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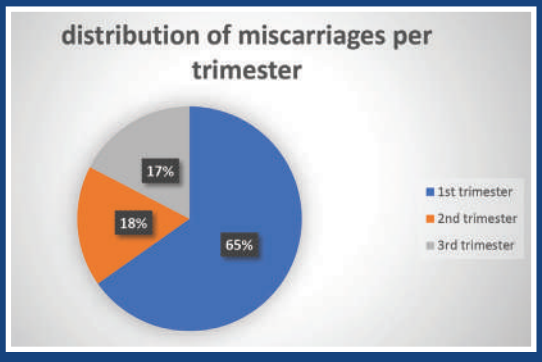

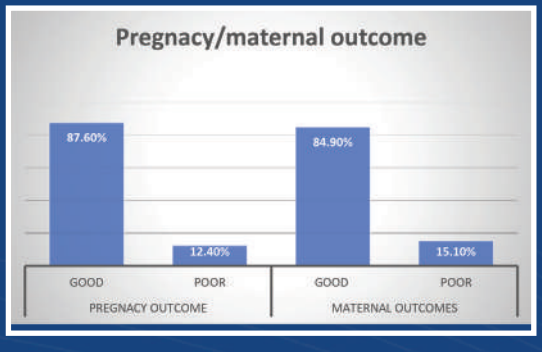

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ASSOCIATION OF PREECLAMPSIA, PLACENTAL PATHOLOGY, AND MATERNAL-FETAL FEATURES WITH PREGNANCY-INDUCED HYPERTENSION AT DIFFERENT GESTATIONAL AGE RANGES

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ABSTRACT

AIM: This study aimed at evaluating the preeclampsia, placental pathology, and maternal and fetal features in women with pregnancy-induced hypertension (PIH) at different gestational age ranges.

METHODS: Data related to this analytical cross-sectional study was collected from 60 pregnant women recruited at Gynecology and Obstetrics Department of Hospital between 21 November 2020 and 22 May 2021. A series of maternal, fetal and placental pathology variables was evaluated and compared between the two 30-tuple groups, including pregnant women with early PIH between 20-34 weeks of gestation and those with late PIH after 34 weeks of gestation.

RESULTS: Preeclampsia was more prevalent in women with early PIH compared with those with late PIH (80% vs 20%, P:0.001), implying that preeclampsia was significantly associated with the early PIH ($p<0.05$). The rate of "syncytial knots" significantly increased with the progression of preeclampsia ($P<0.05$). A significant positive correlation existed between the early PIH and the rate of newborns admitted to NICU, the length of hospitalization, and the levels of the doppler indexes of umbilical and uterine arteries ($p<0.05$). The newborn Apgar scores were also lower in cases with early PIH than those with late PIH ($p<0.05$). The mortality rate in neonates born to mothers with early PIH was higher than neonates delivered from mothers with early PIH, but not significantly so (13.30% vs 3.30%, p:0.16).

CONCLUSION: Early PIH between 20-34 weeks of gestation might be indicative of progression to preeclampsia. Also, higher rates of pregnancy-related complications in mothers with early PIH might be indicative of different impact of PIH and preeclampsia on pregnancy outcomes depending on the gestational age. Nonetheless, further large-scale researches are needed to get a detailed picture of PIH and preeclampsia.

KEYWORDS: Pregnancy-induced hypertension, Preeclampsia, Placental pathology, Pregnancy outcomes

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INTRODUCTION

Hypertensive disorders of pregnancy are still a serious health threat for women and their offspring worldwide. Pregnancy-induced hypertension (PIH) with an overall prevalence of 5–10% of pregnancies, is a condition characterized by high blood pressure (systolic blood pressure (BP) ≥ 140 mmHg or a diastolic BP ≥ 90 mmHg) after 20 weeks of gestation without proteinuria[1, 2]. Although PIH complications are not severe, PIH can subsequently progress to preeclampsia or a severe condition after week 20 of pregnancy [3]. Preeclampsia is generally diagnosed by high BP ≥ 140/90 mmHg and proteinuria ≥ 300 mg /24 h, and or maternal organ dysfunction. Preeclampsia is prevalent in 2%–5% of pregnancies and accounted for nearly 14% of maternal death[3, 4].

The common risk factors for PIH /preeclampsia reported in many epidemiological studies are obesity, older age, stress, multiple-fetus pregnancy, first pregnancy, polycystic ovarian syndrome, diabetes, chronic kidney disease, and autoimmune disease[5, 6]. PIH may cause other fetal and maternal complications, including preterm delivery, intrauterine growth restriction, low birth weight, premature placental abruption, cardiovascular disorders, kidney and/or liver failure, HELLP syndrome, and even high risk of mortality[7, 8]. So, identifying the effects of PIH and preeclampsia on clinical pregnancy outcomes is very useful to clearly understand their pathological mechanism as well as timely prediction and management of complications.

Placenta, as the principal source of oxygen and blood supply to the fetus, can be origin of the majority of adverse pregnancy outcomes, such as fetal growth restriction (FGR) and preeclampsia resulted from the early abnormal placental development[9]. The etiology of preeclampsia is not fully understood, though it is known that the preeclampsia pathogenesis includes poor remodeling of the uteroplacental spiral arteries which lead to placenta perfusion, oxidative stress, chronic hypoxia, and thereby abnormal placentation, and other subsequent clinical disorders[10]. The evidence acknowledged that the placenta can be the source of some common maternal complications during pregnancy, such as inadequate nutrition, diabetes, obesity, and hypertension, which may also influence the infant health[9, 10].

Placental pathology can be clinically useful to perinatal diagnosis as well as explain the pathophysiology of many pregnancy-related complications, such as preterm delivery, intrauterine growth restriction, preterm labor, and preeclampsia[11, 12]. Therefore, gynecologists, pediatricians, and histologists are always looking for the histology changes of the placenta. Also, pathological findings of the placenta may indicate whether or not subsequent pregnancies should be considered at high-risk pregnancies (for example the mild infarction)[13]. Given the previous placental pathological evidences in preeclampsia [e.g., hypoplasia, placental inflammation, and vascular lesions], placental examination plays an important role in the early diagnosis and management of pregnancy and prenatal complications[12].

The current analytical cross-sectional study focuses on evaluating the preeclampsia, placental pathology, and maternal and fetal features in two groups of women with PIH between 20-34 weeks of gestation and those with PIH after 34 weeks of gestation. During the placental pathological examination, a series of variables was evaluated, including syncytial knots, fibrinoid necrosis in placenta, calcification, placental infarction, chorangioma, hyalinized villi, and stromal pathology.

METHOD

Study design

In this analytical cross-sectional study, pregnant women referred to Imam Khomeini Hospital in the city of Ahvaz, Iran, were evaluated. This research was approved by Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran with Ethical Code: IR.AJUMS.HGOLESTAN.REC.1399.099, and all participants signed the informed consent prior to enrollment.

Participants and Methods

Data of the current study was collected from 60 pregnant women recruited at Gynecology and Obstetrics Department of Hospital between 21 November 2020 and 22 May 2021. The inclusion criteria were the presence of PIH, no history of smoking, alcohol, and drug addiction. The exclusion criteria were women who had chronic blood pressure, fetal anomalies, infectious diseases, and/or a history of severe trauma during pregnancy. The participants' information was extracted from their medical records, including demographic data [i.e., age, gender, body mass index (BMI)], underlying disease, and pregnancy health history [e.g., the number of previous pregnancies, history of high BP, time of PIH, history of abortion, maternal diseases, maternal medications, type of delivery and/or pregnancy, neonatal status, birth weight, length of hospitalization in the neonatal intensive care unit (NICU), and the final status of the infant (dead or alive)].

The recruited patients were divided into two 30-tuple groups of mothers with PIH between 20-34 weeks of gestation and those with PIH after 34 weeks of gestation. The placenta samples of mothers were placed in 10% formalin and sent to the pathology laboratory for macroscopic and microscopic examination. The prepared slides were examined by a pathologist for pathological variables, such as syncytial nodule, fibrinoid necrosis in placenta, calcification, placental infarction, chorangioma, hyalinized villi, and stromal pathology (e.g., hypocellular fibrosis, spindle cell stroma, smooth muscle differentiation, edematous stroma, and adipose tissue).

Definitions:

According to National and European scientific society's guidelines, pregnancy-induced hypertension is defined as systolic BP ≥140 mmHg and diastolic BP ≥90 mmHg after the 20th week of gestation in women without previous hypertension, which measured by an oscilometric device for at least two measurements 4 h apart[14]. Preeclampsia was generally diagnosed by high BP ≥ 140/90 mmHg and proteinuria ≥ 300 mg/24 h, and or maternal organ dysfunction[15]. Systolic and diastolic BP were measured after the 20th week of gestation. Gestational age was detected using ultrasound examination.

Statistical analysis

The quantitative variables were described as mean, standard deviation, median and interquartile range while the qualitative variables were expressed as frequency (percentage). The normality of data was checked by the Shapiro-Wilk test. Also, an independent sample T-Test as well as the chi-square test were respectively used to compare the quantitative and qualitative variables between the two studied groups. $P < 0.05$ is considered as statistically significant, and the data were analyzed by SPSS version 26 (SPSS Inc., Chicago, Ill., USA).

RESULTS

Preliminary data analysis showed that there were no significant differences between mothers with early PIH and those with late PIH in terms of the age, height, weight, and BMI ($p>0.05$; Table 1). Preeclampsia were more prevalent in cases with early PIH compared with those with late PIH (80% vs 20%); this indicated a significant positive correlation between preeclampsia and PIH between 20-34 weeks of gestation (p: 0.001; Table 1).

The mean level of systolic BP on admission in women with early PIH (167.17±16.95 mmHg) was partially higher than those with late PIH (160.33±12.17 mmHg), but not significantly so (p: 0.078). The mean level of diastolic BP in women with early PIH (96.17±6.65 mmHg) was significantly higher than those with late PIH (91.33±8.60 mmHg; p: 0.018). But no significant differences were found between the two groups in terms of the mean levels of systolic and/or diastolic BP during care of patients ($p>0.05$; Table 1). Moreover, there was no significant correlation between the history of underlying disease (i.e., brain, liver and or cardiac disorders) and PIH ($P <0.05$; Table 1). Anti-PIH medication use was more prevalent among women with early PIH compared to those with late PIH (46.70% vs 20%, p: 0.04). Also, no significant correlation was found between the history of abortion and PIH (p: 0.99; Table 1).

