

PREVALENCE, STAGING AND ASSOCIATED FACTORS OF UTERO VAGINAL PROLAPSE AMONG GYNECOLOGIC PATIENTS IN KAFFA ZONE HOSPITALS, SOUTH WEST ETHIOPIA, 2021: A MULTI-CENTER CROSS-SECTIONAL STUDY

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ABSTRACT

BACKGROUND: Utero-vaginal prolapse is the descent of the uterus through the vaginal canal due to defects in the support structures of the uterus and vagina because of various factors

OBJECTIVE: This study assessed the prevalence, staging, and associated factors of utero vaginal prolapse among gynecologic patients in kaffa zone hospitals south west Ethiopia, 2021.

METHOD: Institutional-based cross-sectional study design was employed in kaffa zone hospitals among consecutively sampled 287 patients. The odds ratio with a 95% CI at a p-value <0.05 was used to declare the significance level.

RESULTS: Out of 287 study participants, 24(8.3%) were identified to have utero-vaginal prolapse. Being in age group 45 or above (AOR: 4.25, 95% CI: 1.17- 15.43), vaginal delivery for last birth, (AOR: 3.24; 95% CI: 1.01-10.4), staying in labor $\geq$ 24 hours for last birth (AOR: 3.31; 95% CI: 1.10- 9.98), being multi-gravida (AOR: 3.21; 95% CI: 1.11- 9.28) and body mass index <18.5 kg/m² of woman (AOR: 4.94, 95% CI: 1.44- 16.91) were significantly associated with utero-vaginal prolapse.

CONCLUSION: In this study, the prevalence of uterovaginal prolapse was relatively low. Advanced age, vaginal delivery, multi-gravidity, prolonged labor, and low BMI were significant contributing factors. Therefore, strengthening antenatal intrapartum care, promoting nutritional support, and establishing routine gynecological screening for high-risk women are strongly recommended to enable early detection and prevent disease progression

KEYWORDS: Utero-vaginal prolapse, associated factors, Kaffa zone, Ethiopia, gynecologic patients

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INTRODUCTION

Uterovaginal prolapse is a common gynecologic problem. It can occur at any age, but due to injuries to the pelvic floor muscles and fascia during delivery and age-related estrogen deficiency mostly it occurs in postmenopausal women. In young and nulliparous women might be caused by collagen insufficiency or genetically cervical lengthening¹.

Among women younger than 45 years of age, the global prevalence of genital prolapse is estimated to be 2% to 20%⁴. It is one of the most common reproductive morbidity in developing countries⁵. Even in developed countries like the United Kingdom, one out of every 1,000 women is admitted to the hospital due to utero-vaginal prolapse, and around 20% of women with this gynecological problem are awaiting major surgery⁶. In low income countries, the mean prevalence of pelvic organ prolapse is 19.7%⁷. In Africa, the prevalence of UVP varies by countries: 12.7% in Ghana⁸, 5.4% in south west Nigeria⁹, 64.6% in Tanzania¹⁰, according to a population-based study on POP and 22.3% in Ethiopia¹¹.

Women who are suffering from UVP experience a protruding mass inside or outside the vagina accompanied by difficulty sitting, walking, standing, and lifting objects. In developing countries, this can affect the social acceptance of women and can lead to physical and emotional isolation. Because of the stigma associated with UVP in low-income countries, women who are affected by it often hide their situation and do not seek care, and often suffer from the disease and its complications for a long time¹⁶. It is difficult to treat clinically because it requires resolving pelvic floor symptoms, improving quality of life, and minimizing complications¹⁷. It is the third most common reason for hysterectomy¹⁸, and surgery for the treatment of UVP have a high rate of reoperation¹⁹.

Utero vaginal prolapse and its complications have a significant economic burden for those affected. About 11% of American women have surgery for POPs or incontinence before the age of 79, with 29.2% likely to require additional surgery²⁰. In

Ethiopia, there is a significant variation in the magnitude of UVP within and between regions: 12.8% in Addis Ababa²², 22.3% in Gondar¹¹, and 42.3% in Axum²³.

