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Commentary on the Article: Plantar Ulcer as an Atypical Manifestation of Cutaneous Leishmaniasis

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Description

We present here a short commentary of the article published in *Anais Brasileiros de Dermatologia* in 2021, intitled "Plantar ulcer as an atypical manifestation of cutaneous leishmaniasis". In that paper we presented the case of a young male, resident of endemic area of leishmaniasis in Bahia, Brazil, who presents a plantar ulcer, diagnosed as an atypical manifestation of Cutaneous Leishmaniasis. We claim that American Tegumentary Leishmaniasis is an infectious, non-contagious, endemic and neglected zoonosis in Brazil, characterized by various clinical manifestations resulting in mucocutaneous involvement. The disease is caused by several protozoa species of the genus *Leishmania* that is transmitted by the bite of phlebotomine sand fly. Affects about 2 million people per year and it's considered as priority amongst neglected diseases by the WHO. *Leishmania braziliensis* is main causative agent in Brazil's territory. The disease pathogenesis is the result of the interaction between the genetic polymorphism of the parasite, host immune response, and environmental conditions, resulting in different clinical presentations [1-4]. Cutaneous Leishmaniasis (CL) is the most prevalent clinical presentation and is characterized by one or more rounded ulcers, with a granular bottom and raised edges, located mainly in exposed parts of the skin, corresponding to the parasite inoculation site by the vector insect. In addition to localized cutaneous manifestation, ATL can affect mucous membranes (oral and nasal) or even disseminated lesions and atypical forms [4]. The presence of lesions in less accessible body areas constitutes an atypical manifestation of the disease, even if it doesn't fit in the classic description of atypical cutaneous leishmaniasis, which is erysipeloid, sporotrichoid, zosteriform and recidiva cutis [2]. Plantar ulcers, even in endemic areas of leishmaniasis should be differentiated from other etiologies including leprosy, deep fungal infection, atypical mycobacteriosis, gangrenous pyoderma, vasculitis and perforating disease associated with diabetes [3]. In the original article, we reported the case of a twenty-one-year-old male patient, who was referred to the Corte de Pedra Leishmaniasis Reference Center in the municipality of Presidente Tancredo Neves, in the state of Bahia, Brazil. He was previously healthy and had no previous chronic diseases or history of ulcerated skin lesions suspected of leishmaniasis. He observed sudden appearance of a papular and ulcerated lesion in the axillary region with approximately 35 days of evolution. Concomitantly, he had an ulcerated lesion with raised edges on the left plantar region, associated with fever and myalgia. He subsequently evolved with the formation of two erosive lesions in the groin and left buttock regions 20 days after the onset of the manifestations, with lymphadenopathy in the left inguinal region. The physical examination showed a rounded ulcer with a granular bottom on the plantar region of the left foot measuring 11 × 15 mm and three ulcerated papules in the left axilla, buttock, and groin region. The biopsy of the plantar ulcer edge showed positive PCR for *L. braziliensis* and the histopathological analysis showed the presence of amastigotes of *L. braziliensis*, confirming the diagnosis. A successful treatment with meglumine antimoniate was implemented for 30 days, evolving with complete regression of the skin lesions and full healing of the plantar ulcer [1]. In conclusion, we sustain that a round ulcer with raised edges and a granular bottom is the description of the classical presentation of CL, it is located mainly in exposed regions corresponding to the inoculation site of the parasite by the vector insect bite. Ulceration on the plantar region may be considered as an atypical manifestation

of ATL, once the plantar region is not usually accessible to the insect vector, and claims attention to other important differentials diagnosis, such as leprosy, diabetes ulcers and vasculitis. Few reports of CL presentation as plantar ulcers have been described in the literature since it represents an unexposed area of the skin and, furthermore, where the higher thickness of the corneal layer in the volar skin make the inoculation by the vector unfeasible. The histopathological analysis with visualization of the pathogen in the affected tissue and confirmatory PCR analysis are essential in these cases for diagnostic confirmation and implementation of adequate curative treatment. Atypical forms of leishmaniasis are a diagnostic and therapeutical challenge for dermatologists and clinicians around the world.

References

1. Tironi FC, Machado GU, Arruda SM, Machado PRL. Plantar ulcer as an atypical manifestation of cutaneous leishmaniasis. *An Bras Dermatol*.2021.
2. Guimaraes LH, Queiroz A, Silva JA, Silva SC, Magalhaes V, et al. Atypical manifestations of cutaneous leishmaniasis in a region endemic for *Leishmania braziliensis*: clinical, immunological and parasitological aspects. *PLoS Negl Trop Dis*.2016;10: e0005100.
3. Riyaz N, Sehgal VN. Leprosy: trophic skin ulcers. *Skinmed*. 2017;15: 45-51.
4. Machado GU, Prates FV, Machado PRL. Disseminated leishmaniasis: Clinical, pathogenic and therapeutic aspects. *An Bras Dermatol*. 2019;94: 9-16.

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Editorial

Market Analysis on Generic Medicine

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Director, Government & Commercial Strategic Operations at Latham BioPharm Group.

Abstract:

A large number of studies have focussed on the determinants of the entry of generics in the pharmaceuticals market. Most of them focus on the United States market. Much less evidence is found about heavily regulated pharmaceutical markets, such as the Portuguese market. This study uses data from Portugal, for the period 2000–2015. Based on a sample of 50 reimbursable outpatient drugs, that face potential entry of generics, two econometric models were estimated aiming to identify the determinants of entry and penetration of generics. The active substances included were chosen among those that represent the highest financial burden to the National Health System or are the most sold (in volume). To each of those active substances, the most sold pharmaceutical form, dosage, and package size was chosen. Our results suggest that market size is the main determinant of the generics entry. Concerning market penetration, our results show that it is determined by the number of marketed generics, as well as by price differences between brands and generics.