Table 1. Summary of demographic and basic gestational information of pregnant mothers

		Study Group			
	Late GH Mean±SD	Early PIH Mean±SD	P-value		
Age of Pregnant Mothers	32.13±6.84	33.80±6.80			0.38
Height	163.40±4.12	160.37±7.48			0.06
Prenatal Weight	78.47±10.10	78.70±17.07			0.95
BMI	31.25±10.30	30.68±6.36			0.79
Systolic Blood Pressure (on admission)	160.33±12.17	167.17±16.95			0.07
Diastolic Blood Pressure (on admission)	91.33±8.60	96.17±6.65			0.018
Systolic Blood Pressure (during patient care)	120±9.83	125±25.56			0.32
Diastolic Blood Pressure (during patient care)	78.67±6.81	78.67±15.92			0.99
			Total		
The presence of proteinuria, N %No	24 (80)	6 (20)	30 (50)		0.001
	Yes	6 (20)	24 (80)	30 (50)	
Anti-PIH medication use, N %	No	24 (80)	16 (53.3)	40 (66.7)	0.03
	Yes	6 (20)	14 (46.7)	20 (33.3)	
Brain Disorder, N %	does not have	25 (83.3)	21 (70)	46	0.36
	Standard	5 (16.7)	9 (30)	14 (23.3)	
Liver problems, N %	No	27 (90)	25 (83.3)	52 (86.7)	0.7
	Yes	3 (10)	5 (16.7)	8 (13.3)	
Cardiac disorders, N %	Yes	1 (3.30%)	0		
History of Abortion, N %	No	30 (100)	25 (83.3)	55 (91.7)	0.88
	Yes	0 (0) 5 (16.7)	5 (8.3)		

PIH: pregnancy-induced hypertension

A significant correlation existed between the fetal weight on ultrasound and PIH (P<0.05), of which the rate of fetuses with 10_95 fetal weight was more prevalent in cases with early PIH. Also, the mean age of fetuses as well as the mean weight of babies born to women with late PIH were significantly higher than those with early PIH (P<0.05). (Table 2)

Table 2. Summary of descriptive information about the fetal basic conditions

		Study Groups			
		Late GH	Early PIH	Total	P-value
Fetal Age – Days, Mean±SD		246.67±50.90	143.30±112.38	0.001	
Percentage of Fetal Weight on	0	0 (0)	2 (6.7)	2 (3.3)	
Ultrasound, N%	0-10	6 (20)	0 (0)	6 (10)	
	10-50	9 (30)	11 (36.7)	20 (33.3)	0.03
	50-90	15 (50)	16 (53.3)	31 (51.7)	
	90-95	0 (0)	1 (3.3)	1 (1.7)	
Percentage of Fetal Birth Weight, N%	0-5	3 (10)	2 (6.7)	5 (8.3)	
	5-10	3 (10)	4 (13.3)	7 (11.7)	0.13
	10-50	14 (46.7)	14 (46.7)	28 (46.7)	
	50-90	10 (33.3)	5 (16.7)	15 (25)	
	90-100	0 (0)	5 (16.7)	5 (8.3)	

Furthermore, no statistically significant difference in the mean weight of placenta was observed between the two studied groups (p: 0.946). But a remarkable correlation was found between the location of the placenta on ultrasound and PIH ($p<0.05$), as posterior, fundal-posterior, and lateral placenta were more prevalent in those with late PIH. Whereas, most mothers with the early PIH had the anterior placenta ($p<0.05$). (Table 3).

Table 3. Comparison analysis of placental pathological indicators between the two groups.

		Study Groups			
		LLate GH	Early PIH	Total	P-value
Placental Weight, Mean±SD		524.83±91.44	527.37±178.02		0.94
The Location of the Placenta	Posterior	16 (53.3)	14 (46.7)	30 (50)	
on Ultrasound, N%	Anterior	3 (10)	9 (30)	12 (30)	
	Fundal-anterior	3 (10)	1 (3.3)	4 (6.7)	
	Fundal-posterior	4 (13.3)	0 (0)	4 (6.7)	
	Right lateral	2 (6.7)	0 (0)	2 (3.3)	
	Left lateral	2 (6.7)	0 (0)	2 (3.3)	
	left posterior lateral	0 (0)	1 (3.3)	1 (1.7)	
	Posterior midline	0 (0)	1 (3.3)	1 (1.7)	
	Anterior midline	0 (0)	1 (3.3)	1 (1.7)	
	Anterior lateral	0 (0)	3 (10)	3 (5)	
Retroplacental Hemorrhage, N%	0	26 (55.6)	20 (44.4)	46 (76.7)	0.19
	1	3 (30)	7 (70)	10 (16.7)	0.25
	2	1 (50)	1 (50)	2 (3.3)	
	3	0 (0)	2 (100)	2 (3.3)	
Syncytial Knot, N%	1	0 (0)	2 (6.7)	2 (3.4)	0.03
	2	7 (23.3)	16 (53.3)	23 (39)	0.02
	3	20 (66.7)	11 (36.7)	31 (50.8)	
	4	3 (10)	1 (3.3)	4 (6.8)	
Frequency of	0	21 (70)	17 (56.7)	38 (62.7)	0.47
Calcification, N%	1	2 (6.7)	5 (16.7)	7 (11.9)	0.58
	2	7 (23.3)	7 (23.3)	14 (23.7)	
	3	0 (0)	1 (3.3)	1 (1.7)	
Infarcted Area, N%	0	24 (80)	24 (80)	48 (79.7)	0.54
	1	3 (10)	4 (13.3)	7 (11.9)	0.77
	2	3 (10)	1 (3.3)	4 (6.8)	
	3	0 (0)	1 (3.3)	1 (1.7)	
Acute Atherosis, N%	0	26 (89.7)	26 (86.7)	52 (88.1)	0.85
	1	2 (6.9)	2 (6.7)	4 (6.8)	0.99
	2	1 (3.4)	2 (6.7)	3 (5.1)	
Fibrinoid Necrosis, N%	1	12 (40)	15 (50)	27 (44.1)	0.22
	2	8 (26.7)	11 (36.7)	19 (32.2)	0.24
	3	8 (26.7)	4 (13.3)	12 (20.3)	
	4	2 (6.6)	0 (0)	2 (3.4)	
Chorangioma, N%	0	29 (96.7)	28 (93.3)	57 (94.9)	0.61
	1	1 (3.3)	1 (3.3)	2 (3.4)	0.95
	2	0 (0)	1 (3.3)	1 (1.7)	
Hyalinised villi, N%	0	0 (0)	1 (3.3)	1 (1.7)	0.65
	1	12 (40)	15 (50)	27 (45.8)	0.8
	2	16 (53.3)	12 (40)	27 (45.8)	
	3	2 (6.7)	2 (6.7)	4 (6.7)	
Stromal Pathology, N%	0	30 (50)	30 (50)	60 (100)	

No significant association was found between retroplacental haemorrhage of placenta and PIH (p>0.05). There was a significant correlation between the rate of syncytial knots and PIH (P<0.05), as its rate significantly increased with the progression of preeclampsia. But there was no significant correlation between PIH and other placental pathological indicators, including the incidence of calcification, infarction, fibrinoid necrosis, chorangioma, and hyalinised villi (p>0.05). In this study, no evidences of stromal pathology were observed in all patients. (Table 3)

The rate of newborns admitted to NICU who born to mothers with the early PIH was higher than those with late PIH (60% vs 6.70%, p: 0.001). The mean length of NICU hospitalization (day) for newborns in the early PIH group (6.03±10.83) was significantly longer than those of the late PIH group [(0.37±1.45; P<0.05); Table 4].

The postpartum mean level of serum creatinine in mothers with the early PIH, particularly mothers with preeclampsia, was significantly higher than those with late PIH (P=0.008). Also, the postpartum mean level of platelets count in mothers with the early PIH was significantly lower than those with late PIH (P=0.034). (Table 4)

The mean levels of doppler index umbilical artery, doppler index uterine artery right, and the doppler index uterine artery left were significantly higher in cases with early PIH than those with late PIH (p<0.05). Moreover, the minimum and maximum neonatal Apgar scores in babies born to mothers with late PIH were significantly greater than those born to mothers with early PIH (p <0.05). Also, the mean weight of babies born to mothers with late PIH (3034±452.1 grams) was higher than those born to mothers with early PIH (2252.93±974.67 grams; p: 0.001). The results of the first trimester pregnancy-associated plasma protein-P (PAPP-P) test were not statistically different between the two groups (P: 0.671). (Table 4)

The mortality rate among babies born to mothers with early PIH (13.30%) was higher than those born to mothers with late PIH, but not significantly so (3.30%, p:0.161). (Table 4)

Table 4. Analysis of some indicators of newborn and postpartum mothers after delivery in two study groups

Variables		Late GH	Early PIH	P Value
NICU, N %	No	28 (93.3)	12 (40)	0.001
	Yes	2 (6.7)	18 (60)	0.001
		(Mean±SD)	(Mean±SD)	
Number of NICU Hospitalization Days		0.37±1.45	6.03±10.83	0.008
Weight of the Newborn		3034±452.1	2252.93±974.67	0.001
ALT		33.37±89.58	78.10±195.04	0.25
AST		27.40±25.18	75.80±162.83	0.11
Serum creatinine		0.70±0.09	0.80±0.18	0.008
Platelets		213133.33±65526.9	179666.67±52966.05	0.034
First Trimester PAPP-P Test		0.33±0.49	0.27±0.58	0.67
Doppler index Umbilical Artery		0.07±0.27	0.29±0.47	0.027
Doppler Index Uterine Artery Right		0.24±0.56	1.63±0.43	0.001
Doppler Index Uterine Artery Left		0.23±0.47	2.42±0.51	0.001
Minimum Apgar Score of the Baby		8.23±0.82	7.30±2.12	0.03
Maximum Apgar Score of the Baby		10.33±0.66	8.43±2.21	0.041
The Condition of the Baby, N %	Dead	1 (3.3)	4 (13.3)	0.16
	Live	29 (96.7)	26 (86.7)	0.35

Neonatal Intensive Care Unit (NICU)
Pregnancy-associated plasma protein-P (PAPP-P)

DISCUSSION

The present study showed that the preeclampsia was notably more prevalent in mothers with the early PIH before 34 weeks' gestation (80% vs 20% in the late PIH group). The main purpose of this study was to evaluate the preeclampsia, placental pathology, maternal and fetal features in women with pregnancy-induced hypertension at different gestational age ranges.

