unattainable.[5] Pregnancy termination remains the most effective course of action, regardless of gestational age, but especially during the early stages.

The diagnosis of conjoined twins in early pregnancy typically relies on prenatal ultrasound imaging. Some steps involved in diagnosing conjoined twins during the early stages of pregnancy are: early ultrasound examination, identification of gestational sac and embryos, assessment of fetal anatomy, evaluation of the placenta and umbilical cord, and proper follow-up examination. The ultrasound examination enables the identification of conjoined twins during prenatal diagnosis as early as 12 weeks of gestation. However, examination at 18-20 weeks of gestation is recommended for a more comprehensive assessment. Another modality that can be used is magnetic resonance imaging (MRI), which offers enhanced precision in providing anatomically detailed radiological images compared to ultrasound.[12–14]

In the present case, a prenatal ultrasound assessment is performed during the 17th to 18th weeks of pregnancy. The result showed that the cranium and the thalamus are joining, affecting the brain's structure. Furthermore, one of the fetuses exhibited the presence of an omphalocele and spina bifida. A magnetic resonance imaging (MRI) test was conducted to clarify the diagnosis further. The magnetic resonance imaging (MRI) scan reveals an image depicting two vertebrae, each fetus exhibiting distinct anatomical structures such as individual hearts, livers, and kidneys. Additionally, both fetuses exhibit the presence of a single pair of hands and feet. The tests showed that the conjoined twin fetuses, which were diagnosed as cephalo-thoraco-abdominopagus, are babies that cannot be separated and will not live.

In general, conjoined twins have a poor prognosis. The survival rate is indeed 7.5%. Survival rates for surgically separated cases are as low as 60%.[15] An improved prognosis could result from antenatal imaging, postnatal surgery, tissue expansion during surgery, and cadaveric transplantation for important organs shared by the twins, if applicable.[16] Legal abortion should be contemplated in Indonesia when a fetus has a life-threatening congenital abnormality with a poor prognosis, especially cephalon-thoraco-abdominopagus twins, whose survival rate is low and unlikely to be successfully separated.[17]

Early diagnosis of conjoined twins during prenatal examination is critical for ascertaining the prognosis of the fetus, guiding parental counseling over appropriate courses of action, and potentially enabling the termination of the pregnancy. First-trimester ultrasonography continues to be the most effective diagnostic modality in early pregnancy. Additionally, prenatal magnetic resonance imaging can assist in tissue characterization, conjunction type identification, and the detection of embryological malformations.[18] Once applicable, contemporary techniques such as 3D printing may facilitate surgical pre-planning and subsequent separation.[13] A viable pregnancy is easier to terminate vaginally if the diagnosis is made before that time, which may lessen the risk of trauma.[19] As the diagnosis progresses, the probability of achieving termination via cesarean section augments. Early

pregnancy termination is considered a safer option due to its potential to mitigate the emotional impact on the couples, which could be exacerbated by the numerous interdisciplinary follow-ups that are required throughout the prenatal and postnatal phases.[20] The effective management of conjoined twins necessitates the close collaboration of a multidisciplinary team.[21]

CONCLUSION

Conjoined twins of the cephalon-thoraco-abdomino-pagus type are a very rare type of conjoined twin with a poor prognosis. An early prenatal diagnosis provides a good outcome for the mother. Ultrasonography and MRI are complementary modalities in determining the diagnosis and prognosis of conjoined twins.

DISCLOSURES

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Conflict of interest

The author reports there are no competing interests to declare.