Generally, this study is needed because of some reasons. Firstly, UVP is still a problem in low- and middle-income countries, particularly in Sub-Saharan African countries²⁴. As a result, assessing the prevalence and managing the risk factors of UVP early is critical to preventing its occurrence, lowering MMR, and improving maternal quality of life. Secondly, even though some research has been done in Ethiopia based on secondary data covering a small-scale area, the prevalence of UVP varies in each setting because there might be a lack of primary data in different studies, which enhances the variation in magnitude from setting to setting. Thirdly, despite the presence of a few studies regarding the prevalence and risk factors of UVP, there are some contradicting or inconsistent findings on some risk factors for UVP, like BMI^{25,26} and age²⁷, which demand further exploration. Due to these reasons, the investigators believe that there is a need to further investigation to assess the prevalence and risk factors of UVP. So, this study tried to identified the above gaps and assess the Prevalence, staging and associated factors of UVP among gynecologic patients in Kaffa zone hospitals, south west Ethiopia.

METHODS AND MATERIALS

Study Area and Period

This study was conducted among gynecologic patients attending in Kaffa zone hospitals. Kaffa is one of the 15 zones of Southern Nation Nationality People Region (SNNPR) and is located about 449 km southwest of Addis Ababa. There are three governmental hospitals in the kaffa zone, and the study was conducted in these three hospitals (Bonga Gebre-tsadik Shawo Memorial General Hospital, Wacha Primary Hospital, and Tello Primary Hospital). Bonga Gebre-tsadik Shawo Memorial General Hospital (BGSMGH) is located in Bonga town.

Study Design

An institution-based cross-sectional study was conducted.

Study Population

The study population was the selected women with gynecological problems in Kaffa zone Hospitals, South West Ethiopia.

Eligibility Criteria

All women attending the gynecology wards of the study hospitals during the study period were included in the study. Women who were unable to communicate were excluded from the study. Critically ill women were also excluded from the study. Additionally, women with a history of hysterectomy were excluded from the study.

Sample Size and Sampling Technique

Sample Size Determination

The sample size was calculated using a single population proportion formula based on the 22.3% prevalence of UVP in gynecologic hospital admissions, which was obtained from a study conducted in Gondar, Ethiopia¹¹.

Considering the following assumptions, z = standard normal distribution value at 95% confidence level of $z_{\alpha/2} = 1.96$ and margin of error (d) = 5%.

$$n = \frac{(z_{\alpha/2})^2 \cdot P(1-P)}{d^2}$$

Where; n = minimum sample size, p = estimated prevalence of UVP, $Z_{\alpha/2}$ = standard of normal variable, d = margin of error,

$$n = \frac{(1.96)^2 \cdot 0.223(1-0.223)}{(0.05)^2}$$

$n = 261$ then by adding 10% Contingency as non-response rate, $n = 287$ is the final sample size.

Sampling Technique

According to the Health Management Information System (HMIS) reports, the total sample size was allocated proportionally among the three

study hospitals based on the number of women with gynecologic conditions admitted to their gynecology wards during the reference period. Proportional allocation was performed using the formula $n_i = (N_i/N) \times n$, where n_i represents the sample size allocated to each hospital, N_i is the source population in each hospital, N is the total source population across all study hospitals, and n is the total calculated sample size. Finally, after calculating the sample size for each hospital, the study participants were selected by using the consecutive sampling technique

The diagnosis and staging of UVP were considered after the physical examination were done by a gynecologist, general practitioner, or IESO, and if there was a protrusion of mass and/or heaviness in the vagina, which should be documented on the patient's chart before admission.

digital scale

Study Variables

Dependent variable

Utero -vaginal prolapse

Independent variables

- ❖ Socio-demographic characteristics (Maternal, age, Residence, Religion, Educational status, Occupational status of respondents, Marital status), Medical and behavioral related variables (Chronic diarrhea, Chronic cough, Chronic constipation, Smoking, BMI)
- ❖ Gynecologic and obstetric related characteristics (Parity, Gravidity, Family planning, Duration of labor in last birth, Age at first marriage, Mode of delivery for last birth, Age at first pregnancy, Place of delivery for last child Duration of rest after last delivery)

Data Quality Assurance

Pre-testing was carried out on 5% of the sample size at Mizan Tepi University Teaching Hospital, which is nearer but outside the proposed study area. After pre-testing, the questionnaire was evaluated for clarity, understandability, length, and completeness.

Data processing and Analysis

After all the necessary data had been collected, the data was checked, coded, and entered into Epi-Data version 4.6, and the data from three hospitals were merged together and exported to SPSS (Statistical Package for Social Science) version 23 for analysis. For categorical variables, the results were reported as proportions and frequency tables. Variables with a p-value < 0.25 at 95% CI in the bivariate logistic regression were entered into a multivariable logistic regression³². Multiple logistic regressions were carried out by using the backward stepwise method to identify the factors associated with UVP in gynecologic patients. Then all the candidate variables were entered into a multivariate model since collinearity was not found between them. Finally, an AOR with a 95% CI and value <0.05 were considered as statistically significant.

