

Clinical Presentation and Associated Factors of Lower Limb Chronic Venous Insufficiency at a Tertiary Hospital in Uganda: A Cross-Sectional Study

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Abstract

Background: Lower limb chronic venous insufficiency (CVI) is a common disorder associated with sequelae of changes that lead to varicose veins and skin trophic changes. There is limited data on potential associated factors from representative studies yet its burden and impact on the quality of life is quite significant. We evaluated the clinical presentation and associated factors of lower limb CVI among patients at Mulago National Referral Hospital (MNRH).

Methods: We conducted a cross-sectional study of 104 consecutive participants with CVI aged ≥ 18 years attending the outpatient clinics of MNRH. Limbs of participants with history of surgery pertaining to CVI were excluded. We recorded information on demographics, relevant medical history, symptoms, lifestyle and clinical presentation. We described CVI using the clinical and anatomical components of the clinical-etiological-anatomical and pathophysiologic (CEAP) scale. Data was analyzed at both bivariate and multivariate levels using Stata version 14.1

Results: Altogether, 104 participants were enrolled with a male: female ratio of 2:1, age range of 18 to 85 years and median age of 43 years. The commonest venous symptoms included; venous pain (96.2%), sensation of swelling (93.3%) and heaviness (79.8%). Of the 146 affected limbs, CEAP clinical class included; C0:59.6%, C1:40.4%, C2:80.8%, C3:88.5%, C4:73.1%, C5:30.8%, C6:51.9%. The anatomical class identified superficial veins in 138 (90.5%), deep veins in 46 (29.7%) and perforator veins in 122 (79.7%) affected limbs. Men had significantly higher proportions of skin trophic changes 88.7% vs 63.6% ($p=0.003$) while females had significantly higher proportions of venous symptoms compared to men 57.6% vs 32.4% ($p=0.015$). All participants with a smoking history had skin changes. Obese and overweight patients had higher proportions for venous symptoms 13 (54.2%) and 14(50%) respectively as compared to those who had a normal BMI 14(28.6%).

Conclusions: Most participants are symptomatic with advanced disease, young and predominantly male. Males had 4.5 times higher odds of having skin changes as compared to females. Although some associated factors such as age, gender are immutable, others can be modified, such as physical activity, cigarette smoking.

Keywords: Chronic Venous Insufficiency, CEAP Scale, Associated Factors

Background

Chronic venous insufficiency describes a condition that affects the venous system of the lower extremities with venous hypertension causing various pathologies including pain, swelling, edema, skin changes and ulceration [1]. It causes significant morbidity in diverse populations and socioeconomic cost owing to its high prevalence, cost of investigation, treatment and loss of working days.

Around 3% of total health care expenditures are linked to venous disorders [2].

Globally, reports of prevalence vary from less than 1% to 40% in females and less than 1% to 17% in males. The reported ranges in prevalence estimations presumably reflect differences in the population distribution of risk factors, accuracy in diagnostic criteria

and availability of medical diagnostic and treatment resources. However studies done have shown the prevalence to be increasing with age [3]. The diversity of the associated factors indicates that early diagnosis and treatment can be more complex in resource-limited settings.

In sub-Saharan Africa, there are a few anecdotal reports dating back to the 1970's [4, 5]. They used visual inspection methods and focused only on varicose veins and not the full spectrum of CVI. In Uganda, there is limited data on the magnitude of this condition. Therefore, the purpose of this study was to determine the clinical presentation and the associated factors of lower limb chronic venous insufficiency among patients at Mulago National Referral Hospital.

Methods

Study Design and Setting

During a 6-months period from September 2019 to February 2020, a cross-sectional study was conducted on all consecutive participants with evidence of chronic venous insufficiency (CVI) who were ≥ 18 years old and attending the outpatient clinics of Mulago National Referral Hospital (MNRH). MNRH is a public-general and teaching hospital with modern facilities to perform vascular surgery. The vascular outpatient department receives about 5 patients on a weekly basis from all sources (e.g. other physicians, clinics, private hospitals). We excluded limbs of participants with a history of surgery pertaining to CVI (venous stripping) or sclerotherapy and those who were unable to consent.

Study Variables

The independent variables included; age (in completed years), gender, body mass index (BMI), employment status and lifestyle (e.g. smoking history, alcohol intake). The dependent variables were varicose veins, skin trophic changes and venous symptoms (e.g., edema, leg cramps, and heaviness).