Patient consent for publication

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REFERENCES

1. Bindlish A, Sawal A. A Detailed Description and Discussion on Conjoined Twins. Cureus. 2022; 14(9):e29526. doi: 10.7759/cureus.29526. PMID: 36312620; PMCID: PMC9595239.
2. Spitz L. Conjoined twins. Prenat Diagn. 2005;25 (9):814-9. doi: 10.1002/pd.1268. PMID: 16170846.
3. Spencer R. Theoretical and analytical embryology of conjoined twins: part II: adjustments to union. Clin Anat. 2000;13(2):97-120. doi: 10.1002/(SICI)1098-2353(2000)13:2<97::AID-CA5>3.0.CO;2-I. PMID: 10679855.
4. Kapoor R, Bansal A, Aggarwal A, et al. Prenatal diagnosis of cephalophagus conjoined twins by ultrasonography and magnetic resonance imaging. Journal of Fetal Medicine. 2015;02(01):45–50. doi: 10.1007/s40556-015-0039-x.
5. Liang XW, Cai YY, Yang YZ, et al. Early ultrasound diagnosis of conjoined twins at eight weeks of pregnancy: A case report. World J Clin Cases. 2020;8(21):5389-93. doi: 10.12998/wjcc.v8.i21.5389. PMID: 33269274; PMCID: PMC7674739.
6. Kaufman MH. The embryology of conjoined twins. Childs Nerv Syst. 2004;20(8-9):508-25. doi: 10.1007/s00381-004-0985-4. Epub 2004 Jul 27. PMID: 15278382.
7. Kuroda K, Kamei Y, Kozuma S, et al. Prenatal evaluation of cephalopagus conjoined twins by means of three-dimensional ultrasound at 13 weeks of pregnancy. Ultrasound Obstet Gynecol. 2000; 16(3):264-6. doi: 10.1046/j.1469-0705.2000.00263.x. PMID: 11169294.
8. Singh M, Singh KP, Shaligram P. Conjoined twins cephalopagus janiceps monosymmetros: a case report. Birth Defects Res A Clin Mol Teratol. 2003; 67(4):268-72. doi: 10.1002/bdra.10042. PMID: 12854662.
9. Burans C, Smulian JC, Rochon ML, et al. W. 3-dimensional ultrasound assisted counseling for conjoined twins. J Genet Couns. 2014;23(1):29-32. doi: 10.1007/s10897-013-9623-1. PMID: 23797965.
10. Willobee BA, Mulder M, Perez EA, et al. Predictors of in-hospital mortality in newborn conjoined twins. Surgery. 2019;166(5):854-60. doi: 10.1016/j.surg.2019.06.028. Epub 2019 Aug 8. PMID: 31402130; PMCID: PMC10353765.
11. Syngelaki A, Cimpoca B, Litwinska E, et al. Diagnosis of fetal defects in twin pregnancies at routine 11-13-week ultrasound examination. Ultrasound Obstet Gynecol. 2020;55(4):474-81. doi: 10.1002/uog.21938. Epub 2020 Mar 6. PMID: 31788879.
12. Sabih D, Ahmad E, Sabih A, et al. Ultrasound diagnosis of cephalopagus conjoined twin pregnancy at 29 weeks. Biomed Imaging Interv J. 2010;6(4):e38. doi: 10.2349/biij.6.4.e38. Epub 2010 Oct 1. PMID: 21611074; PMCID: PMC3097803.
13. Mathew RP, Francis S, Basti RS, et al. Conjoined twins - role of imaging and recent advances. J Ultrason. 2017;17(71):259-66. doi: 10.15557/JoU.2017.0038. Epub 2017 Dec 29. PMID: 29375901; PMCID: PMC5769666.
14. Vagyannavar R, Bhattacharyya A, Misra G, et al. Craniopagus twins for magnetic resonance imaging. Saudi J Anaesth. 2017;11(4):509-10. doi: 10.4103/

sja.SJA_89_17. PMID: 29033747; PMCID: PMC 5637443.
15. Brizot Mde L, Liao AW, Lopes LM, et al. Gêmeos unidos: diagnóstico pré-natal, parto e desfecho após o nascimento [Conjoined twins: prenatal diagnosis, delivery and postnatal outcome]. Rev Bras Ginecol Obstet. 2011;33(5):211-8. Portuguese. PMID: 21860927.
16. Afzal AR, Montero FJ. Conjoined Twins. 2023. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 32809674.
17. Regulation of the Government of Republic of Indonesia no. 61 year 2014 on Reproductive Health. Available from: https://gizikia.kemkes.go.id/assets/file/pedoman/PP%20No.%2061%20Th%202014%20ttg%20Kesehatan%20Reproduksi.pdf
18. Mehollin-Ray AR. Prenatal and postnatal radiologic evaluation of conjoined twins. Semin Perinatol. 2018;42(6):369-80. doi: 10.1053/j.semperi.2018.07.015. Epub 2018 Jul 26. PMID: 30170825.
19. Wataganara T, Ruangvutilert P, Sunsaneevithayakul P, et al. Three-dimensional ultrasound for prenatal assessment of conjoined twins: additional advantages? J Perinat Med. 2017;45(6): 667-91. doi: 10.1515/jpm-2016-0381. PMID: 28231064.
20. Vayna AM, Veduta A, Duta S, et al. Diagnosis of Fetal Structural Anomalies at 11 to 14 Weeks. J Ultrasound Med. 2018;37(8):2063-73. doi: 10.1002/jum.14561. Epub 2018 Feb 24. PMID: 29476550.
21. Luton A, Estrada N, Barrientez K, et al. Nursing considerations and interdisciplinary coordination in the care of conjoined twins. Semin Perinatol. 2018; 42(6):340-9. doi: 10.1053/j.semperi.2018.07.012. Epub 2018 Jul 27. PMID: 30185382.

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