Graphical Abstract:

Frank Orłowski Director, Government & Commercial Strategic Operations at Latham BioPharm Group. As a Retired Executive, Frank worked for over 25 years at Pfizer in positions of responsibility in Finance, Strategy, & Operations. Frank lead the Supply Chain & Finance function across Asia, Middle East, South America & Eastern Europe developing business, operational & financial product localization strategies. He had direct financial control of over \$2 Billion with a team of over 100 in-country operational colleagues across 35 Markets.

Publication of speakers:

1. One Billion USD FCPA Fine imposed by DOJ, but Goldman not admitting any wrongdoing.
2. A Human Perspective – Global Business in the Post COVID-19 World and The New Norm.
3. The Human Factor of the Novel Coronavirus (COVID-19) and Corruption.

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Editorial

Medicine and Infertility

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Abstract

Endometriosis may reflect one of the underlying factors of infertility. This estrogen-dependent disease affects up to 10% of reproductive-aged women and up to 50% of women with infertility. Infertility is a major cause of morbidity in women with endometriosis. Thirty to fifty percent of endometriosis patients face infertility, and the condition reduces fecundity from 15% to 20% per month in healthy women to 2% to 5% per month in women with endometriosis. The exact cause of infertility is not definitively known, both pathologic and iatrogenic causes may exist. It has been hypothesized that several factors (anatomical, immunological, hormonal, genetic and environmental) may play a role in the pathogenesis of this chronic disease. The first step towards an accurate and prompt diagnosis of endometriosis includes physical examination of the pelvis and the abdomen that are followed by the imaging techniques, namely transvaginal sonography, rectal endoscopic sonography and magnetic resonance imaging (MRI), which are mainly employed for infiltrating lesions as well as for the detection of a possible ovarian endometrioma. The ultimate diagnosis could be accomplished through the method of laparoscopy.

Medical therapy can be helpful in managing symptoms, but does not improve pregnancy rates. The role of surgical treatment remains controversial. Superovulation with intrauterine insemination has shown modest improvement in pregnancy rates in women who may have endometriosis. The most effective treatment for endometriosis associated infertility is in-vitro fertilization. Recent focus on proteomics and genetics of the disease may aid in optimizing treatment options.

Graphical Abstract

Mohammad Ebrahim Parsanezhad has graduated from Tabriz Medical School in 1979 and completed Obstetrics and Gynecology Specialty Board at Shiraz Medical School in 1986. He has also completed 2.5 years of Infertility Fellowship at Gotingen University, Diako Medical Centre, Bremen Germany in 2003. He is currently a Professor and Chair, Infertility and Reproductive Medicine Division, Department of Gynecology & Obstetrics, Shiraz University, Iran. He is the Reviewer of Fertility & Sterility Journal, Member of Editorial board in Middle East Fertility Journal, Chairman of Educational Planning of Nursing and Midwifery School, Member of Editorial Board of Iranian Journal of Medical Sciences (IJMS), Member of National OB & GYN Board Examination at Ministry of Health and Medical Education. He has published 106 papers in reputed journals.

Speaker Publications

1. Determining an optimal cut-off value for follicle-stimulating hormone to predict microsurgical testicular sperm extraction outcome in patients with non-obstructive azoospermia” Archives of Endocrinology and Metabolism 64(AHEAD);
2. “The effect of antidepressant treatment on the HPA axis, changes in depression score and serum levels of TNF- α in depressed infertile women” Revista de Psiquiatria Clínica

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The Prevalence of Anorectal Disorders among Residents of Kirtipur Municipality in Nepal

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Abstract

Background: Epidemiological knowledge is very poor in regards to anorectal disorders. The patients do not often discuss perianal symptoms leading to late diagnosis and treatment. There is a need of doing systematic questioning and clinical evaluation of the population to assess the prevalence of anorectal disorders.

Aim and objectives: The aim of this study is to assess the prevalence of anorectal disorders among the residents of Kirtipur municipality in Nepal.

Methods: The first section was the cross-sectional survey to assess the demographic and lifestyle characteristics of the study population. The second section was the observation study to assess the prevalence of anorectal symptoms. 1483 patients were recruited from 10 wards of Kirtipur municipality. We analyzed the comparison of diagnostic approach between patients with perianal symptoms spontaneously visited and those revealed after targeted questioning. We further analyzed the reason for not performing perianal examination by both patients and general practitioners. Factors associated with referral to a proctologist and diagnosis rate were also evaluated.

Results: The study showed that the prevalence of anorectal symptoms increased from 9.4% to 21.2% after systematic targeted questioning by general practitioners. Spice intake was the only covariate associated with decrease risk of proctological symptoms. Haemorrhoids (31.2%) and anal fissure (28.7%) were the most prevalent anorectal disorders. However, physicians have diagnosed anorectal disorders in 20.2% of patients without performing any perianal examination. Diagnosis of haemorrhoids and fistula in ano were significantly associated with referral to a proctologist.

Conclusion: This study may contribute to epidemiological knowledge about the prevalence of anorectal disorders among Nepalese population.

Keywords: Anorectal disorders; Prevalence; Nepal

Abbreviations

NARTC: National Ayurveda Research and Training Center; CI: Confidence Interval; OR: Odds Ratio; SPSS: Statistical Package for Social Sciences; ENT: Ear: Nose and Throat; VDC: Village Development Committee.

Background

Anorectal disorders are one of the most common reluctant disorders and affect about one-fourth of the population [1]. Anorectal disorders are either structural or functional abnormalities of the pelvic floor in patients with symptoms, such as difficulty in defecation, fecal incontinence, rectal bleeding, anorectal pain, and rectal prolapse [2,3]. Anorectal disorders include benign conditions such as haemorrhoids to severe conditions such as anorectal cancers. The most common anorectal disorders are haemorrhoids, anal fissures, anorectal abscesses and fistulae, fecal incontinence and pruritus ani. A careful history taking of presenting symptoms, visual inspections, digital rectal examinations along with relevant tests help in diagnosis of anorectal disorders [4].