Ethical Consideration

An ethical approval letter was secured from the Institutional Review Board (IRB) of Insitute Health of Jimma University (Ref.no: IHRPGJ/535/21). A permission letter was written to the Kaffa Zone Hospitals administration office. Written consent from each respondent was obtained after a detailed explanation of the main purpose of the study.

RESULTS

Socio demographic Characteristics

A total of 287 study participants were included in the study with response rate of 100%.

Among the two hundred eighty-seven participants, majority, 133(46.3%) was in the age group of 18-34 years and the minimum and maximum ages 21 and 53 years (see table 1).

Table 1: Socio demographic characteristics of the study participants in kaffa zone Hospitals October 6-December 6, 2021(n=287)

Variables	Category	Frequency (%)
Age of respondents	18-34 years	133(46.3)
	35-44 years	61(21.3)
	45 and above	93(32.4)
Religion	Orthodox	107(37.3)
	Protestant	104(36.2)
	Muslim	61(21.3)
	Catholic	12(4.2)
	Others *	3(1.0)
Residence	Rural	142(49.5)
	Urban	145(50.5)
Level of education	Unable to read and write	63(22)
	Read and write only	60(20.9)
	Primary education	67(23.4)
	Secondary education	65(22.6)
	Higher education and above	32(11.1)
Occupational status	Housewife	63(22)
	Farmer	53(18.5)
	Merchant	49(17.1)
	Daily laborer	9(3.1)
	Government employee	52(18.1)
	Private employee	61(12.2)
Marital status	Married	255(88.9)
	Single	4(1.4)
	Divorced	19(6.6)
	Widowed	9(3.1)

*Others =Traditional religion ("barri kocho")

Gynecologic and Obstetric Characterstics of the Study Participants

Most (37.7%) of the participants, were multiparous had vaginal delivery (51%) And delivered at health institutions (70%) (see table 2).

Table 2: Gynecologic and obstetric related characteristics of the study participants in kaffa zone hospitals October 13 -December 13, 2021(n=287)

Variables	Category	Frequency (%)
Experience of pregnancy	Yes	284(98.1)
	No	3(1.1)
Age at first pregnancy	≤18 years	5(1.8)
	>18 years	279(98.2)
Gravidity	Multigravida	114(40.1)
	Primi-gravida	170(59.9)
Parity	Multiparous	107(37.7)
	Primi-parous	177(62.3)
Mode of delivery for last birth	Vaginal delivery	145(51.1)
	Cesarean-section	139(48.9)
Place of delivery for last birth	Home	85 (29.9)
	Health institution	199 (70.1)
Rest after last delivery	≤ 42 days	139(48.9)
	>42 days	145 (51.1)
Duration of labor for the last birth	≥ 24 hours	119(41.9)
	<24 hours	165(58.1)
Family planning	Yes	169(58.9)
	No	118(41.1)

Medical and Behavioral Characterstics of the Study Participants

The majority of participants, 278(96.9%) had no history of smoking. However, 7(2.4%) of the respondents were exposed to other smokers, only 2(0.7%) had a previous history of smoking. Of the total number of participants, some of them had medical problems like chronic cough, chronic constipation, and chronic diarrhea that were present

in 35 (12.2%), 85 (29.6%), and 73 (25.4%) of these patients, respectively. Regarding participants' BMI, 108 (37.6%) of the respondents had a BMI of 18.5-24.9 kg/m² while the remaining respondents had BMI of above 25 kg/m² and below 18.5 kg/m² 107 (37.3%) and 72 (25.1%), respectively (Table 3).

Table 3: Medical and behavioral characteristics of the study participants in Kaffa zone Hospitals October13- December 13, 2021(n=287)

Variables	Category	Frequency (%)
History of smoking	Former	2 (0.7)
	Current	0 (0)
	Passive	7 (2.4)
	Never	278 (96.9)
History of chronic cough	Yes	35(12.2)
	No	252(87.8)
History of chronic constipation	Yes	85(29.6)
	No	202 (70.4)
History of chronic diarrhea	Yes	73 (25.4)
	No	214 (74.6)
Body mass index in kg/ m2	<18.5 kg/ m2	72 (25.1)
	18.5-24.9 kg/ m2	108 (37.6)
	25 and above	107(37.3)

5.4 Prevalence of Utero-vaginal Prolapse

Out of the two hundred eight seven patients attended in the selected hospitals who underwent gynecological evaluation, 24 were identified to have UVP resulting in a prevalence of 8.3%. The overall distribution of UVP in participants who lives in rural area is higher, The R: U ratio is 3.8:1, with rural accounting for 19 cases and urban 5 cases. The distribution of UVP in those who used family planning was 14(58.3%), in respondents who had a history of chronic cough was 5(20.8%), had history of chronic diarrhea was 4 (16.7%), had chronic constipation was 11(45.8%), and in those participants who had no history of smoking was 20 (83.3%).