Study Procedure

Patients who consented to participate in the study were subjected to a medical interview, a physical examination of the lower extremities and a review of the Doppler or duplex scan results. The structured interview documented the following data: age, gender, body mass index (BMI), level of education, years since onset of CVI and presence of comorbid conditions. Special consideration was also given to information suggesting family history, symptoms potentially related to venous disease (leg heaviness, painful legs, sensation of swelling, itching, heaviness, night cramps, and sensation of pins and needles) and lifestyle habits (e.g. posture assumed at work, alcohol intake). For women: parity, use of contraception for women younger than 49 years and use of hormonal replacement therapy (HRT) for those older than 49 years and in menopause was also evaluated.

We conducted a comprehensive standardized clinical examination with the participant standing for more than 2 minutes to determine

the magnitude of visible disease. The method of examination and classification was adapted from the method used in the Basle study and Edinburgh vein study as this was considered the best available to provide the most detailed classification for the different degrees of venous insufficiency [6-8].

We classified participants' limbs using the clinical category of CVI according to the clinical component (C) of the CEAP classification that categorizes patients into one of seven classes based on clinical signs. Class 0, no visible or palpable signs of venous disease; class 1, telangiectasia's or reticular veins; class 2, varicose veins; class 3, edema; class 4, skin changes due to venous disease; class 5, skin changes with healed ulceration; and class 6, skin changes with active ulceration [9]. Each category can include signs present in a lower order category; for example, edema could be present in classes 4 through 6.

We obtained information about functional disease at various anatomic sites (superficial, deep and perforator veins) from the Doppler or duplex ultrasound scans of the participant. For participants with bilateral disease, the highest CEAP classification of the most affected limb was determined. We described CVI using the clinical (C) and anatomical (A) components of the CEAP classification [9].

Quality Control Measures

Included use of a standardized internationally approved data collection tool, the CEAP assessment tool.

Statistical Analysis

All data obtained were entered into a computer database using Epi Data Classic Version 3.1 and exported to STATA Version 14.1 for analysis. We also tabulated baseline characteristics for the study population as a whole and by CEAP class. Statistical data analysis was done according to participant or limb as appropriate. We summarized continuous variables using means, standard deviations, and medians where appropriate, while categorical variables were summarized using proportions and percentages. Frequencies and proportions were used to describe associated factors of CVI. We used Fischer exact test and Chi square to test the difference between the proportions.

Ethical Considerations

Approval was obtained from Makerere University School of Medicine Research Ethics Committee- (SOMREC) #REC REF 2019-160. For all study procedures, participants provided informed consent after a detailed explanation of the study.

Results

There were 104 participants (146 affected legs) enrolled for the study. The male: female ratio was 2:1. The participants' ages ranged from 18 to 85 years with a median age of 43 years (IQR; 31-52 years). Among the females, 28 (85%) had at least one birth while 15 (45%) had more than three births. The main characteristics of the participants are as shown in **Table 1** below.

Forty-nine out of 104 participants (47.1%) were in occupations that involved prolonged standing (peasant farmers, teachers and security workers) and 35 (33.7 %) spent most of the day seated (secretaries and drivers). 25 % of participants had comorbid conditions. Among the females, 25 (75%) had a history of hormonal contraceptive use. The rest of the characteristics are as shown in

Table 2. The overall median duration of symptoms was 36 months (IQR; 15- 60 months). In total, majority of the participants 94 (90.4%) had at least three symptoms of CVI. The most common venous symptoms were venous pain 96.2%, sensation of swelling (93.3%) and sensation heaviness (79.8%). (See **Figure 1**)

Table 1: Baseline Characteristics of the Participants

Characteristic	Frequency	Percentage
Age (years)		
Median (IQR)	43(31-35)	
≤20	2	1.92
21-30	24	23.08
31-40	22	21.15
41-50	24	23.08
51-60	20	19.23
>60	12	11.54
Gender		
Female	33	31.7
Male	71	68.3
Body Mass Index		
Underweight	2	1.94
Normal weight	49	47.57
Overweight	28	27.18
Obese	24	23.30
Education level		
None	2	1.9
Primary	34	32.7
Secondary	38	36.5
Tertiary (Vocational/University)	30	28.8
Occupation		
Businessman/woman	23	22.12
Employed	25	24.04
Not employed	27	25.96
Self-employed/Informal	29	27.88
<i>IQR; interquartile range</i>		