Most of the studies have evaluated anorectal disorders based only on questionnaires and without any clinical examinations of the patients. Thus, the prevalence of anorectal disorders differs from 20% to 40.5% [5-7]. Most of the patients are reluctant to disclose the anorectal problems and do not seek medical attention [8-11]. Furthermore, physicians seldom performed the perianal examination [10]. Anorectal disorders seem to increase progressively and their prevalence in the general population probably tends to be higher than seen in clinical practice. After targeted systematic questioning to the patients, the prevalence of proctological symptoms seems to be increased [10,11].

In context of Nepal, one study showed 2.0% of individuals over 18 years old who have experienced rectal bleeding [12]. The study focused on anorectal disorders is very rare in Nepali population. Therefore, we aim to design the study to assess the prevalence of anorectal disorders by systematic questioning and clinical examination among residents of Kirtipur municipality in Nepal.

Materials and Methods

Study design

The study was conducted according to the national ethical guidelines for health research in Nepal [13]. The ethics committee of the National Ayurveda Research and Training Center (NARTC) approved the study protocol. The study design consisted of two sections. The first section was a cross-sectional survey among usual members of households in Kirtipur municipality. Hundred households were randomly selected from each ward of Kirtipur municipality. Any two eligible participants of the households were interviewed for demographic and lifestyle questionnaires after receiving a verbal consent. The participants were then asked to visit NARTC at Kirtipur for their health examination.

The second section was a descriptive study. Systematic questioning and clinical examinations of those participants who visited NARTC at Kirtipur were recorded. Health professionals of NARTC performed the systematic questioning of perianal symptoms and clinical examination. The study participants were recruited from each ward of Kirtipur municipality and the study duration were carried for eight weeks at NARTC.

Study participants

The eligible participants for the study were those aged 18 years and above who were usual members of the selected households in Kirtipur municipality and gave informed consent for the study. We included the participants who were those aged 18 years old and above residing in Kirtipur municipality and gave informed consent. Participants were excluded for the following criteria: those with aged less than 18 years old and have undergone recent major surgical procedure; and pregnant women.

Tools and procedures

Training of field staff: The main training for the study was started on January 24, 2020 at NARTC. The training included orientation on anorectal disorders and on use of questionnaires. Expert proctologists gave the training on anorectal disorders and study design, respectively. Two volunteer female members from each ward and 10 staff members of NARTC participated in the training program. Field work: The fieldwork for the study was started from January 29, 2020. One representative from each ward along with one field staff of NARTC visited on randomly selected 100 households of respective ward for the survey. The interviewer representing NARTC filled the demographic and lifestyle related questionnaires of the participants. The interviewer invited each verbally consented participant to visit NARTC for the clinical examination by health professionals. They provided referral card with a code number for the consented participants [Appendix 1]. The participants were asked to visit at NARTC hospital with respective timeframe and days. For instance, ward 1 and ward 2 were invited to visit within February 9 to 15, 2020 between 10:00 am to 4:00 pm.

Health professional recruitment: All the registered doctors working at NARTC took part in the second section of the study design. Health professionals asked systematic questioning of anorectal symptoms and did proper clinical evaluation [Appendix 2]. The questionnaires were adopted from the questionnaire prepared by Abramowitz et al. and Tournu et al., and modified as requirement [10,11].

Prior to the study, medical lecture on anal disorders was given to all the doctors taking part in the research.

Outcome measures: The primary outcome measure was the prevalence of anal symptoms and diagnosis approach.

Secondary outcomes monitored were demographic characteristics and behavioral factors of the study participants.

Statistical analysis: Characteristics for categorical variables were expressed as frequencies and that for continuous variables were shown as a median and range, or mean (standard deviation). Chi-square test was used to compare the distribution of qualitative variables. But, Fisher's exact test was used when expected frequencies is less than 5 in frequency table. We calculated the exact Clopper-Pearson confidence interval (CI) for the observed proportion [14,15]. Logistic regression analysis was used to estimate the odds ratio (OR) and the 95% CI for the association between lifestyle factors and proctological symptoms. Statistical significance was declared if the two-sided p value <0.05. Statistical analyses were carried out using Statistical Package for Social Sciences (SPSS).

Results

The median age of the participants was 45 years (range 18-83 years). Out of 1483 participants, 483 (33%) and 1000 (67%) participants were male and female, respectively. Participants predominantly belonged to indigenous ethnicity (71.9%) with Chhetri 17.6%, Brahman 7.6%, Madheshi 0.8% and others 2.0%.

139 patients (9.4%) visited spontaneously for a proctological problem (median age: 40 years; range: 18 – 80 years), whereas 1344 (90.6%) visited for other problems than proctological symptoms (median age: 46 years; range 18 – 83 years). Among those visited other than a proctological problem, 175 patients (11.8%) reported proctological symptoms after systematic questioning. Thus, following systematic questioning to investigate possible anorectal disorders, 314 patients had proctological symptoms (21.2%, 95% CI: 19.14% -23.37%) with a mean age of 45.5 years.

Demographic characteristics of patients with or without proctological symptoms after targeted questioning are shown in Table 1. Likewise, association between lifestyle factors and proctological symptoms are shown in Table 2. There was no statistically significant association between lifestyle factors and proctological symptoms except for intake of spice. Intake of spice showed a statistically significant decrease in odds of proctological symptoms (OR, 0.74; CI, 0.57 – 0.96) when compared with non-spice intake (Table 2).