Previously (2014), Nelson et al assessed the placental pathology of 1210 women with preeclampsia at various gestational ages. Their findings showed that the placental hypoplasia was considerably associated with early preeclampsia in the third trimester, and the placental vascular lesions was notably increased at gestational ages of 240/67 to 336/7 weeks (53%) compared with 340/7 (34%) to 366/7 (26%) and 37 weeks or longer, respectively (P <0.001) [16]. Our results were in consistent with Nelson et al.'s reports and indicated a significant positive correlation between the percentage of syncytial knots with high hypertension before 34 weeks' gestation and preeclampsia. Also, based on our findings, there was no significant correlation between PIH and other placental pathological indicators, including the incidence of calcification, infarction, fibrinoid necrosis, chorangioma, and hyalinised villi. In this regard, Ezeigwe et al reported that there were no statistically significant differences in placental calcifications, stromal edema, obstructive fibrosis, and nodules. The degree of placental infarction was related to fetal birth weight, and the association between fetal birth weight and placental involvement was more than 10% [17]. The anatomopathological features of early onset preeclampsia are significantly different from late onset preeclampsia, as cases with early onset preeclampsia are characterized with hypoxia, villous infarctions, and hypoplasia[18].

Previous scientific evidence reported that overweight (excess BMI) is significantly associated with an increased risk of preeclampsia and can predict the preeclampsia[19]. By contrast, our analysis showed that neither age and nor BMI can predict PIH and preeclampsia, except for weight of fetus during pregnancy. Also, our findings showed no evidence of a significant correlation between the history of underlying disease and PIH.

Recently, Awuah et al (2020) conducted a prospective case-control study in Ghana to assess the placenta growth, and perinatal outcomes of 84 hypertensive women. Their findings showed that 52%, 33.30%, 7.10%, 4.80%, and 2.40% of the hypertensive women had respectively preeclampsia, PIH, eclampsia, chronic hypertension, and preeclampsia superimposed on chronic hypertension. Also, they indicated a significant positive correlation between PIH and the incidence of placental infarction, placental calcification, and placental haematoma (p= 0.001). The mean weight of placental, placental diameter, placental volume, and placental thickness of the hypertensive women were significantly lower than those of the normotensive women (p<0.05). Moreover, the number of babies born to hypertensive women was considerably more than those born to normotensive women (p= 0.001)[20]. The present study did not evaluate the normotensive women. Nevertheless, the percentage of newborns admitted to NICU who were arisen from mothers with the early PIH was significantly more than those delivered by the late PIH mothers (60% vs 6.70%). The mean length of NICU hospitalization (day) for babies born to mothers with early PIH was significantly longer than those born to the those with late PIH.

Our findings showed no correlation between the fetal birth weight and PIH, yet the mean weight of the babies born to the mothers with a late PIH was notably higher than those delivered by mothers with early PIH. Maybe, the higher incidence rate of preeclampsia in mothers with early PIH led to a reduction in the mean weight of their newborns.

Based on the prior clinical evidences, the placental histological findings can differentiate hypertensive women from normotensive. However, placental pathology was almost similar between high hypertensive mothers and those with mild to severe preeclampsia[17, 20]. Accordingly, differentiation between the early and late PIH in clinical practice can

be useful in the early predicting of the preeclampsia as well as explaining its pathophysiology. Our study is one of the rare studies in this field and has succeeded in identifying a series of maternal risk factors of PIH and preeclampsia. Moreover, this study indicated that maternal-fetal features and pregnancy outcomes may significantly affected by PIH or preeclampsia depending on the gestational age.

In this study, the prevalence of preeclampsia was higher in mothers with early PIH. So, a series of changes in the early PIH group compared with the late PIH group are clinically predictable and logical [e.g., a more frequent use of PIH drug, a more percentage of fetal admitted into NICU, the longer length of NICU hospitalization, the lower weight of newborns, and the higher level of serum creatinine]. In this regard, the mean levels of the umbilical and uterine artery doppler indices were also remarkably higher in the early PIH group than in the late PIH group, which is consistent with the results of Adekanmi et al.'s study[21].

CONCLUSION

This comparative analysis showed that the early PIH between 20-34 weeks of gestation might be indicative of progression to preeclampsia. Placentas from women with early PIH significantly differ from those with late PIH histopathologically (i.e., syncytial node and placental location on ultrasound). Higher rates of maternal and fetal pregnancy-related complications in mothers with early PIH may be indicative of different impact of PIH and preeclampsia on pregnancy outcomes depending on the gestational age. Nonetheless, further comprehensive and large-scale researches are needed to get a detailed picture of PIH and preeclampsia.

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OBSTETRIC HDU: A SUPPLY-BASED ALTERNATIVE FOR ICU CARE IN A LOW-INCOME SETTING: A DESCRIPTIVE STUDY

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ABSTRACT

BACKGROUND: The demand of ICU care for obstetric patients is rising in low-income settings, where there is low ICU-bed capacity. Introduction of obstetric High-dependency unit (HDU) has been described as an effective strategy to bridge this gap in resource-restricted settings.

OBJECTIVE: To describe the clinical characteristic and maternal outcomes of obstetric patients admitted to the first obstetric HDU in Ethiopia.

STUDY DESIGN: This was a descriptive study on clinical characteristics and maternal outcomes of obstetric patients admitted to obstetric HDU over one year (October 2021 to September 2022) at St. Paul's Hospital Millennium Medical College (Ethiopia). Data were collected retrospectively through reviewing patients' medical records using a data extraction format with KOBO collect tool. Data were analyzed using SPSS version 23 and simple descriptive statistics were employed. Proportions and percentages were used to present the results.

RESULTS: After excluding 18 patients who did not meet the inclusion criteria, a total of 355 obstetric patients who were admitted to an obstetric HDU were included in the final analysis. Among these all-obstetric patients admitted to obstetric HDU, pre-eclampsia/ eclampsia (82/355, 23.1%) and postpartum hemorrhage (66/355, 18.6%) were the most frequent reasons for admission to the HDU whereas cardiac disease constituted 14.1% (50/355) of the indication for admissions to the unit.

Majority (318/355, 89.6%) from the study participants were transferred to other wards with im-provement, while 37(7.9%) deteriorated with 9(2.53%) of them died. Septic shock (6/9, 66.6%) and DIC (2/9, 22.2%) were the leading causes of death in the HDU.

CONCLUSION: Findings of our study demonstrate that opening HDU in a low-income setting is feasible and results in favorable maternal outcomes. Introduction of obstetric HDU in low-income settings is an effective intervention to reduce severe maternal morbidity and mortality associated with low ICU-bed capacity in those settings.

KEYWORDS: ICU; maternal mortality; critical obstetric care; Ethiopia; preeclampsia

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INTRODUCTION

Estimates show that 1 in 100 pregnant women suffer a life-threatening event during pregnancy and delivery[1]. The global estimates of maternal mortality for the year 2017 indicate that there were 295 000. Globally MMR in 2017 is estimated at 211 maternal deaths per 100 000 live births, many more suffer varying degrees of acute maternal morbidities resulting in critical maternal illness necessitating critical care at the Intensive Care Unit during pregnancy or puerperium[2]. Although maternal mortality ratio has decreased from 676 per 1000 live births in 2011 to 267 per 1000 live births in 2020[3,4], the rate of maternal death in intensive care units is significant, like in the other of low-income countries.[5]

The concept of HDU has been instituted as a bridge between routine obstetric care and ICU in order to bypass and decrease the ICU burden.[6] HDU care is required for women requiring more detailed observation, intervention including basic support for a single failing organ system, extended post-op care and those stepping down from higher levels of care.[7,8] The presence of a well-developed critical care unit (HDU/ICU) with appropriate infrastructure, equipment's and trained staff is key for providing necessary and timely intensive management to critical mothers.[9] In low-income settings, HDUs may represent frugal innovations incorporating few but essen¬tial lifesaving interventions to critically ill women.[10] With deep understanding of this concept, we recently opened an obstetrics HDU in our hospital (St. Paul's Hospital Millennium Medical College) in Ethiopia. This HDU is the first HDU in Ethiopia, which is well-equipped with mechanical ventilators and ideal critical care personnel.

Though this new obstetric HDU unit in our hospital has been instrumental in decreasing the need for ICU admission among our obstetric patients, it's overall impact in improving the care has never been documented in terms of research. Our study sought to describe the clinical patterns and maternal outcomes of obstetric patients admitted to HDU at a tertiary setting in Ethiopia.

METHODS AND MATERIALS

Study design, study setting, and study period

This was a retrospective descriptive study on clinical characteristics and patient outcomes of obstetric patients admitted to high dependency unit (HDU) at St. Paul's Hospital Millennium Medical College in Ethiopia over 1 year (from October 2021 to September 2022). St. Paul's Hospital Millennium Medical College is a leading national tertiary hospital and medical college in Ethiopia with various sub-specialty care and training available in it, including a Maternal-fetal medicine unit. The hospital attends approximately 10,000 to 11, 000 deliveries per annum and receives one of the highest referral cases that require tertiary level of care, including ICU admission. Often, this hospital is struck with shortage of ICU beds and delay in accessing ICU beds had a detrimental effect on patient outcomes until recently, before we opened the first Obstetrics high dependency unity (HDU) in Ethiopia in 2021, at this hospital. Our positive experience of temporary utilization of mechanical ventilators in our obstetric recovery ward for patients that need intubation in the past, few years prior to the opening this HDU unit when we had ICU bed shortages, was fundamental in making our bold decision to develop a full concept of pioneering obstetric HDC care in Ethiopia. Beyond being the first obstetrics HDU in Ethiopia, our HDU is unique from the other HDU centers across the low-income countries, in that it is well-equipped with mechanical ventilators along with the medical personnel to handle the care. There are 4 beds equipped with oxygen source and vital sign monitors, two mechanical ventilators, advanced high-resolution ultrasound utilized in obstetric and non-obstetric diagnostics including bedside echocardiography. We have 24-hour duty consultant MFM specialist, anesthesiologists, and critical care nurses assigned at the HDU ward. For patients that need multidisciplinary team approach, the

unit has a direct access to consultations from other disciplines including cardiologists, hematologists, and neurosurgeons.