Table 2: Health-Related Lifestyle and Clinical Characteristics

	Frequency (n=104)	Percentage
Most assumed posture at the workplace		
Sitting	35	33.7
Standing	49	47.1
Mobile	20	19.2
Prior lower limb trauma/injury		
Yes	28	26.9
No	76	73.1
Prior lower limb surgery after trauma		
Yes	10	9.6
No	94	90.4
Family history of lower limb CVI		
Yes	15	14.4
No	89	85.6
Chronic co-morbid conditions or diseases		
Yes	26	25
No	78	75
Comorbidities n=26		
Hypertension	16	61.54
HTN and DM	1	3.85
Sickle cell	4	15.38
Others	5	19.23
Smoking history(former or current)		
Yes	17	16.3
No	87	83.7
Alcohol intake history		
Yes	45	43.3
No	59	56.7
<i>CVI; chronic venous insufficiency, DM; Diabetes Mellitus, HTN; Hypertension</i>		

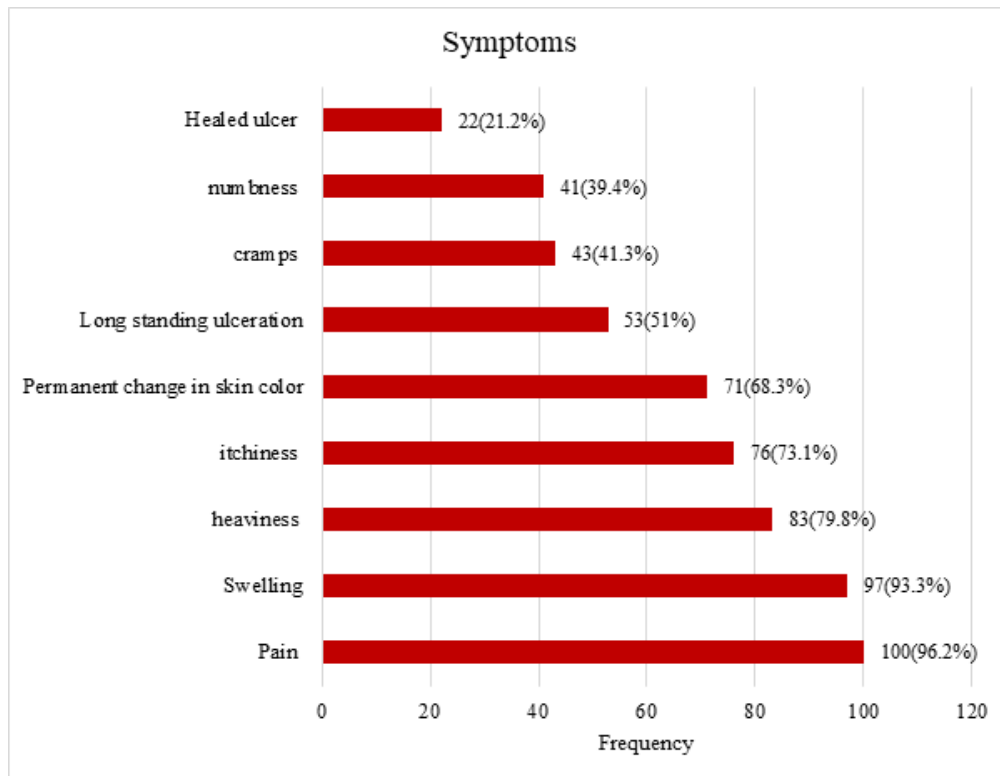


Figure 1: Distribution of Venous Symptoms among Participants

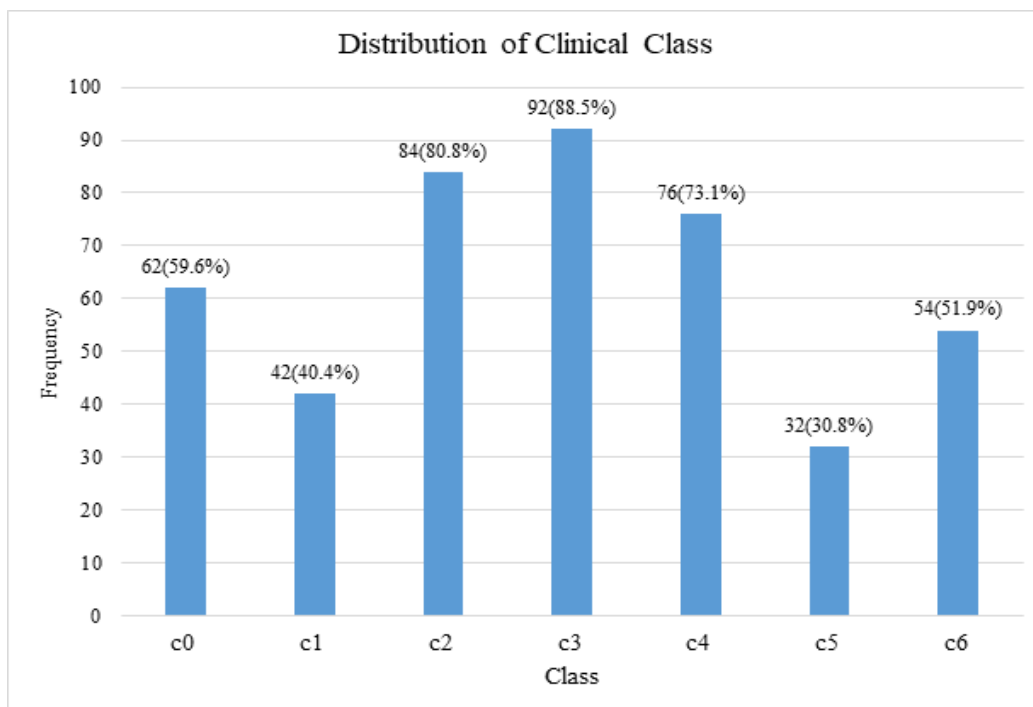


Figure 2: Distribution of the Clinical Class of CEAP

Of the 104 participants, 62 (59.6%) had unilateral disease (C0) with the left limb being most affected (See figure 2). Out of the 146 affected limbs, majority were clustered into CEAP classes 2

through 4. (I.e. varicose veins, limb edema and skin trophic changes). The rest of the characteristics of the clinical class is as shown in Figure 2.

Table 3: Distribution of the anatomical classification of CEAP

Venous Segment	Right Lower Limb (RLL)	Left Lower Limb (LLL)	Both limbs	RLL Total	LLL Total
Superficial Veins	27(42.9)	41(39.8)	35(50)	62(46.6)	76(43.9)
Perforators	25(39.7)	41(39.8)	28(40)	53(39.8)	69(39.9)
Deep veins	11(17.5)	21(20.4)	7(10)	18(13.5)	28(16.2)
Total	63	103	70	133(100)	173(100)

Chronic venous insufficiency was present in the following venous segments: superficial veins, perforators and deep veins as shown in

Table 3. The left limb was the most affected in all venous segments considered (See Table 3).