Of the 1344 patients visited for other disorders, 20.6% were seen for rheumatology, 16.4% for gastroenterology, 8.5% for endocrinology, 8% for gynaecology and obstetrics, 7.1% for neurology, 6.8% for ear, nose and throat (ENT), 4.7% for respiratory, 4.1% for dermatology, 4.0% for cardiology and 5.8% for other disorders, such as psychiatry, ophthalmology, nephrology, urology and haematology. Among 175 patients who revealed proctological symptoms after systematic questioning, 29.7% for gastroenterology, 20.6% for rheumatology, 8.0% for gynaecology and obstetrics, 6.9% for neurology, 5.1% for dermatology, 4.6% for endocrinology, 4.0% for urology, 3.4% for ENT, 2.3% for cardiology, 2.3% for respiratory and 13.3% for psychiatry, nephrology, haematology and other disorders were reported. Some patients had more than one reason for consultation, but we analyzed only for one primary reason for consultation based on chief complaints of the patients.

After targeted questioning, the frequency of anal symptoms revealed by patients were constipation (43.0%); pain/burning during/after defecation (36.3%), bleeding (30.9%), perianal mass (22.0%), pruritus ani (21.3%), diarrhoea (1.3%), perianal discharge and uncontrolled (0.6%) anal leakage (0.6%). Haemorrhoids (31.2%) was the most prevalent anorectal disorder followed by anal fissure (28.7%), fistula in ano (2.2%), dermatological disorder in perianal region (2.2%), and perianal wart (0.9%). 109 cases (34.7%) was not diagnosed as anorectal disorders. Based on diagnosis approach by proctological symptoms; of 97 patients who reported symptoms of anal bleeding, haemorrhoids and

anal fissure were diagnosed in 44 patients (45.4%) and 47 patients (48.5%), respectively. Of the 67 patients who had pruritus ani, 27 patients (40.3%) were diagnosed with haemorrhoids and 24 patients (35.8%) with anal fissure. Of the 114 patients with complaints of perianal pain, 45 patients (39.5%) diagnosed with haemorrhoids and 57 patients (50%) diagnosed with anal fissure. Of the 69 patients who presented with perianal mass, 61 patients (91%) had haemorrhoids. Examination of the perianal region, digital rectal examination and proctoscopy was performed in 118 (37.5%), 66 (21.0%) and 6 (1.9%) patients, respectively.

With regard to perianal symptoms, bleeding, perianal pain, perianal mass and constipation showed statistically significant differences between patients spontaneously consulting for proctological symptoms and patients who revealed proctological symptoms by questioning. Constipation seemed to be less likely proctological symptom for the patients to visit spontaneously for consultation (Table 3).

Digital rectal examination was significantly more prevalent in patients spontaneously consulting for proctological symptoms than patients who revealed proctological symptoms by questioning (Table 3). Diagnosis of haemorrhoids was significantly better in patients who visited spontaneously for a proctological problem in compared with patients who had proctological symptoms after targeted questioning (Table 3). There was a statistically significant difference in past history of treatment between spontaneously visiting patients for a proctological problem and patients visiting for other reasons (Table 3).

After an anal disorder diagnosis by the general practitioner, only 77 cases (24.5%) were referred to a proctologist. Factors of perianal symptoms significantly associated with referral to a proctologist were bleeding, pain, and perianal mass. Constipation symptoms were significantly associated with non-referral to a proctologist (Table 4). In context of diagnoses, there was a statistically significant association between haemorrhoids and fistula in ano and referral to a proctologist. For diagnostic tools, digital rectal examination and proctoscope were significantly associated with referral to a proctologist, while questioning was significantly associated with non-referral to a proctologist (Table 4).

Diagnosis and non-diagnosis rate when compared with performing perianal examination (digital rectal examination and proctoscopy also included) was 94.7% versus 5.3% (Fig not shown). Not performing perianal examination resulted in decreased risk of diagnosis rate with a Relative Risk (RR) 0.21 (95% CI: 0.15 – 0.30).

Degree of pain and discomfort induced by perianal symptoms were reported in 150 and 214 patients, respectively. Pain and discomfort in the patients were 3 out of 10 (range 1-10) and 2 out of 10 (range 1-9), respectively. There was no difference in median of pain between patients consulting spontaneously for perianal symptoms and patients revealing perianal symptoms after targeted questioning 3 out of 10 (range 1-10). Likewise, there was no difference in the median of discomfort rate in perianal symptoms between patients visiting spontaneously for proctological problems and patients visiting for other reasons.

Of 314 patients having perianal symptoms, examination was not done in 124 patients whereas digital rectal examination was not done for 242 patients for various reasons (Table 5). 60 patients refused to undergo the perianal examination and the most frequent reason being discomfort (38.3%) followed by anal symptoms considered of minor importance (31.7%). Absence of indication (49.5%) and patient's reluctance (26.4%) were the two primary reasons for not performing digital rectal examination. However, 48 patients who were reluctant to do digital rectal examination had consented for perianal examination.

Of 314 patients who had proctological symptoms, only 104 individuals (33.1%) had visited to a health facility or seen a doctor for the proctological problem (Fig not shown). Among 104 individuals who had treatment history for proctological symptoms; 57 patients had allopathy treatment, 39 patients had ayurveda treatment, 6 patients had done surgical management and 2 patients had homeopathy treatment (Fig not shown). With regard to diagnosis; out of 98 patients with haemorrhoids, 23 patients (23.5%) were treated with allopathy medicine, 24 patients (24.5%) were treated with ayurveda medicine, 5

patients (5.1%) had surgical management and 1 patient (1.0%) had homeopathic medicine. In 90 patients with anal fissures, 21 patients (23.3%) had treatment history of allopathy medicine and 8 patients (8.9%) had treatment history of ayurveda medicine. In 7 patients with fistula, 5 patients (71.4%) had allopathy treatment, 1 patient (14.3%) each had homeopathy treatment and ayurveda treatment.