Stage of Utero-vaginal Prolapse

Gynecologic evaluation of the study participants revealed 4 different types of staging, Of the 24 patients with utero vaginal prolapse, the majority 11 (45.8%) had stage IV UVP, 8(33.4%) had stage III, 3(12.5%) had stage II and 2(8.3%) had stage I utero vaginal prolapse and None of the women examined had stage 0 pelvic prolapse (Figure 2).

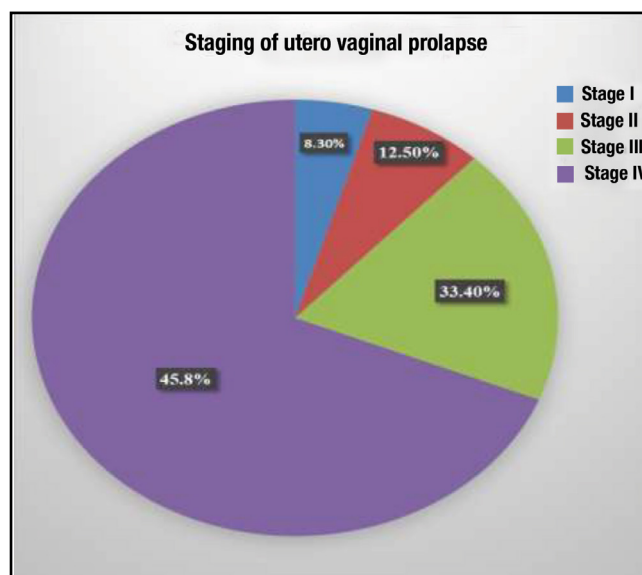


Figure 1: Distribution of UVP based on staging among admitted gynecologic patients in Kaffa Zone hospitals October 13, December 13 2021(n=287)

Factors Associated with Utero-vaginal Prolapse in Gynecologic Patients

Bi-variable and multivariable logistic regressions were used to assess factors associated with utero vaginal prolapse among gynecologic patients in the selected hospitals. Age, residence, mode of delivery in last birth, place of delivery in last birth, gravidity, duration of labor in last birth, rest after last delivery, chronic cough, chronic constipation, and body mass index showed significant association in the bi-variable model and were selected as candidates for multivariable logistic regression. Those candidates were entered into the multivariable model and age, mode of delivery for last birth, gravidity, duration of labor for last birth, and body mass index were found to be significantly associated with the development of UVP.

The odds of developing UVP among gynecologic patients whose age 45 and above was 4.25 times (AOR= 4.25, 95% CI: 1.17-15.43) when compared to those patients whose age between 18 and 34. History of vaginal delivery for the last birth was also one of the significantly associated variables with UVP (AOR = 3.24, 95% CI: 1.01- 10.4). The finding indicated that, those patients who had a history of vaginal delivery for the last birth were 3.24 times more likely to develop UVP compared to those patients who had a history of caesarian section delivery for their last birth.

Multi gravidity increases the chance of developing UVP among respondents by 3.21 times (AOR= 3.21, 95% CI: 1.11- 9.28) when compared to those respondents who had a history of Primi-gravida. In addition, the duration of labor for the last delivery was also found to raise the likelihood of developing UVP. Hence, those respondents who had a duration of labor for last birth ≥ 24 hours had 3.31 odds of developing UVP (AOR= 3.31, 95% CI: 1.10-9.98) when compared with those respondents who had duration of labor for thier last birth<24 hours

Lastly, the body mass index of the respondent was found to be significantly associated with the development of UVP among participants. Accordingly, those respondents whose BMI <18.5 kg/m² were 4.94 times (AOR=4.94, 95%CI: 1.44-16.91) more likely to develop UVP when compared with those respondents whose BMI 18.5-24.9 kg/m² (Table 4).