Table 4: Bivariate Analysis for Factors Associated With Chronic Venous Insufficiency

Variable	Varicose veins (C2)		Venous symptoms		Skin Change (C4 –C6)	
	Present	p value	Bilateral	p value	Present	p value
Age (yrs.)						
21-30	20(83.3)	0.661	7(29.2)	0.697	19(79.2)	0.905
31-40	18(81.8)		10(45.5)		19(86.4)	
41-50	17(70.8)		9(37.5)		19(79.2)	
51-60	17(85)		9(45)		17(85)	
>60	11(91.7)		6(50)		9(75)	
Gender						
Female	26(78.8)	0.727	19(57.6)	0.015	21(63.6)	0.003
Male	58(81.7)		23(32.4)		63(88.7)	
Body mass index						
Normal BMI	42(85.7)	0.141	14(28.6)	0.055	42(85.7)	0.491
Overweight	24(85.7)		14(50)		21(75)	
Obese	16(66.7)		13(54.2)		19(79.2)	
Most assumed posture						
Sitting	28(80)	0.866	15(42.9)	0.214	30(85.7)	0.356
Standing	39(79.6)		16(32.7)		40(81.6)	
Mobile	17(85)		11(55)		14(70)	
Family history of lower limb CVI						
No	73(82)	0.481	33(37.1)	0.094	73(82)	0.481
Yes	11(73.3)		9(60)		11(73.3)	
Chronic co-morbid conditions or diseases						
No	66(84.6)	0.085	29(37.2)	0.249	63(80.8)	1
Yes	18(69.2)		13(50)		21(80.8)	
Obstetric history in females						
Nulliparous	4(80)	1	2(40)	0.628	4(80)	0.63
Parity	22(78.6)		17(60.7)		17(60.7)	
History of smoking						
No	72(82.8)	0.244	39(44.8)	0.057	67(77)	0.038
Yes	12(70.6)		3(17.6)		17(100)	
History of Alcohol intake						
No	47(79.7)	0.743	27(45.8)	0.201	46(78)	0.406
Yes	37(82.2)		15(33.3)		38(84.4)	

At bivariate regression analysis, males had significantly higher proportions of skin trophic changes ($P=0.003$) while females had significantly higher proportions of venous symptoms compared to men ($P=0.015$). Overweight participants had significantly higher proportions for venous symptoms as compared to those who had normal BMIs. All the participants with history of smoking had skin changes ($P= 0.038$) (See table 4).