Proportion of patients with proctological symptoms not to go to a health facility before was no need 41.0%, feel ashamed 29.0%, fear/no trust 17.1%, no time 12.4% and no money for healthcare 0.5% (Fig not shown). The impact in the patient's daily life from the proctological symptoms was also assessed. Of the 314 patients, 196 patients (62.4%) revealed the condition is not disabling; 102 patients (32.5%) reported no able to work like he/she used to and 12 patients (3.8%) need help with daily living (Fig not shown).

Discussion

To our knowledge, the present study is the first comprehensive study to assess the prevalence of anorectal disorders in Nepal. The study showed that the prevalence of anorectal symptoms increased from 9.4% to 21.2% after systematic targeted questioning by general practitioners. Spice intake was the only covariate associated with decrease risk of proctological symptoms. Haemorrhoids (31.2%) and anal fissure (28.7%) were the most prevalent anorectal disorders. However, physicians have diagnosed anorectal disorders in 20.2% of patients without performing any perianal examination. Diagnosis of haemorrhoids and fistula in ano were significantly associated with referral to a proctologist.

The prevalence of perianal symptoms increased from 9.4% to 21.2% after systematic targeted questioning by general practitioners in our study. A study by Nelson et al. showed the prevalence of anal symptoms was 20.0% [5]. There was also a high incidence of anal symptoms in patients from 2.0% to 14.2% following targeted questioning [10]. In another cohort of 1061 patients, after questioning all patients the prevalence of perianal symptoms increase from 2.3% to 15.6% [11]. This shows the fact that perianal symptoms are not well presented by patients and underestimated by the physicians not only in Nepalese population but also in another study population.

In the present study, the frequency of female patients is higher than male patients (67.4% vs. 32.6%). Some previous studies showed that the prevalence was higher for female than male [5-7,9,10], whereas prevalence was higher in male than female in other studies [8,11]. The increase of female participants in our study is more likely to occur because during time of survey female respondents were highly available at their residence than male. Likewise, indigenous ethnicity was predominant in the study population because Newar community which belongs to indigenous group largely reside in the study area [14]. There was no significant association between demographic characteristics and proctological symptoms in our study. But, we have found one study in Nepalese population which showed occupation was associated with rectal bleeding for homemakers, non-government employees and government employees, when compared to those who are unemployed [12]. Tessler et al. showed that the prevalence of rectal bleeding among Nepalese population over 18 years was 2.0% [12]. Our study is inconsistent with this finding and reported 6.5% patients over 18 years had symptoms of bleeding. The randomly selected population in the present study was from one particular municipality whereas the previous study has randomly selected from 3 Village Development Committees (VDC) of 15 districts proportional to population. Thus, inconsistency between the studies in Nepalese population in prevalence of rectal bleeding may have occurred due to ethnic variability. The majority of patients who did not seek health facility cited their primary reason as no need followed by feel ashamed and fear/no trust as that of previous study [12]. Thus, the proctological symptoms are considered to be of minor importance and reluctant disorders in Nepalese population. These findings may suggest importance of comprehensive epidemiological study to assess the prevalence of anorectal disorders among the population.

This is also the first study to assess the relationship between lifestyle factors and anorectal disorders in Nepalese population. However, in the present study intake of spice was significantly related

with decrease in proctological symptoms when compared to those who do not intake spice (ORs, 0.74; CI, 0.57–0.96). Other lifestyle factors exercise, alcohol consumption, tobacco users and meat consumption was not significantly associated with proctological symptoms. In study by Pigot et al., perianal symptoms were associated with ingestion of spices and alcohol [7]. Nonetheless, in one retrospective study, haemorrhoids and anal fissure was associated with consumption of spices or alcohol and physical activity in another population [13]. Current status of lifestyle activities at the time of interview may have resulted inconsistent findings in our study. To elucidate the association between lifestyle factors and anorectal disorders, retrospective study is more appropriate.

Proctological symptoms in the study were constipation (43.0%); pain/burning during/after defecation (36.3%), bleeding (30.9%), perianal mass (22.0%), pruritus ani (21.3%), diarrhoea (1.3%), perianal discharge (0.6%) and uncontrolled anal leakage (0.6%). Common anal symptoms revealed by Tournu et al. were bleeding (46.4%), anal pruritus (44.6%), pain (34.3%), constipation (30.1%), anal swelling (27.1%), anal discharge (10.2%) and uncontrolled anal leakage (9%) [11]. Likewise, Abramowitz et al. reported perianal symptoms were: constipation (33.3%), bleeding (32%), pain (31%), pruritus ani (22%), swelling (22%), oozing (14%) and anal discharge (14%) [11]. Similarly, another study showed the prevalence of perianal symptoms were pain (48%), bleeding (37%), swelling (26%) and pruritus ani (24%) [7]. Bleeding, pain, pruritus ani, swelling and constipation are commonly prevalent perianal symptoms similar to previous studies [2,3,7,10,11]. Despite having perianal discharge and uncontrolled anal leakage less prevalent proctological symptoms similar to other studies, our study tentatively has much less prevalence of these symptoms when compared with other studies. This might suggest anal incontinence varies significantly among different races as such South Asian versus European population.

Like previous studies, significant differences were found in pain and perianal swelling between those visited for proctological consultation and those visited for other reasons. There is also increase in frequency of constipation among those who revealed proctological symptoms after questioning, similar to the study by Abramowitz et al. [10].

In our study, digital rectal examination was significantly more frequent in patients visiting spontaneously for a proctological problem when compared with patients visiting for other reasons. This finding suggested patients who spontaneously visited for perianal symptoms were better clinically investigated than the patients who revealed perianal symptoms after questioning [10].