The primary outcome of our study was frequent indications for HDU admission during the study period in our hospital and overall patient outcomes of the study subjects included in the study. We specifically looked into the progress of the patients (whether they have improved or deteriorated, including mortality rate and transfer to ICU), after admission to HDU.

Data collection and Procedures

We accessed medical records for HDU patients included in this study by reviewing our HDU registry. Data for study participants included in this study were collected by reviewing the patient medical records. Data was collected using a simple data extraction format with KOBO collect tool. The data extraction format had 3 sections, socio-demographic data, clinical characteristics of patients, and patient outcomes after admission to HDU. A formal ethical clearance letter was obtained from St. Paul's Institutional Review Board (IRB). The ethical clearance didn't require getting informed consent from study subjects included in this study, hence informed consent was not obtained from the study subjects. The inclusion criteria were: obstetric patients, admitted to HDU, clinical characteristic and patient outcomes are known, antepartum and post-partum patients, and post-abortion patients. The exclusion criteria were stepped down patients from ICU (transferred from ICU for transition before admitted to respective ward).

Statistical analysis

No sample size calculation was used. Patients who were admitted to our HDU during the study period and meet the inclusion and exclusion criteria were included. Data were analyzed using SPSS version 23. Simple descriptive statistics were employed. Proportions and frequency were used to present findings significance.

RESULTS

A total of 355 patients were included in this study after 18 patients were excluded because they did not meet the inclusion criteria. The mean age of the study participants was 28+5.3 years. Majority of the patients were post-partum mothers (306/355, 86.2%) while 20 (5.6%) were pregnant at the time of admission to the HDU. The remaining 29(8.16%) were post abortion patients (Table-1).

Table 1: Clinical characteristics of the participants involved in the study of Admission and outcome of obstetric patients admitted to the obstetrics HDU of SPHMMC, 2021-2022

Variable	Category	n	%
Age(years)	**Mean**	**28+5.3**	
	< 19	13	3.7
	20-34	290	81.7
	35-49	52	14.6
Parity	Nulliparous	15	4.2
	Parous	340	95.8
Condition at admission to Obstetrics HDU	Pregnant	20	5.6
	Postpartum	306	86.2
	Post abortion	29	8.2

Among the indications for HDU admission, pre-eclampsia/ eclampsia (82/355, 23.1%) and postpartum hemorrhage (66/355, 18.6%) were the most common ones while cardiac disease accounted for 14.1% (50/355) of the admissions (Table-2).

Table-2 Indications for HDU admission in Ethiopia, 2021-2-2022

Indication for HD admission	n	%
Preeclampsia /eclampsia related complications	82	23.1
PPH	66	18.6
Post delivery / post- cs observation	53	14.9
Cardiac disease	50	14.1
Others	41	11.6
Sepsis	28	7.9
Abortion related complications	20	5.6
Chronic hypertension	15	4.2

The average length of HDU stay was 1.86 + 2.68 days ranging from 12 hours to 32 days. The majority 318(89.6%) of the study participants were transferred to other wards with improvement, while 37(7.9%) deteriorated with 9(2.53%) of them died. Septic shock (66.6%) and DIC (22.2%) were the leading causes of death in the HDU. The 9 mothers who died in the HDU stayed for 2.1(6 patients stayed for 1, one patient each stayed for 2 days, 5 days, and 6 days respectively). The average length of HDU stay for those mothers who died was 2.11 days ranging from 1 to 6 days.

Table-3: Patient outcomes after HDU admission in Ethiopia, 2021-2022

Outcome	Category	n	%
Length of stay at HDU	**Mean (days)**	**1.86 + 2.68 days**	
Improved	Transferred to other wards or discharged after improvement	318	89.6
Deteriorated	Total	37	10.4
	Transferred to ICU Kept at HDU	18	5.1
	for longer time and transferred to other wards without improvement	10	2.8
	Died	9	2.5

DISCUSSION

In this study, Preeclampsia/eclampsia related complications and post-partum hemorrhage were the most frequent indications for HDU admission. Nine in 10 of patients admitted to our HDU were transferred to other wards after improvement. The death rate among HDU patients was very low, septic shock and DIC being the most frequent immediate causes of death.

Different studies show that the need of ICU admission for obstetric conditions across low-income countries(considered to have a very low ICU bed capacity) is on rising trend.[11,12] Though the pattern of the disease necessitating such admissions influences maternal mortality to a great extent, in general obstetric patients are often young and healthy with their spectrum of sickness being very much reversible with timely intensive care.[13] The introduction of HDU helps to reduce ICU utilization and mortality in obstetric population.[14,15] A recent study of 40,412 deliveries, among which there was a need for ICU care in 447 (1.11%) of the deliveries over a 6-year period found that the rate of ICU admission dropped from 1.59% before the introduction of obstetric HDU to 0.67 after the introduction of obstetric HDU.16 According to some reports, maternal death among obstetric patients admitted to ICU is high in Ethiopia. In a recent case-control study (n=427), obstetrics mortality in intensive care unit was 27% from the total intensive care unit were due to obstetric causes.[5] Although difficult to speculate on the relationship between delay in accessing an ICU bed and risk of maternal mortally based on this study, shortage of ICU bed is often encountered in Ethiopia, like in the rest of the developing countries. Hence, introduction of HDU aiming at improving critical care outcomes for obstetric patients through accessing critical care timely and decreasing the burden of ICU care in our setting is crucial.

The present study found that the majority (1 in 10) of the patients admitted to our obstetric HDU had a favorable outcome. There were 9 deaths among the 355 patients included constituting 2.5%, septic shock and DIC being the main orchestrates of these

deaths. This rate of maternal death in our study is lower than maternal mortality of 4.1% (n=17) found among 413 obstetric patients admitted to HDU in a study done in India.[17] Among the important findings in our study is that Preeclampsia/ eclampsia related complications (82/355, 23.1%) and post-partum hemorrhage (66/355, 18.6%) were the most common reasons for admission to HDU. This finding is consistent with previous reports from UK and India that found hypertensive disorders and PPH as the top indications for HDU admission.[18,19]

We do not have any other study that focused on obstetric HDU in Ethiopia to align with our findings in discussion. However, studies that focused on ICU care outcomes for obstetric patients and maternal death reviews reveal that preeclampsia followed by PPH remain the most frequent indications for admission to ICU as well as the top causes of maternal mortality. Matiyas A. etal found that the leading causes of the direct maternal deaths were hypertensive disorders of pregnancy (32.5%) and postpartum hemorrhage (25%) in his review of 40 in-hospital maternal deaths.[20] Similarly, another study conducted in Ethiopia found that severe preeclampsia was the most frequent indication for ICU admission represented in 35% among the total (225) obstetric ICU patients included in the study. The study also found severe pre-eclampsia (AOR: 6.33; 95% CI: 2.25–17.79) is among factors associated with obstetrics mortality after admission to ICU and further recommended that all pregnant women should have proper antenatal care in order to decrease preeclampsia-related complications through early intervention[5], central to which is preeclampsia prevention through effective screening and providing ASA prophylaxis to those at risk. Recent studies on preeclampsia prevention in Ethiopia also underscore this recommendation. A prospective study of 395 pregnant women with preeclampsia at tertiary hospital in Ethiopia found that 49.4% of them had an indication for preeclampsia prevention intervention however ASA prophylaxis was utilized in less than 2% of them.[21] Though the reasons for this low uptake of ASA prophylaxis for preeclampsia prevention could be multiple, another study shows that there is significant gap in the knowledge and practice of preeclampsia predication and prevention among prenatal care providers attending antenatal care for pregnant mothers in Ethiopia (the mean score of knowledge and practice of prevention for pre-eclampsia using Aspirin among the providers was 42.9[±0.13] and 45.8[±0.07], respectively).[22]

Being the first study in Ethiopia and from the Sub-Saharan region, which may policy-brief the opening of other obstetric HDU units in Ethiopia and beyond in the region is the main strength of this study. Lack of analysis impact of opening HDU on ICU admission rates among obstetric patients and the overall impact of HDU in reducing in-hospital deaths are the major limitation of this study. The retrospective nature of the data and lack of analysis of factors associated with patient deterioration after admission to HDU are the other limitations of this study.

Our study adds useful information on effective utilization of HDU in low-income settings, which is often married by low ICU bed capacity. Being among the first study on this from the Sub-Saharan Africa, it implies that obstetric critical patients who thought to have most of the time reversible causes can access critical care by being admitted to HDU early instead of facing a deterioration in their clinical conditions associated with delays in accessing ICU bed. We underscore that introduction of HDU in low-income settings is an alternative solution to decrease maternal mortality among critically ill obstetric patients. There is a gap in understanding the cost-benefit analysis of introducing obstetric HDU in low-income settings (including care cost for patients and the financial expenses needed to construct such advanced care centers) which should be explored in future studies.

CONCLUSION

Our study shows that opening HDU in a low-income setting is feasible and results in favorable maternal outcomes. Though it did not measure this in terms of reducing in-hospital maternal deaths and need for ICU care among obstetric patients in exact figures, our study supports that introduction of obstetric HDU in low-income settings as an alternative solution to address low ICU-bed capacity which is rampant in such settings.

DECLARATIONS

Ethical consideration

Formal Ethical clearance letter was obtained from Institutional review board of St. Paul Hospital Millennium. The ethical clearance didn't require us to obtain informed consent from patients, hence informed consent was not obtained from the study subjects included in this study.

Conflicts of Interest

The authors report no conflicts of interest (financial or non-financial)

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Authors Contribution

IT, DB, LBT, and AFS contributed conception and development of the study protocol. AFS, DB, and WG contributed data collection and data analysis. AFS, LBT, MB, WG, and DB contributed data interpretation and manuscript write up. The final manuscript was edited by DB , MB, and AFS. All authors critically revised the article for intellectual content. All authors reviewed the final manuscript and approved its submission for publication.

Data Availability Statement

All data generated or analyzed during this study are included in this published article.