At multivariable analysis, males had 4.5 times higher odds of developing skin changes as compared to females (OR=4.5, 95% CI: 1.62-12.5). Patients with history of surgery following trauma were 77% less likely to have varicose veins as compared to patients with no history of surgery (AOR=0.23, 95% CI: 0.05-1). Majority of our participants 85 (82%), presented with severe grades of C4-C6.

Discussion

This is the first study to analyze the clinical presentation and associated factors of chronic venous insufficiency at a tertiary hospital in Uganda. Our patients are young (mean, 43 years) which is a true representation of the generally young Ugandan population and Africa as a whole. It is also comparable to studies done in Cameroon (4) and Kenya [10]. In Western countries, advanced age is a common risk factor [11, 12]. If it is well known that the African population is young, then the presence of the disease in the young people cannot be clearly explained. One hypothesis may be the exposure to a hot climate. It is postulated that when patients are in a hot environment, the manifestations of venous disease worsen [13, 14].

The male predominance is contrary to findings in other studies. The reasons that explain a higher prevalence in women are well documented in the medical-surgical literature and include hormonal factors and pregnancy [15-17]. In our female participants, the pregnancy rate is high and thus the prevalence of varicose veins increases with parity as documented in literature [16]. Even though a high percentage of the women were using hormonal contraception, no women were using postmenopausal hormone replacement therapy. This is similar to findings from a study done in Mengo [17]. Very few studies have investigated the effect of oral contraceptives on varicose veins. The Basle study reported no association between varicose veins and oral contraceptive use. A limitation of studies measuring the relationship between oral contraceptives and varicose veins has been selection bias [18]. It is not surprising that majority of the participants had their body mass index within the normal weight. This is similar to findings done in Cameroon and Kenya [4, 10]. In Africa in general, obesity is not yet a common issue as compared to western countries [19].

All participants were symptomatic in at least one limb and the most encountered symptoms included sensation of leg heaviness, pain, and sensation of swelling. This was similar to what was reported in large studies like the Vein Consult Program, which was performed in 22 countries around the world [20]. The prevalence of symp-

toms in the Vein Consult Program was high in all geographical areas studied. Moreover, the distribution of symptom prevalence (by decreasing frequency: heavy legs, pain, sensation of swelling) was similar whatever area considered as reported in this study. Symptom prevalence by decreasing frequency of symptoms in our study included pain, sensation of swelling, and heavy legs.

We observed a long duration of symptoms for most participants with the majority having more than three symptoms. The same long duration was noted in a Kenyan study [10]. The pattern of disease presentation was consistent with chronicity of symptoms in that participants with more symptoms had higher grades of the clinical class. This delay in seeking medical attention may be due to the difficulty in accessing health services and lack of investigative tools at the primary health institutions [21]. Varicose veins, edema, skin trophic changes were the three commonest clinical manifestations. This was quite similar to a study done by Omulo et al in Kenyatta hospital [10]. The prevalence of C3-C6 was higher as compared to most reports and this being a hospital-based study done at a referral hospital higher grades of CVI were encountered [1, 22]. In addition, in dark-skinned C1 patients, telangiectasia's tend to be particularly difficult to detect, and therefore only later stages are obvious. No difference was found between men and women unlike in other studies that have shown that varicose veins are more common in women [23, 24]. The prevalence of ulcers (healed and active) was high compared to figures from western countries, where it is described mostly in patients older than 60 years. The young age pattern of patients with ulcers was noted in Asian and Cameroon populations respectively [4, 25].

We observed more superficial vein involvement as compared to the other vein segments. The left limb was most affected compared to the right one. Basing on the highest CEAP score per participant, majority of the affected participants were in the older age group. This is not surprising because older age means an increased number of insufficient venous segments and increased risk of clinical progression from varicose veins to trophic skin changes [26].