In this study, haemorrhoids (31.2%) was the most prevalent anorectal disorder followed by anal fissure (28.7%). The sequence of prevalence of anorectal disorders in our study was similar in previous studies [1,4-7,10,11,15,16]. Even though, there is disparity among races of study population, the trend of prevalence of anorectal disorders did not vary globally. However, 34.7% of patients had no diagnosis in the present study. Only 60.5% of those with perianal symptoms were performed perianal examination by the physicians. Nonetheless, our study shows that diagnosis and non-diagnosis rate when compared with performing perianal examination was 94.7% versus 5.3%. This suggests similar findings of the importance of the examination in the diagnosis approach [11]. Of the 69 patients who presented with perianal mass, 61 patients (91%) had haemorrhoids. Similar result was found in another study where all anal swelling 94% was attributed to haemorrhoids [10]. studies have also shown that anal pain is often secondary to an anal fissure rather than anal disease [17]. This reason is very relevant to our study, where 50% of the patients with anal pain had anal fissure.

In this study, 104 patients had past history of treatment. Proctological complaints are a reason for repeated visits to the general practitioner and lead to repeated prescriptions [7].

Anal incontinence was the only factor that was associated with referral to a proctologist [10]. Nonetheless, our data showed bleeding, pruritus ani, pain and constipation were the factors associated with referral to a proctologist. This dissimilarity may be due to prevalence of anal incontinence in our

study population (1.3%) is tentatively lower than the previous study. However, all the patients with anal incontinence have been referred to a proctologist in this study. Diagnosis of haemorrhoids and fistula in ano are only anorectal disorders that showed statistically significant association with referral to a proctologist. This diagnostic factors influencing referral to a proctologist were not found in the study by Abramowitz et al. [10]. Digital rectal examination and proctoscope were the diagnostic tools referred to proctologist. Hence, the prevalence of anorectal disorders' diagnosis is more likely to be precise in the present study.

In this study, 39.5% of patients did not perform anal examination. 19.1% patients refused to undergo the perianal examination and the most frequent reason being discomfort (38.3%) followed by anal symptoms considered of minor importance (31.7%). Similar results were shown in the previous studies [18]. Absence of indication (49.5%) and patient's reluctance (26.4%) were the two primary reasons for not performing digital rectal examination in our study. In addition to these two primary reasons, fear of causing pain was the main reason for not performing digital rectal examination in another study [11]. Hence, physician's motivation to influence the patients is very important in performing perianal or digital rectal examination.

We also evaluated the impact on patients having perianal symptoms like a study by Tourneau et al. But, for our patients, the mean discomfort was 3 unlike the previous study [11].

Patients are reluctant to reveal their perianal symptoms even when they consult with their general practitioners. This is not just limited to patients, but general practitioners usually do not perform clinical examination of perianal region. Eventually, this underestimation by patients and physicians in regards to anorectal disorders may lead to late diagnosis and complications of anorectal disorders. Similarly, screening for anorectal disorders seems to be a major problem in late diagnosis of anorectal disorders for instance rectal cancer. Most of the patients with perianal symptoms were not referred to a specialist. Despite having prominent perianal symptoms for further investigation, indication of colonoscopy was not prescribed in our study. Spread of awareness about the frequency of anal disorders and its complications due to late diagnosis is crucial role for both patients and physicians. Late diagnosis of anal fissure and haemorrhoids can lead to fecal incontinence and complications due to necessary surgery, respectively. Likewise, there is probable risk of avoiding anorectal cancer if systematic screening is not applied [19].

To best of our knowledge, this is the first comprehensive study to assess the prevalence of perianal symptoms and disorders in Nepalese population. The study population is randomly selected and has fairly large sample size in compare to previous studies done in different countries. We adopted the simple and brief questionnaires of our study from the previous studies elucidating epidemiological values and easy comparisons between the studies [20-23]. This study unavoidably has several limitations. The sample population was recruited from 10 wards of one municipality in Nepal. The lifestyle and demographic characteristics vary largely according to geographical location in Nepal. Thus, the sample may not represent and validate the extrapolation of our findings even in Nepalese population. Participation rate was lower than targeted (74.2%), minimizing the study's strength. The female health volunteers and health workers of the institution who surveyed the first questionnaire were likely to be familiar about the study. The participants who gave informed consent for the study may indicate volunteer bias. Physicians, involved in reporting the questionnaires and diagnoses of the anorectal disorders, were aware of our study design and it may have resulted biased outcome. Only 24.5% of patients having proctological symptoms were referred to a proctologist and thus only few cases were confirmed diagnoses. We cannot also draw a clear inference of causality between diagnostic approaches and proctological symptoms.

Conclusion

This study reports that the prevalence of perianal symptoms increased from 9.4% to 21.2% after

systematic targeted questioning. Despite patients with perianal symptoms, 39.5% of patients still did not undergo any perianal examination by patient's reluctance and physician's consideration of perianal symptoms to be of minor importance. It is of noteworthy that performing perianal examination is associated with higher diagnosis rate (94.7% vs. 5.3%). Hence, to elucidate the prevalence of anorectal disorders and its management, it is very important to educate both patients and physicians about perianal symptoms' diagnostic approach and complications.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Yadav R and Joshi AM conceived and designed the study. Shrestha S and Joshi AM carried out literature search, interpretation of data and drafted the manuscript. Shrestha S, Shrestha J and Joshi AM participated in study design and edited the manuscript. All authors have seen and approved the final manuscript.