Table 4: Bi-variable and multi-variable binary logistic regression results of the factors associated with UVP in Kaffa zone Hospitals October 13, December 13 2021(n=287)

Independent variable	Category	UVP		COR (95 %CI)	P value	AOR (95 %CI)	P value
		Yes	No				
Age	18-34 years	4	130	1			
	35-44 years	6	55	3.51(0.95-12.9)	0.059	2.15(0.49-9.39)	0.30
	45 and above	14	79	5.71(1.81-17.9)	0.003*	4.25(1.17-15.43)	0.028**
Residence	Urban	5	140	1			
	Rural	19	124	4.32(1.56-11.83)	0.005*	2.94(0.88-9.79)	0.078
Mode of delivery for last birth	Cesarean-section	5	134	1			
	Vaginal delivery	19	126	4.04(1.46-11.18)	0.007*	3.24(1.01-10.4)	0.047**
Place of delivery for last birth	Health institution	10	190	1			
	Home	14	71	3.72(1.58-8.77)	0.003*	2.66(0.94-7.48)	0.063
Gravidity	Primi-gravida	7	164	1			
	Multigravida	17	97	4.08(1.63-10.19)	0.003	3.21(1.11-9.28)	0.031**
Rest after last delivery	>42 days	7	139	1			
	≤ 42 days	17	122	2.74(1.10-6.84)	0.03*	1.87(0.59-5.92)	0.28
	R54						
Duration of labor for last birth	<24 hours	7	159	1			
	≥ 24 hours	17	102	3.76(1.50-9.39)	0.005*	3.31(1.10-9.98)	0.033**
Chronic cough	Yes	5	30	2.04(0.71-5.87)	0.185*	2.61(0.61-11.14)	0.19
	No	19	234	1			
Chronic constipation	Yes	11	75	2.16(0.92-5.04)	0.07*	2.73(0.92-8.05)	0.068
	No	13	189	1			
Body mass Index	<18.5 kg/ m2	11	61	2.25(0.85-5.97)	0.099*	4.94(1.44-16.91)	0.011**
	18.5-24.9 kg/ m2	8	101	1			
	25 kg/ m2 and above	5	102	0.61(0.19-1.94)	0.40	0.88(0.22-3.46)	0.86

NB. * = $P \leq 0.25$, ** = $P < 0.05$, AOR= Adjusted Odds Ratio, CI= Confidence Interval, 1= reference Hosmer Lemshow test=0.46

DISCUSSION

The current study showed that the prevalence of UVP among admitted gynecologic patients was 8.3%. The prevalence of uterovaginal prolapse observed in this study is comparable to reports from China (9.6%) and rural Pakistan (10.3%), but substantially lower than those reported in Nepal (35.97%) and Brazil (52.3%)³⁶. The variation may be explained by differences in population demographics (i.e, racial or ethnic), and cultural diversity with time. Our finding is also lower than that reported in a study conducted in Gondar, which found a prevalence of 22.3%.¹¹ The variation might be, due to the fact that the study done in Gondar was a retrospective analysis chart review, and many patients were referred from different parts of the region, for better evaluation and management.

In contrast, the prevalence of UVP in the present study was higher than that reported in studies from South India (1.6%)³⁷, Nepal (2.6%)³⁸, southwest Nigeria (5.4%)⁹, and Bangladesh (4.2%)³⁹. The observed differences may be attributed to variations in study design, study setting, participant characteristics (particularly age), and maternal healthcare utilization. Additionally, genetic and environmental factors may have contributed to the variation in prevalence across countries. The most commonly diagnosed stage in the current study was stage IV followed by Stage III and Stage II. This finding is comparable with that reported by Shireen Akhter Khanam, et al. in Bangladesh, identified stage IV (76 %), Stage III (9%), Stage II (6%) Stage I (6%) and stage 0 (3%)³⁹.

In contrast to this, a study done in Ghana revealed that Stage II was the commonest symptomatic UVP which revealed that 33.3%⁸. Our finding is also not comparable with a study done in Brazil regarding the stage of UVP, which revealed that the prevalence of UVP in relation to stage were as stage I (27.8%), stage II (23.1%), and stage III (1.4%) and none of the women examined had stage

IV pelvic organ prolapse³⁶. The variation may be due to delayed in the treatment of POP due to lack of support, low income, and fear of social stigma across the countries. A study conducted in Turkey found that 27.1% of prolapses were stage II⁴⁰. A similar study in China revealed that, symptomatic POP-Q stage II, was the most common which shows that 7.52%³⁴. The possible reason for the variation in this finding may be due to environmental and geographical factors.