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INVESTIGATING THE EFFECTS OF PAUSINYSTALIA YOHIMBE AQUEOUS LEAVES EXTRACT ON PARAMETERS FOR REPRODUCTIVE PERFORMANCE IN EXPERIMENTAL RATS

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ABSTRACT

BACKGROUND: Herbal plants and herbal preparations are widely used as immunomodulatory medicines that helps in improving reproductive health in humankind, and they are globally used and have rapidly grown in economic developmental importance.

OBJECTIVE: The study was conducted to investigate the effects of the aqueous extract of P. yohimbe leaves on sexual reproductive performance in Wistar rats. The primary outcome of the study is the reproductive performance sexual rate.

METHODS: The experimental study was carried out on albino rats of the Wistar strain, weighing between 150 and 200g sexually naive. The animals were raised in polyethylene cages and divided into four groups, which received a saline solution (control group), 2, 5, and 10 mL/kg of the aqueous extract of P. yohimbe leaves for fourteen days orally. The sexual behavior test was performed according to three types of crossing.

RESULTS: The results of the treated groups showed a significant increase in mating frequency compared to the control group. Overall, the results showed that P. yohimbe significantly affects sexual behavior. The aqueous extract of P. yohimbe leaves increased sexual behaviour and orientation activity performance recorded in the treated rats.

CONCLUSION AND RECOMMENDATION: The enhanced reproductive performance appetitive detected in the study, justify the indigenous use of the herbal plant in reproductive medicine and could be a precursor in the synthesis of useful drugs. However, based on the current findings, we recommend that careful administration be considered as a better option justifying human circumstances for patient with advanced mankind age in low dosage resource settings, as it achieves a better reproductive performance rate at a lower dose dependent increase.

KEYWORDS: Aphrodisiac effect; herbal plant; reproductive performance parameters; experimental rat.

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INTRODUCTION

Medicinal plants serve as critical therapeutic agents and valuable raw materials for manufacturing numerous traditional and modern medicines. In many developing countries, traditional medicine is still the mainstay of health care, and most of the drugs and cures come from natural sources of plant origin[1]. Many herbal Plants and plant preparations produces a wide range of secondary metabolites such as phenolic compounds, alkaloids, flavonoids, and other secondary metabolites with proven aphrodisiac[2], spermatogenic[3] and antioxidant activities[4, 5, 6].

The aphrodisiac therapy, Pausinystalia yohimbe (K. Schum.) Pierre ex Beille, belongs to the family Rubiaceae. It is an evergreen species growing in West and Central Africa in lowland forests. The tree grows about 30 m tall, with a straight boles/trunk that is rarely larger than 50-60 cm in diameter. The leaves grow in groups of three, with short (about 2 cm) petioles. The blades are oval-shaped, 11-47 cm long and 5-17 cm wide. Its geographical spread is from South-Western Nigeria to Gabon and Zaire[7, 8].

The aphrodisiac activity of some plants like Tribulus terrestris and Microdesmis keayana have been implicated due to their androgen increasing properties[9, 10]. Since the Pausinystalia yohimbe leaf has been acclaimed to be used as an aphrodisiac8, there is the need to provide scientific information on its androgenic potentials which appear not to be, to the best of my knowledge, in existence of the open scientific literature. This study therefore attempts to provide scientific evidence to the androgenic potentials inherent in the aqueous extract of Pausinystalia yohimbe leaf, and focuses on evaluating the effect on sexual behavior and its sequences leading to the mating of Wistar rats.

MATERIALS AND METHODS

Animals

The Animal, Herbal Plants and Plant Preparations Ethics Committee of Olusegun Agagu University of Science and Technology, Okitipupa, Nigeria has approved the experimental protocol. We used adult rats, Wistar strain for all experiments. These animals were acclimatized to laboratory conditions (temperature 25±2 °C and humidity 70-80% and photoperiod 12:12h); with free access to rat's pellet and water. And after extract administration, they were subjected to various sexual behavioural study using the methods of Yakubu *et al*[11].

Ethical approval was obtained before the start of the research study from the Institutional Ethical Committee on Use of Experimental Animal and Procurement of Herbal Plants of Olusegun Agagu University of Science and Technology, Okitipupa, Ondo State, Nigeria.

Procurement, Authentication and Preparation of the Plant Sample

The plant material was collected at Arakhuan village in the boundary of Okomu National Park, Udo, Edo State. It was authenticated in Botanical Systematic Unit of Eureka Herbal Clinic, IgboEgunrin, Ondo State. Aqueous maceration of P. yohimbe powdered leaves sample was done by macerating 400g of plant powder for 24 hours in two liters of distilled water at (99.8%) at room temperature and in the shade for 72 days. After filtration, the solution obtained was evaporated in the shade. With the help of a magnetic stirrer to drive out the solvent using a hot plate at 50 °C until a paste was obtained, kept at 4 °C until its use.

Treatments, Dosage of Test Drug and Route of Administration

Forty rats were separated into four groups, a control group and three treatment groups (5 males and 5 females each), which were subjected to treatment by gavage, of 2, 5 and 10 mL/kg of P. yohimbe for fourteen successive days.

Reproductive Performance

In mammals, male sexual behavior includes a precopulatory phase (motivational or appetitive) and a copulatory (or consummatory) phase leading ultimately to ejaculation12. During the precopulatory phase, male rats sniff the genitals of females, emit ultrasonic vocalizations, mark their territory with urine, and show a clear preference

for oestrus (or receptive) females[12]. During the consumptive phase, the male performs climbs followed by intromissions, during which he performs back-and-forth movements corresponding to rhythmic pelvic thrusts, culminating in ejaculation[12]. Thus, in rats, copulatory parameters take place chronologically according to Yakubu *et al*[11]: (1) In the *mounting*, the male rat climbs on the receptive female in heat from the rear flank and makes pushing movements with his pelvis. The latency is generally 3 to 6 seconds; (2) The intromission occurs similarly to the mating but is immediately followed by a deep pelvic thrust when the penis enters the vagina; this penetration phase lasts about 200 to 400 ms in well-trained rats.

Reproductive Performance Measurements

After the last administration, the animals were placed in a mating cage (one couple per day) in a quiet room at room temperature (24±2 °C) with a light/dark cycle of 12:12h and a humidity of 60 to 65%. Before each test, the male rat was placed in the observation cage (42 cm x 10 cm x 21 cm), he was allowed to get used to the test chamber for 5 min. Afterward, a female was introduced into the cage, and the mating behavior observation started immediately after the introduction of the female, and the parameters were recorded as the test progressed. The copulatory activity (rise latency, intromission latency, rise frequency, and intromission frequency) of each male was evaluated in the presence of a female in a quiet room as described by Watcho et al13.

Reproductive Orientation Activities

Male rat orientation activities towards females (riding, licking, and sniffing), and towards oneself (genital grooming, non-genital grooming) were observed during the period of the copulatory behavior test, according to the method described and evaluated according to Zade et al[14]. No male was exposed to the same female more than once during the experiment. These tests are carried out according to three types of crosses: control male × control female, treated male × treated female, and treated male × control female. Examinations usually are completed immediately after the first post-ejaculatory intromission. In this test, female rats were introduced into the cages of the male animal with a ratio of one female to one male[11].

Reproductive Performance Parameters

The following parameters of sexual behavior were measured as described by Yakubu et al[11]. Mating latency time (ML) is the time between introducing a female into the cage and the first breeding; The latency time of the intromission (IL) is the time that separates the introduction of the female and the first intromission; The frequency of mounts (MF) is the mounts numbers, with or without intromissions preceding ejaculation; The frequency of intromissions (IF) corresponds to the number of intromissions preceding ejaculation; Penile licking (PE) is the number of times the rat bent over to lick the penis.

Plate 1: A pictorial relay of reproductive performance test

Data Analysis

All parameters measured in this study were statistically analyzed by SPSS computer software (version 20) and Microsoft Excel (2013) software, using descriptive metric methods giving the mean, and the standard deviation of the mean. The results were, also, analyzed by a variances comparison (ANOVA, whose significance level is $p < 0.05$).

RESULTS

From our findings, we noted that the first contact time is 25.60±5.30 seconds in the control rats, while

the treated rats took less time to establish the first contact with their partner than the control rats; these times are significantly different (Table 1). For the intromission latency time, the aqueous extract of P. yohimbe acts on this time, and we recorded less time in the treated rats compared to the control (Table 1). Aqueous extract significantly increased the intromission frequency in treated rats compared to control rats, which had lesser frequency (Table 1). Similarly, we recorded a significantly decreased mounting latency in the treated rats compared to control rats (Table 1).

Table 1 Effect of the aqueous leaves extract of P. yohimbe on 1st contact, the latency time of the intromission, the frequency of intromission, and mating latency time of Wistar rats.

Group	1st Contact time (s)	Contacts number	Intromission latency time (s)	Intromission frequency	Mounting latency time (s)
Control	25.60± 5.30	111.20± 36.51	12316.20±11444.51	3.80±1.39	14.60±6.12
2 mL/kg	19.20±8.03	120.40± 25.33	12107.60±9877.75	15.60±8.80	5.00±1.41
5 mL/kg	9.20±0.80	168.40±15.68	6693.60±3374.76	19,40±8,90	4.20±1.20
10 mL/kg	21.40±8.17	140.40± 15.37	7673.40±1334.36	17.20±6.40	6.00±3.40
P-value	0.05*	0.05	0.05	0.05**	0.05**

The mounting frequency is increased in the treated rats compared to the control (Table 2). We found highly significant differences between the mount's frequencies ($P < 0.05$; Table 2). For the rise latency time, P. yohimbe affects significantly, the rise latency time ($P < 0.05$; Table 2). The P. yohimbe aqueous extract has a highly significant influence on the mating time ($P < 0.05$; Table 2). In the end, we show that the males lick their penises; we noted that the P. yohimbe aqueous extract does not act on this sequence, and we recorded no significant effect between the licking times (Table 2).

Table 2 Effect of the aqueous leaves extract of P. yohimbe on the frequency of mounts, mating time, time of licking, and number of lickings of Wistar rats.