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References

1. Wu JM, et al. "Prevalence and trends of symptomatic pelvic floor disorders in U.S. women". *ObstetGynecol* (2014);123: 141–148.
2. Pfenninger JL. "Common anorectal conditions: Part I. Symptoms and complaints". *Am Fam Physician* (2001);63: 2391–2398.
3. Patcharatrakul T. "Update on the pathophysiology and management of Anorectal Disorders". *Gut Liver*. 2018;12: 375–384.
4. Foxx-Orenstein AE. "Common anorectal disorders". *GastroenterolHepatol (NY)* (2014);10: 294–301.
5. Nelson RL et al. "Prevalence of benign anorectal disease in a randomly selected population". *Dis Colon rectum* (1995);38: 341–344.
6. Siproudhis L, Pigot F, Godeberge P, Damon H, Soudan D et al. "Defecation Disorders: a French populationsurvey". *Dis Colon rectum*. (2006);49: 219–227.
7. Pigot F, et al. "Ano-rectal complaints in general practitioner visits: consumer point of view". *GastroenterolClinBiol* (2006);30: 1371–1374.
8. Hennigan TW, et al. "Rectal examination in general practice". *BMJ* (1990);301: 478–480
9. Damon H, Guye O, Seigneurin A, Long F, Sonko A. "Prevalence of anal incontinence in adults and impact on quality of life". *GastroenterolClinBiol* (2006);30: 37–43.
10. Abramowitz L, Benabderrahmane M, Pospait D, Philip J, Laouénan C. "The prevalence of proctological symptoms amongst patients who see generalpractitioners in France". *Eur J Gen Pract* (2014);20: 301–306.
11. Tournu G, et al. "Prevalence of anal symptoms in general practice: a prospective study". *BMC Fam Pract* (2017);18: 78.
12. Tessler R, Gupta S, Pathak J, Ghimire P, Kingham TP, et al. "Rectal bleeding and implications for surgical care in Nepal". *J Surg Res* (2015);197: 12–17.
13. Pigot F, et al. "Risk factors associated with hemorrhoidal symptoms in specialized consultation". *GastroenterolClinBiol* (2005);29: 1270–1274.
14. Ravindranath GG, et al. "Prevalence and risk factors of hemorrhoids: a study in a semi-urban centre". *IntSurg J* (2018);5: 496–499.

15. Basava AH, et al. "Demography, epidemiology, clinical presentations, diagnoses and management of various anorectal diseases: An article review". *Journal of Universal Surgery* (2019);7: 1–3.
16. Everhart JE, et al. "Burden of digestive diseases in the United states part II: lower gastrointestinal diseases". *Gastroenterology* (2009);136: 741–754.
17. "Nepal Demographic and Health Survey 2016". Kathmandu, Nepal: Ministry of health. Ministry of health, Nepal; New ERA and ICF (2017).
18. Government of Nepal, National Planning Commission, Central Bureau of statistics. Local Unit; Population and household data of Kathmandu: Kirtipur Municipality.
19. Clopper CJ, et al. "The use of confidence or fiducial limits illustrated in the case of the binomial". *Biometrika* (1934);26: 404–413.
20. Fleiss JL, et al. "statistical methods for rates and proportions 3rd Edition" (2003);10: 26.
21. "Ethical guidelines for health research in Ayurveda 2013". Ministry of Health, Nepal (2013).
22. Villalba H, et al. "Anal fissure: A common cause of anal pain". *Perm J.* (2007);11: 62–65.
23. Springall RG, et al. "General practitioner referral of patients with lower gastrointestinal symptoms". *J R Soc Med* (1988);81: 87–88.

Table 1: Demographic characteristics of patients with and without proctological symptoms.

D e m o g r a p h i c characteristics	Frequency with proctological symptoms n (%)	Frequency without proctological symptoms n (%)	Total patients n
Sex			
Male	120 (24.8)	363 (75.2)	483
Female	194 (19.4)	806 (80.6)	1000
Ethnicity			
Brahman	27 (23.9)	86 (76.1)	113
Chhetri	46 (17.6)	215 (82.4)	261
Indigenous	227 (21.3)	840 (78.7)	1067
Madhesi	4 (33.3)	8 (66.7)	12
Others	10 (33.3)	20 (66.7)	30
Education			
Primary	65 (23.5)	212 (76.5)	277
Lower secondary	66 (26.4)	184 (73.6)	250
Higher secondary	43 (21.9)	153 (78.1)	196
Graduate and above	62 (24.9)	187 (75.1)	249
None	78 (15.8)	433 (84.7)	511
Occupation			
Farmer	13 (15.9)	69 (84.1)	82
Business	80 (27.6)	210 (72.4)	290
Government employee	23 (29.1)	56 (70.9)	79
Private employee	39 (23.8)	125 (76.2)	164
Housewife	106 (17.8)	488 (82.2)	594
Student	24 (14.6)	140 (85.2)	164
Retired	7 (22.6)	24 (77.4)	31
None	22 (27.8)	57 (72.2)	79

Table 2: Association between lifestyle factors and proctological symptoms in patients OR, odds ratio; CI, confidence interval.

Lifestyle factors	Patients with proctological symptoms (n)	Patients without proctological symptoms (n)	OR (95% CI)*	p – value
Exercise				
No physical activity	190	721	reference	
Physical activity	124	448	1.06 (0.81 – 1.38)	0.698
Alcohol				
Non-alcohol consumers	189	761	reference	
Alcohol consumers	125	408	0.88 (0.66 – 1.18)	0.391
Tobacco				
Non tobacco users	259	1014	reference	
Tobacco users	55	155	0.83 (0.56 – 1.23)	0.355
Meat				
Vegetarian	27	117	reference	
Non-vegetarian	287	1052	0.83 (0.56 – 1.46)	0.712
Spice				
No spice intake	161	695	reference	
Spice intake	153	474	0.74 (0.57 – 0.96)	0.024

*Adjusted for sex, ethnicity, education, occupation, and exercise, intake of alcohol, tobacco, meat and spice

Table 3: Comparison of diagnostic approach for patients spontaneously consulting for proctological problems versus patients who revealed proctological symptoms by questioning.