More than three quarters of the participants had no familial history of CVI. The genetic predisposition that explains family history of venous insufficiency has not been clearly elucidated. However, some studies have confirmed heredity as a contributing factor to varicose veins most especially among 1st degree relatives [27-29]. Most of the participants were in occupations that necessitated prolonged orthostatic postures, making it an associated factor for aggravation or initiation of CVI as it causes increased pressure on the valves leading to incompetence [30-32]. A study done by Finn et al showed that working in a standing position is associated with subsequent hospitalization for varicose veins for both men and women [33].

It has been postulated that subcutaneous deposition of adipose and fibrous tissue disrupts cutaneous venous network impairing

drainage and promoting stasis [19]. Nearly half of the participants had BMIs above the healthy weight range of 25 with a slight increase seen in the overweight range as compared to the obese range. However, some African studies have not confirmed obesity as a significant factor as it is not yet a common issue compared to western countries [4]. Obesity also played a significant role for CVI in this study as there was a significant association observed between obesity and venous symptoms. The study did not confirm any association between varicose veins, skin changes and obesity. A quarter of our participants had chronic co-morbid conditions with the majority of these presenting with hypertension and a few with Diabetes mellitus. This is similar to a study done by Auzky et al in which CVI symptoms were strongly associated with a higher prevalence of manageable cardiovascular risk factors [34]. As has been documented in literature, dense sickled cells impair endothelial function by causing mechanical obstruction, venous incompetence, bacterial infections and vasoconstriction [35]. Thus, it is not surprising that some of our participants had CVI in addition to sickle cell disease.

Although a small number of our participants had a positive history of smoking (16%), as compared to the alcoholics (43%), there was a significant association between smoking and CVI (skin changes) but not alcohol intake. Smoking is a major factor in causing oxidative stress, hypoxia through carbon monoxide and nitric oxide fixation to hemoglobin and endothelial damage [36]. All the participants with history of smoking had skin changes compared to those who reported no smoking history. This was similar to a study done in France [36]. Smoking is significantly associated with CVI in accordance with the biological data and pathophysiological mechanisms already documented in medical literature. Hormone replacement therapy in women was not of relevance in our population because it is not frequently used.

Study Limitations

There was difficulty in clearly differentiating normal from abnormal skin in some participants. (dark-skinned). For example, early skin manifestations of CVI (CEAP C1 with intradermal visible veins, telangiectasia, "hyphen webs" reticular veins, CEAP C1) due to our dark skin.

Conclusions

The results clearly show that chronic venous insufficiency (CVI) is present in our population with some associated factors being frequent. The patients tend to be young, and males are more affected. The morbidity is high as most patients by presentation have more than three symptoms and advanced disease. CVI affects a significant part of the population, underlining the importance of screening and modification of some associated factors. We recommend further studies in the general population will contribute to a better understanding of the full magnitude of the problem.

Abbreviations

BMI: Body mass index, CEAP: Clinical, etiological, anatomical, pathophysiological system, CVI: Chronic Venous Insufficiency, HRT: Hormone Replacement therapy, LLL: Left lower limb, MNRH: Mulago National Referral Hospital, MUK: Makerere University, OPD: Outpatient Department, RLL: Right lower limb, SOMREC: School of Medicine Research Ethics Committee, UNCST: Uganda National Council for Science and Technology.

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Authors' Contributions

EK, PM, RO, WK and JPM contributed to the conception and design of the study. EK collected data and was involved in data analysis. EK, PM and RO contributed to drafting of the initial manuscript. WK, JPM supervised the study, participated in analysis and interpretation of data. WK and JPM critically reviewed and revised the manuscript. All authors read and approved the final version of the manuscript.

Availability of Data and Materials

The datasets generated and analyzed are available from the corresponding author upon request.

Declarations

Ethics Approval and Consent to Participate

This study was approved by the School of Medicine Research Ethics Committee- (SOMREC) of Makerere University (MUK), under registration number #REC REF 2019-160. All study participants obtained written informed consent before recruitment and participation. For participants who were unable to read and write, they gave their consent using a thumbprint as approved by SOMREC. Approval was also sought from the Department of Surgery of MUK and Mulago National Referral Hospital (MNRH) administration provided access to the study participants. We followed the Human Subjects Protection guidelines- July 2014 as documented by the Uganda National Council for Science and Technology (UNCST) avoiding any type of physical or moral harm.

Consent for Publication

Not applicable

Competing Interests

The authors declare that they have no competing interests regarding the publication of this article.

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