This study revealed that several factors like age of the respondents, mode of delivery for the last birth, number of pregnancies (gravidity), duration of labor for the last delivery, and BMI of the respondents were associated with the development of UVP.

In this study, the age of the respondents was found to be significantly associated with UVP. Women with the age of 45 and above were more likely to develop UVP than women under the age of 18-34 years. This finding is supported by studies conducted in Korea⁴¹, Brazil⁴² and USA⁴³. This might be due to; increasing age which leads to the age-related loss of muscle function known as Sarcopenia⁴⁴. As a result, loss of strength in pelvic muscles and ligaments occurs, which increases the risk of vaginal prolapse with age. In addition to this, the hormonal changes related to menopause, which are common in this age group, may have an effect on prolapse. Moreover, women of advanced age had reduced collagen content, lower collagen solubility, and higher collagen turnover, all of which contribute to the progression and development of UVP⁴⁵. In addition, the advanced age of the respondents, especially during the menopausal state due to a decrease in pelvic connective tissue resilience and genital atrophy, plays the most important role in the pathogenesis of utero-vaginal prolapse⁴⁶. In contrast, a study conducted in North west Ethiopia reported a contradictory finding²⁷. This might be due to a small sample size that may fail to show associations due to low statistical power.

Vaginal delivery for the last birth is also one of the independent factors of UVP in the current study. Specifically, women with vaginal delivery for their last birth had higher odds of experiencing UVP

than women with cesarean-section delivery for thier last birth. Different studies reported that the risk of UVP increases with vaginal delivery⁴⁷⁻⁵⁰. More over our study is consistent with studies done in USA⁵¹ and Australia⁵². The possible justification could be that following vaginal delivery, UVP is thought to develop as a result of the structural disruption caused by overstretching, compression, and avulsions during childbirth, or as a result of levator ani muscle injury, particularly to the pubococcygeal muscle⁵³.

The current study, also revealed that the number of pregnancies (gravidity) was one of the significantly associated variables with UVP. Women with multigravida, were more likely risk to develop UVP than women with primigravida. Our finding is supported by a report done in Gambia¹⁶ and Ethiopia⁵⁵. This could be due to repeated pregnancy and childbirth that damage the sphincter and ligaments, sometimes failing to regain full strength and elasticity. In addition, as abdominal pressure increases, the length and angle of the cardinal and sacral ligaments change depending on the force exerted on the pelvic organs⁵⁶.

The duration of labor for the last birth was found to be significantly associated with UVP. The duration of labor greater than or equal to 24 hours was significantly associated with the development of utero-vaginal prolapse. This finding is consistent with previous reports from Nepal⁵⁷, Tanzania¹⁰, and Nigeria⁵⁸. This could be because prolonged labor causes more damage to the supportive structures of the uterus and other pelvic organs. Prolonged labor can also be complicated by obstructed labor, which might need aggressive interventions like operative deliveries that might worsen damage to the supportive structure of the pelvic organ which increase the occurrence of POP⁵⁹. Moreover, the most common cause of levator ani muscle damage is prolonged labor. The principal contributors to the levator hiatus (weakest area in the pelvic floor) are the levator ani and puborectalis, which play a crucial and central role in the management of urination and defecation. This study has several limitations. First, the use of self-reported data may

have introduced recall bias. Second, the relatively small sample size may limit the generalizability of the findings. Finally, the cross-sectional study design precludes the establishment of causal relationships between the independent and dependent variable

Conclusion and Recommendations

The magnitude of Utero-vaginal prolapse was low in this study. Older age, vaginal delivery, prolonged labor, multigravidity, and undernutrition were independently associated with the condition. Targeted preventive strategies, including improved intrapartum care, nutritional support, and early identification of women at increased risk, are warranted to reduce the burden of utero-vaginal prolapse.

Abbreviations:

BMI	Body mass Index,
CI	Confidence interval,
CSI	Central Statistical agency
ETB	Ethiopian Birr,
FP	Family planning,
G.C	Gregorian calendar,
GP	General practitioner,
HMIS	Health management information system,
IRB	Institutional review board,
IESO	Integrated emergency surgery &obstetric,
JUMC	Jimma university Medical center,
OR	Odd ratio,
POP	pelvic organ prolapses,
SNNPR	South nation nationality people region,
SPSS	Statistical package for social science,
UNPF	United nation population fund agency,
UVP	Utero-vaginal prolapse

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article.

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Disclosure

The authors report no conflicts of interest in this work

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