Group	Mounts frequency	Mating time (s)	Licking time (s)	Lickings number	Ejaculation
Control	3.80±1.39	7.60±2.78	165.20±104.30 12.	40±6.54	Absent
2 mL/kg	11.20±6.40	30.10±15.20	163.00± 75.27	14.00±3.16	Present
5 mL/kg	19.40±8.90	38,80±17,81	214.40±144.91	23.00±7.42	Present
10 mL/kg	15.60±8.80	31.20±17.60	167.00± 79.87	18.00±5.16	Present
P-value	0.05**	0.05**			

Also, administration of aqueous extract of P. yohimbe leaves affects specific performance parameters and sexual motivation in treated rats, thereby, causing a stimulatory effect, increasing sexual performance and orientation activity towards the female when compared with the control rats (Table 3).

Table 3 Effect of the aqueous leaves extract of P. yohimbe on the exploration, raring, climbing, genital grooming, and non-genital grooming of Wistar rats.

Group	Exploration	Raring	Climbing	Genital grooming	Non-genital grooming
Control	14.33±1.86b	4.00±2.00c	0.00±0.00	0.67±0.67d	1.00±0.58b
2 mL/kg	12.33±0.33a	1.33±0.67b	0.00±0.00	3.33±0.67b	1.33±0.88b
5 mL/kg	10.33±0.33a	0.67±0.57a	0.00±0.00	4.00±2.00a	2.33±0.33a
10 mL/kg	11.67±0.33a	2.00±0.00b	0.00±0.00	2.67±0.67c	1.67±0.67b

(n=4), $p < 0.05$ – Significant, $p > 0.05$ – Not Significant; Different letters in superscript across the columns are significant from others

DISCUSSION

Several studies reported that herbal plants are good sources of aphrodisiac alternatives for improving sexual functions in mammals, human beings inclusive[15], probably due to their bioactive agents, resulting in efficacy and potency[10]. This sexual behavior may also be due to androgenic and gonadotropic activities of P. yohimbe aqueous extract; these results were also observed for M. acuminata stem in male rats[16].

The frequencies of mounts and intromission remain sufficient valuable indices of vigour, libido, and power[17]. As observed in this study, treated animals with the aqueous extract of P. yohimbe show that the treated males go directly towards their treated females in the first 30 seconds of the test, contrary to the control rats, which take a little more time to join their females. This rapid orientation step towards the conspecific indicates the extract's stimulating effect, which probably includes aphrodisiac compounds. Our results are consistent with those of Yakubu and Akanji[16], which suggest that male rats, upon introduction to the test cage, responded with immediate advances toward females and showed precopulatory behaviors such as chasing anogenital sniffing that eventually resulted in mounting.

ML and IL are considered indicators of sexual motivation16. The significative reduction in these parameters observed in rats treated with aqueous extract of P. yohimbe could imply an improvement in sexual motivation and sexual appetite. Besides, increased MF is an indicator of vigor, libido, and potency. Increased MF indicates sexual motivation[18]. The pro-sexual effect of P. yohimbe was also established by increasing the MF after treatment.

When tested with a female, the copulatory behavior of the male rat consists of a repeated series of mounts and intromissions culminating in ejaculation[19]. The administration of an aqueous extract of P. yohimbe caused a stimulatory effect, increasing sexual performance and orientation activity towards the female. These results are similar to those of Watcho et al[13], and Watcho et al[20], where long-term administration of the aqueous and methanol extracts of Ficus asperifolia and Raphia vinifera leaves significantly increased the sexual behavior of the animals during the observation period.

The precopulatory behavior of the extract-treated male rats indicated that the animals were generally aroused. Several precopulatory behavior parameters of males were observed on the cage side when extract-treated male rats were presented to receptive female rats. Also, there was genital grooming after each mounting by the male which resulted in intromission. The effect of the aqueous extract of P. yohimbe leaves in rats was similar to that of the aqueous extract of the plant Massularia acuminata[16]. The present study results demonstrate the potency of P. yohimbe leaves stimulating the

copulatory activity of sexually naïve rats.

Our findings highlight the sexually stimulating effects of the aqueous extract of P. yohimbe leaves in rats and thus give credence to its aphrodisiac reputation. It appears from this work that this extract has a sexually stimulating activity which would confirm the interest of its traditional use as a reproductive performance stimulant. Based on these findings, we recommend that further studies with larger doses be conducted to confirm the results. However, based on the current findings, we recommend that careful administration be considered as a better option justifying human circumstances for patients with advanced mankind age in low dosage resource settings, as it achieves a better reproductive performance rate at a lower dose-dependent increase.

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PREMARITAL SEX AND ASSOCIATED FACTORS AMONG UNMARRIED STUDENTS OF A PRIVATE COLLEGE IN ADDIS ABABA, ETHIOPIA

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ABSTRACT

BACKGROUND: Premarital sex may result in sexually transmitted infections (STIs) and unwanted pregnancy. Published reports on the prevalence of premarital sex among private college students in Ethiopia are limited. This study aimed to assess the prevalence of premarital sex and associated factors among unmarried students of a private college in Addis Ababa, Ethiopia. Methods: A cross-sectional study was conducted and a structured questionnaire was used to collect data from 390 unmarried students of the college selected by stratified random sampling. Associations between variables were determined using binary and multiple logistic regression at P-value less than 0.05.

RESULTS: Eighty-one percent (316/390) and about 62% (241/389) of the participants were females and 18-21 years of age, respectively. The prevalence of premarital sex was 23.3% (88/290), and 20% (18/86) of the participants started sex before 18. About 68% (58/85) did not use condom at the first sex. Nearly 15.5% (9/58) had multiple sexual partners. About 14.5% (48/332) said oral contraceptive pills prevent STIs. Nearly 59 % (47/80) did not request a new sexual partner for STIs status. Multiple logistic regression analysis showed that religion (AOR,4.282; CI95%, 1.229-14.913; P, 0.022), study program (AOR, 3.417; CI95%,1.423-8.206; P, 0.006), having a boyfriend or girlfriend (AOR, 6.259; CI95%,2.866-13.672; P, 0.000), misconception that oral contraceptive pills prevent STIs (AOR, 3.345; CI95%,1.317-8.499; P, 0.011) and taking alcohol (AOR, 3.304; CI95%, 1.319-8.501; P, 0.011) were significantly associated with having premarital sex.

CONCLUSION: The prevalence of premarital was high among participants. Effective intervention strategies are needed to reduce the prevalence of premarital sex.

KEYWORDS: COLLEGE STUDENTS, ETHIOPIA, PREMARITAL SEX, PREVALENCE

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INTRODUCTION

Premarital sex is sexual intercourse performed before marriage. Many students start in premarital sex in educational institutions. The rate of premarital sex among university/college students is increasing globally and it varies from country to country. In Iran, it was 15.1% among non-medical students of a great university of Mashhad [1] . It was 63.9% among the unmarried youth of Vientiane, Laos[2]. It was 8.1% among unmarried female undergraduates in China (Wuhan)[3, 4].The rate of premarital sexual intercourse was low (4.3%) among students of Dicle University in Turkey[5].The prevalence of premarital sexual practice in Africa seems to be higher compared to other continents. In Nigeria the prevalence of premarital sex was 45.8% among nursing students[6]. A higher prevalence of premarital sex (70.4%) was found among female undergraduate students of Muhimbili and Dar es Salaam Universities, Tanzania[7], and university students in Uganda (74%)[8] and Botswana (65.35%)[9].

In Ethiopia, the prevalence of premarital sex among university/college students ranged from about 23% to 68% (10-23). The associated factors with premarital sex were watching pornography, alcohol use, attending night clubs, khat chewing[10,13,24,25]. Unsafe premarital sex may lead to unwanted pregnancy and STIs. It is estimated that 50% of pregnancies among girls between 15 and 19 years of age in developing countries are unintended[26]. The prevalence of unintended pregnancy is about 34% among college students in China[27]. Among female students of Ethiopian universities and colleges, it is 6.6% (28). World Bank estimates that 5% to 33% of girls between 15 and 24 years of age in some countries drop out from schools due to early pregnancy or marriage[29]. This is also a problem among female students in Ethiopian universities[30,31].

There are a few published reports on the prevalence of premarital sex among unmarried students of private colleges, particularly in Addis Ababa. This study aim to determine the prevalence of premarital sex and associated factors among students of Ayer Tena Health Science and Business College (ATHSBC).

MATERIALS AND METHODS

Study Setting and Design

A cross-sectional survey was used. ATHSBC, located in Addis Ababa, Ethiopia, runs degree and level programs in regular and extension modalities.

Population

The source population was all students of ATHSBC. The study population included randomly selected unmarried students.

Sample size determination

Sample size (n) was calculated to be 384 using a single population proportion formula.

$n = z^2p(1-p)/w^2$

where,

p = proportion (50%)

n = sample size

z = confidence interval (with 95% level of certainty)

w = margin of error (5%)

When a 10% non-response rate was considered, the sample size became 422.

Sampling methods and procedure

A source population of about 2900 students was stratified by division of study, field of study, department, section and sex. Systematic random sampling was used to select females and males from each section in proportion to their numbers, resulting in the selection of 422 students from all sections.

Exclusion and inclusion criteria

Married students were excluded from this study, whereas single students who were not widowed or divorced were included.

Study variables

The independent variables were sex, age, religion, frequency of religious service attendance, study field, place of residence, cohabitant type and place of high/preparatory school completion. The dependent variable was having premarital sex.

Data collection and analysis

Data were collected using a self-administered, close-ended questionnaire that was pretested.The questionnaire included questions about socio-demographic characteristics and behavior of the study participants. Data were entered into Excel before export to SPSS v20 for management and analysis. Missing data were excluded from prevalence calculations. Associations between variables were determined using binary and multiple logistic regression. P-value less than 0.05 was considered statistically significant. First, binary logistic regression was used to determine the existence of association between having premarital sex and many independent varaiables (Table 3). Variables that showed statistically significant associatation at P-value less than 0.05 were analysed for further association by multiple logistic regression (Table 3).

Ethics approval

This study was approved by the Ethical Review Committee of ATHSBC. Informed written consent was obtained from study participants before data collection.

RESULTS

Socio-demographic characteristics of the study participants

From a total of 422 unmarried students recruited to participate in this study, 390 (92.4%) filled the questionnaire. The majority of them were 18-21 years old (61%; 241/389), females (81%; 316/390), Christians (61.6%; 282/381), business students (58.8%; 228/388), degree students (56.8%; 221/389) and regular students (62.1%; 242/390). Most of them lived together with both parents (35.7%; 138/387), did not have income (69%; 256/371), lived in and around Addis Ababa for five or more years (63.7%; 246/386), and completed grade 10 or 12 in and around Addis Ababa (55.7%; 215/386) (Table 1).