Diagnostic approach	Patients spontaneously consulting for proctological symptoms (n=139)	Patients who revealed proctological symptoms by questioning (n=175)	p –value*
	n (%)	n (%)	
Perianal symptoms			
Bleeding	52 (37.4%)	45 (25.7%)	0.026
Pruritus ani	36 (29.7%)	31 (37.3%)	0.079
Pain/Burning during/after defecation	71 (51.1%)	43 (24.6%)	<0.001
Perianal mass	50 (36.0%)	19 (10.9%)	<0.001
Perianal discharge	0 (0.0%)	2 (1.1%)	0.505+
Uncontrolled anal leakage	0 (0.0%)	2 (1.1%)	0.505+
Constipation	24 (17.3%)	93 (53.1%)	<0.001
Diarrhoea	1 (0.7%)	3 (1.7%)	0.633+
Examinations			
Examination of perianal region	60 (43.2%)	58 (33.1%)	0.069
Digital rectal examination	44 (31.7%)	22 (12.6%)	<0.001
Proctoscope	3 (2.2%)	3 (1.7%)	1.000+
Diagnoses			
Haemorrhoids	61 (43.9%)	37 (21.1%)	<0.001
Anal fissure	46 (33.1%)	44 (25.1%)	0.122
Ano-rectal abscess/ Fistula in ano	5 (3.6%)	2 (1.1%)	0.248+
Dermatology disease	0 (0.0%)	7 (4.0%)	0.019+
Perianal wart	0 (0.0%)	3 (1.7%)	0.257+
Treatment			
Past history of treatment	66 (47.5%)	38 (21.2%)	<0.001

*Chi-square test for p-value +Fisher's exact test for p-value

Table 4: Factors associated with referral to a proctologist

*Chi-square test for p – value

+Fisher's exact test for p – value

Factors	Referral to a proctologist	Non referral to a proctologist	p – value*
	(n=77) n (%)	(n=237) n (%)	
Perianal symptoms			
Bleeding	39 (50.6%)	58 (24.5%)	<0.001
Pruritus ani	17 (22.1%)	50 (21.1%)	0.855
Pain	51 (66.2%)	63 (26.6%)	<0.001
Perianal mass	33 (42.9%)	36 (15.2%)	<0.001
Anal discharge	2 (2.6%)	0 (0.0%)	0.060+
Anal leakage	2 (2.6%)	0 (0.0%)	0.060+
Constipation	15 (19.5%)	120 (50.6%)	<0.001
Diarrhoea	0 (0.0%)	4 (1.7%)	0.575+
Diagnoses			
Haemorrhoids	49 (63.6%)	49 (20.7%)	<0.001
Anal fissure	17 (22.1%)	73 (30.8%)	0.141
Fistula in ano	6 (7.8%)	1 (0.4%)	0.001+
Dermatological disease	0 (0.0%)	7 (3.0%)	0.201+
Perianal wart	0 (0.0%)	3 (1.3%)	1
Diagnostic tools			
Questioning	9 (11.7%)	115 (48.5%)	<0.001
Perianal examination	22 (28.6%)	96 (40.5%)	0.06
Digital rectal examination	41 (53.2%)	25 (10.5%)	<0.001
Proctoscope	5 (6.5%)	1 (0.4%)	0.004+

*Chi-square test for p – value +Fisher's exact test for p – value

Table 5: Proportion of reasons for not performing digital rectal examination

Reasons	Patients (n%)
Patients refused the perianal examination (n = 50)	
Discomfort	23 (38.3%)
Anal symptoms considered of minor importance	19 (31.7%)
Examination already performed for the symptom	5 (8.3%)
Lack of time	4 (6.7%)
Knowing the examination would be repeated by the specialist	2 (3.3%)
Other	7 (11.7%)
General physicians did not propose a digital rectal examination (n= 182).	
Fear of causing pain	16 (8.8%)
Absence of indication	90 (49.5%)
Patient's reluctance	48 (26.4%)
Embarrassment	21 (11.5%)
Lack of knowledge	1 (0.5%)
Lack of time	6 (3.3%)
Other	0 (0.0%)

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Editorial

A retrospective analysis of the oncological outcomes of T3a Renal Cell Carcinomas which have undergone Partial Nephrectomy

Theo Reback

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Introduction:

Radical Nephrectomy is the gold standard surgical approach for T3a Renal Cell Carcinomas. However, a small but not insignificant number of patients pre-operatively staged cT1/cT2 are treated with a partial nephrectomy but at final pathology are subsequently upstaged to pT3a.

Materials and Method:

Data was collected retrospectively using the Royal Free database. 16 of the 306 partial nephrectomies demonstrated stage T3a at final histology. Primary outcome analysed was Recurrence-Free Survival. Secondary outcome analysed was Renal Function Preservation (post-operative eGFR/ pre-operative eGFR).

Results:

Of the 16 patient, 14 patients presented with localised T3a RCC at presentation with an average follow up of 17.3 months. No evidence of local or metastatic recurrence was found in this series of 14 patients. 2 patients were excluded as they presented with metastatic disease. This study found a respectable Renal Function Preservation. In this series, the eGFR \pm SD (mL/min/1.73m²) was 77.3 \pm 18.8 pre-operatively and 69.7 \pm 19.7 post-operatively, displaying a Renal Function Preservation (post/pre eGFR) of 90.2%.

Conclusion:

This pilot study concluded that a partial nephrectomy is oncologically safe for certain T3a kidney renal cell carcinomas. The main implications are that: 1) Current practice should shift and start considering a partial nephrectomy in certain selected patients with clinical T3a tumours, especially in patients with imperative reasons for nephron-sparing surgery as long as a negative margin can be achieved. 2) This study seeks to advise that surgeons should not be deterred from carrying out a partial nephrectomy for fear of pathological upstaging.

Abbreviations:

PN: Partial Nephrectomy

RN: Radical Nephrectomy

RCC: Renal Cell Carcinoma

cT3a: clinically staged T3a

pT3a: pathologically staged T3a

RFS: Recurrence-Free Survival

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