Table 1. Socio-demographic characteristics of students of ATHSBC, Addis Ababa, 2019

Variable	Measurement level	Frequency	Percent
Sex	Male	74	19.0
	Female	316	81.0
Age	16-17	22	5.7
	18-19	128	32.9
	20-21	113	29.0
	22-23	65	16.7
	24-25	37	9.5
	≥ 26	24	6.2
Religion	Orthodox	221	58.0
	Islam	90	23.6
	Protestant	60	15.7
	Catholic	1	0.003
	Other	9	2.4
Frequency of religious service attendance	Daily	99	25.6
	1-2 times per week per week	126	32.6
	3 times or more	74	19.1
	Occasionally	78	20.2
	Never	10	2.6
Field of study	Health	160	41.2
	Business	228	58.8
Program of study	Level	168	43.2
	Degree	221	56.8
Division of study	Regular	242	62.1
	Extension	148	37.9
Have income	Yes	115	31.0
	No	256	69.0
Place where Grade10 or 12 Completed	In or around Addis Ababa	215	55.7
	Amhara	61	15.8
	Oromia	50	13.0
	Debub	47	12.2
	Tigray	6	1.6
	Other	7	1.8
Number of years lived in or around Addis Ababa	1-2 years	92	23.8
	3-4 years	48	12.4
	≥ 5 years	246	63.7

Prevalence of pre-marital sex

The prevalence of premarital sex was 23.3% (88/378) among the students (Table 2). Of those who experienced sexual intercourse, 43.5% (37/85) had sex in the last 12 months, 14.3% (12/84) practiced sex with individuals of the same sex , and 51.3% (41/80) did not plan for the first sexual intercourse. From the total participants who answered a relevant question, 11.4 % (40/352) had sex in the last 12 months. The most common reasons reported for having premarital sex were falling in love (69.3%; 52/75), development of sexual desire (16%; 12/75) and peer pressure (9.3%; 7/75) (Table 2).

Table 2. Premarital sexual activity of students of ATHSBC, Addis Ababa, 2019

Variable	Measurement level	Frequency	Percent
Ever had sex	Yes	88	23.3
	No	290	76.7
Age at first sex	12-13	4	4.7
	14-15	5	5.8
	16-17	9	10.5
	18-19	31	36.0
	20-21	21	24.4
	22-23	14	16.3
	24-25	2	2.3
Used condom at first sex	Yes	27	31.8
	No	58	68.2
Reason for premarital sex	Fell in love	52	69.3
	Peer pressure	7	9.3
	Developed desire for sex	12	16.0
	Raped	2	2.7
	Drunk	1	1.3
First sex planned	Yes	39	48.8
	No	41	51.3
Had sex in the last 12 months	Yes	40	11.4
	No	312	88.6
Number of lifetime sex partners	1	54	65.9
	2	12	14.6
	3	7	8.5
	4	3	3.7
	5-10	4	4.9
	> 10	2	2.4
Number of current sex partners	1	49	84.5
	2	3	5.2
	4	2	3.4
	5-10	3	5.2
	>10	1	1.7
Ever had sex without condom	Yes	52	61.2
	No	33	38.8
Reason for having sex without condom	The sex was accidental and I did not have condoms with me.	18	40.0
	I believed that my sex partner was free from STIs.	12	26.7
	My sex partner refused.	6	13.3
	I did not know that I had to use condom.	2	4.4
	To get better sexual satisfaction	2	4.4
	Other	5	11.1
Ever requested a new sex partner for STIs and HIV test	Yes	33	41.3
	No	47	58.8
Seduce opposite sex	Yes	19	5.3
	No	337	94.7
Frequency of pornography watch	Always	4	1.1
	Most of the time	15	4.1
	Sometimes	44	12.1
	Never	302	82.7
Ever had sex with a person of the same sex	Yes	12	3.3
	No	352	96.7
Drink alcohol	Yes	63	17.1
	No	306	82.9
Take drugs	Yes	11	3.0
	No	356	97.0

Risky sexual practice

About 21% (18/87) of the participants who had practiced sex started it before the age of 18, whereas 76.4% (66/86) began sex between 18 and 23, inclusively (Table 2). Regardless of whether it was the first sex or not, 70% (49/70) had a history of having sex without a condom, and 47.3% (35/74) had never used a condom for

sex. About 68% (27/85) did not use condom for the first sex. The most common reasons reported for having unprotected sex were that they had sex accidentally and they did not have condoms with them (40%;18/45) and that they believed that their new sexual partner was STI-free (26.3%; 12/45) (Table 2). Out of 82 respondents, 28 (34.1%) had two or more sexual partners in their lifetime. About 58.8% (47/80) of respondents established a new sexual partner without asking for STI and HIV status. About 14.5% (48/332) responded that oral contraceptive pills protect against STIs.

Factors associated with having premarital sex

In bivariate analysis, sex, religion, study field, study program, income, seducing the opposite sex, having a boyfriend or girlfriend, misconception that oral contraceptive pills protect from acquiring STIs, watching pornography and alcohol drinking were statistically significantly associated with having premarital sex (Table 3). In multivariate analysis, religion (AOR, 4.282; CI95%, 1.229-14.913; P, 0.022), program of study (AOR, 3.417; CI95%,1.423-8.206 ; P, 0.006), having a boyfriend or girlfriend (AOR, 6.259; CI95%, 2.866-13.672; P, 0.000), misconception that oral contraceptive pills protect from STIs (AOR, 3.345; CI95%, 1.317-8.499 ; P, 0.011) and taking alcohol (AOR, 3.304; CI95%, 1.319-8.501; P, 0.011) were independently associated with having premarital sex, after controlling other variables (Table 3). Thus multiple logistic regression analysis showed that premarital sex was found to be more common among Christians, degree students, those who have a boyfriend or girlfriend, those who believe that oral contraceptive pills provide protection against STIs and those who take alcohol (Table 3).

Table 3. Factors associated with having premarital sex among students of ATHSBC, Addis Ababa, 2019

Variable	Category	Had premarital sex		cOR	CI 95%	p-value	AOR	CI 95%	p-value
		Yes (%)	No (%)						
Sex	Male (ref)	30 (41.7)	42(58.3)				1		
	Female	58(19)	248(81)	3.050	1.764-5.288	0.000	1.844	0.699-4.868	0.216
Religion	Christian (ref)	76(27.9)	196(72.1)				1		
	Muslim	7(7.8)	83(92.2)	4.598	2.034-10.393	0.000	4.282	1.229-14.913	0.022
Field of study	Health (ref)	52(32.9)	106(67.1)				1		
	Business	36(16.5)	182(83.5)	2.480	1.523-4.039	0.000	1.889	0.901-3.960	0.092
Program of study	Level	20 (12.3)	142(87.7)	3.284	1.896-5.689	0.000	3.417	1.423-8.206	0.006
	Degree (ref)	68(31.6)	147(68.4)				1		
Have income	Yes (ref)	39(35.8)	70(64.2)				1		
	No	44(17.5)	208(82.5)	2.634	1.583-4.382	0.000	1.912	0.888-4.118	0.098
Seduce opposite	Yes (ref)	14(73.7)	5(26.3)				1		
sex	NO	68(20.7)	261(79.3)	10.747	3.741-30.878	0.000	1.229	0.290-5.200	0.780
Have boy-/	Yes (ref)	65(44.8)	80(55.2)				1		
girl-friend	No	21(9.7)	196(90.3)	7.583	4.347-13.229	0.000	6.259	2.866-13.672	0.000
Do contraceptive	Yes (ref)	26(53.1)	23(46.9)				1		
pills protect	No	54(19.4)	224(80.6)	4.689	2.485-8.847	0.000	3.345	1.317-8.499	0.011
from STIs?									
Ever watched	Yes	29(34.5)	31(65.5)				1		
Pornography	NO	31(11.4)	242(81.5)	4.116	2.293-7.388	0.000	2.180	0.866-5.485	0.098
Take alcohol	Yes (ref)	36(60)	24(40)				1		
	No	49(16.3)	252(83.7)	7.714	4.232-14.061	0.000	3.304	1.319-8.501	0.011

CONCLUSION

This study showed that the prevalence of premarital sex and risky practices is high among students of ATHSBC. Therefore, effective reproductive and sex health education must be provided to college and secondary school students by colleges and other stakeholders in order to save them from being victims of unwanted pregnancy and sexually transmitted infections. In providing health education, it is important ensure that students get rid of misconception about function of oral contraceptive pills. Moreover, parents and guardians need to advise their children not be engaged in premarital sexual intercourse and risky sexual behaviors. Furthermore, the usual role of religious institutions in solving these problems has to be emphasized and promoted.

DECELARATIONS

Authors' contribution

All authors contributed to the conceptualization, design and implementation of the study, data collection, analysis and interpretation, and writing the manuscript.

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A RETROSPECTIVE ANALYSIS OF MATERNAL AND PREGNANCY OUTCOMES FOLLOWING PMTCT MATERNAL COHORT REGISTRATION IN A DISPLACED SETTING

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ABSTRACT

BACKGROUND/AIM: This study assessed maternal and pregnancy outcomes following the Prevention of Mother-to-Child Transmission (PMTCT) cohort registration in a displaced setting.

Methods: A retrospective analysis of HIV-positive pregnant women's outcomes following enrollment in the maternal PMTCT register between January 2019 and December 2021 in FSP Daudu. Using a checklist, data was collected from the folders and PMTCT maternal register. Measures of interest included sociodemographic characteristics maternal outcomes and pregnancy outcomes.

RESULTS: Of 223 HIV-positive pregnant women, 201 were enrolled in the program. However, only 189 maternal records met the inclusion criteria. Registration for the PMTCT program occurred primarily during the prenatal period, between the ages of 26 and 30, with a mean gestational age of 15.2 weeks. Only 5.95 reported facility delivery, and up to 70% had over 4 PMTCT follow-up visits before delivery ($\chi 2 = 6.825$, $P = 0.03$). The retention rate among the cohort was 98.4%, with 62 % of the women being active throughout the program and over 86% having a live birth. Most miscarriages occurred during the first trimester. Bivariate analysis suggested that aside from maternal age, similar factors affected maternal and pregnancy outcomes. These factors include maternal prior PMTCT experience, total number of visits, and the place of delivery.

CONCLUSIONS: Active follow-up and documentation constitute an effective strategy to improve PMTCT maternal retention in care and improve patient outcomes. Ensuring that women are active in PMTCT care by engaging community health workers in service delivery will create positive outcomes in the program.

KEYWORDS: PMTCT, HIV, Maternal health, Pregnancy.

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INTRODUCTION

The Prevention of Mother-to-Child Transmission (PMTCT) of the Human Immunodeficiency Virus (HIV) follow-up program for pregnant women program focuses on Prongs 3 and 4 of the PMTCT, which are: to prevent HIV transmission from a woman living with HIV to her infant (prong 3); and to provide appropriate treatment, care, and support to women living with HIV and their children and families (prong 4)[1]. In most facilities that run the PMTCT program, health providers Integrate information about HIV and Acquired immunodeficiency syndrome (AIDS) as well as education on PMTCT care options to empower women/men about the need to be retained in care during pregnancy. In most countries, Nigeria inclusive, the Option B+ approach has been implemented in the PMTCT care[2,3]. Option B+ is a vertical transmission prevention strategy in which pregnant HIV-positive women are offered lifelong medication regardless of their CD4 status. This strategy offers benefits such as protection for the partner(s) and (unborn) kid, as well as health benefits for the woman[4]. However, there exist numerous challenges with implementing the PMTCT program and the Option B+ approach. In a study in Nigeria and Malawi, findings suggested that challenges in PMTCT program implementation centered around economic and sociocultural factors, limited male involvement, the organization of PMTCT service delivery, as well as factors centered around health workers' inefficiency[5,6]. These same factors affect sexual and reproductive health and rights (SRHR) services including PMTCT in displaced settings[7,8]. In a study by Wut et al., (2017), that examined the outcomes of women in a PMTCT cohort it was highlighted that there was a low mother-to-child transmission rate but high loss-to-follow-up of mother-infant pairs[9]. This same finding has been discovered in other places like Ethiopia, where pregnant women on lifelong antiretroviral therapy (ART) had improved health outcomes than those on short term prophylaxis[10]. Although there are many studies evaluating the PMTCT program, there is little literature on maternal outcomes following PMTCT registration. Most studies have focused on, retention, LTFU and infant outcomes[10,11]. The exposure to sexual and reproductive health and right (SRHR) challenges and risk of LTFU in care due to migration by women in this area is a major public health concern. However , there are limited studies that examine or evaluate the outcomes of maternal PMTCT follow-up in displaced settings. Maternal PMTCT outcomes as prescribed by the Federal ministry of Health (FMoH) include: active in PMTCT, transferred out, transferred to another PMTCT, transition to an ART clinic, LTFU, and death[12]. According to Resnik, (2019), one major outcome of every pregnancy that needs to be examined is the proportion of life births, still births and miscarriages amongst others[13]. Based on this background, this study examines pregnancy and maternal outcomes following PMTCT cohort registration in a displaced setting in Nigeria.

Background of PMTCT services at the Family Support program (FSP) Clinic Daudu

The FSP Daudu clinic is located in the Guma local government area (LGA) of Benue state. It provides SRHR care, pediatric and general medical care in the community. The facility provides PMTCT care as part of its ART clinic. When a pregnant HIV positive woman presents at the facility, she is enrolled into the PMTCT program and is registered in the PMTCT maternal cohort register. She is then encouraged to seek ANC care alongside PMTCT care. ANC and PMTCT services are integrated however, records are kept separately. The woman is then scheduled for follow-up visits with the facility. During each visit, she is clinically assessed, and records are kept in her folder and in the PMTCT maternal cohort register. To aid follow-up and improve attendance, trained community health workers, including mentor mothers and traditional birth attendants function, as adhoc staff who assist with PMTCT activities. This practice has been recommended to improve program performance[14].

These volunteers assist with maternal follow-up, drug pickup, health education, tracking of LTFU and other activities aimed at improving maternal health and having a positive PMTCT experience. The facility also runs a mother-to-mother support group activity, in which women in the PMTCT program come together to share experience on how to live healthy with HIV and bring forth healthy HIV-negative babies. All HIV services including PMTCT services are offered free.

MATERIAL AND METHODS

This was a retrospective analysis of PMTCT pregnancy outcomes of HIV women's outcomes who enrolled in the PMTCT maternal cohort register between January 2019 and December 2021 in FSP Daudu. Since 2018, the people of Benue and the Fulani have been in a clash over farming and grazing land and this clash has caused the displacement of over one million people (IDMC & NRC, 2019). These displaced persons are faced with SRHR issues, including HIV and AIDS. According to the Nigeria HIV/AIDS Indicator and Impact Survey (NAIIS) report, the state has an HIV prevalence of 4.3%[15].

Both patient folders and the PMTCT maternal cohort register of those who enrolled in the PMTCT maternal cohort register were reviewed. Figure 1 shows the flow chart of studies included in the study. A checklist which was developed following a review of literature and indicators listed in the PMTCT register was used. The checklist was pilot tested on 18 records of women who used the PMTCT maternal service in 2018. The Cronbach's Alpha test was used to test for reliability and the instrument was found reliable at 0.927, (P value =0.000). The checklist was inputted into the Kobo toolbox to collect the data. Four research assistants were trained in data collection. Permission was sort form the State ministry of Health and head of the facilities clinic to assess the records.

Source of data and measures

Each mother's demographic and clinical data was captured in her folder and in the register during each visit. These included, age, date of enrollment in the ART, gestational age (GA) of registration and point of entry (Antenatal, intra-natal or post-natal). Each time a mother or mother/infant pair reported to the clinic for follow-up , the outcome measures were evaluated.

Measures of interest included sociodemographic characteristics, maternal outcomes as prescribed by the maternal cohort register and pregnancy outcomes. Maternal outcomes included: active in maternal PMTCT, transfer to an ART clinic (positive outcomes), transfer to another maternal PMTCT ,loss to follow-up (LTFU), death of the woman(negative outcomes), while pregnancy outcomes included miscarriage/still-birth (negative outcomes) or life birth (positive outcomes) . Active in PMTCT was defined as having over 4 PMTCT visits while out of facility delivery included delivery out of a hospital setting.

Data Analysis

Data were imported into SPSS 23, cleaned, and analyzed. The data was represented in charts and tables. Bivariate analysis of chi-square/Fisher's exact test was used to associate the sociodemographic characteristics of respondents to maternal outcomes and pregnancy outcomes. Outcomes were classified as good or poor by scoring participants' responses. Negative maternal outcomes were assigned a -1 and positive outcomes were assigned a +1. After summations, outcomes with a negative sum were classified poor. Retention in care was defined as mothers who stayed in care till the end of her pregnancy. Maximum score of maternal and pregnancy out comes was 2 and 1 respectively.

RESULTS

A total of 223 women were pregnant during the study period, however, only 201 women were registered in the PMTCT maternal cohort register, of this,189 records met the inclusion criteria. However only 186 were examined (figure 1)

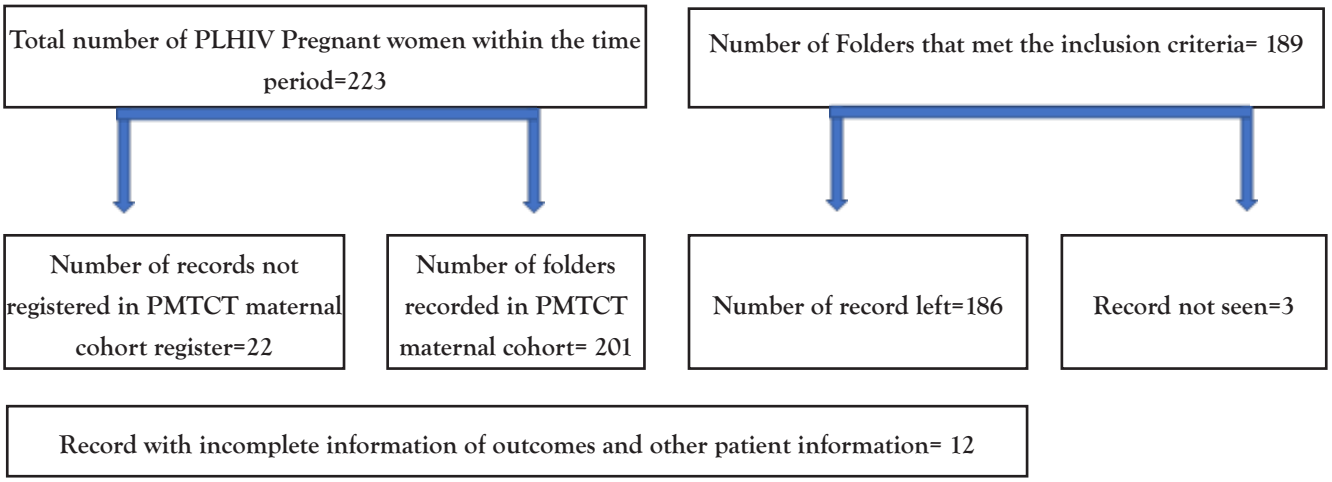

Fig. 1: Flow chart of records included in the study

Sociodemographic characteristics of respondents

Table 1 shows that about one-third of the respondents 68(36.6%) were between 26-30 years of age, with a mean age of 28.8 ±5.6 years. The major point of entry was during the antenatal care total of 99% of the respondents were on a first-line regimen. Most women were enrolled into the PMTCT program in their first trimester (64.5%) and the mean gestational age at PMTCT registration was 15.2weeks. Up to 64% of the respondents started PMTCT after 1 year of enrollment in ART, while 58.1% had prior PMTCT experience. Most participants 116 (62.4%) had a minimum of four a PMTCT visits however, majority 175(94.1%) of the women gave birth out of the facility.

Pregnancy/maternal outcomes of women who received maternal PMTCT services

In Figure 2, of the 186 respondents, 116 (62.4%) were active throughout the PMTCT visit. 171(91.9%), transferred to an ART clinic after PMTCT while 12(6.5%) transferred from PMTCT to another PMTCT program. Only 2 (1.1%) women were LTFU while 1 maternal dead was recorded (giving a retention rate of 98.4%) and 163(87.6%) had a live birth

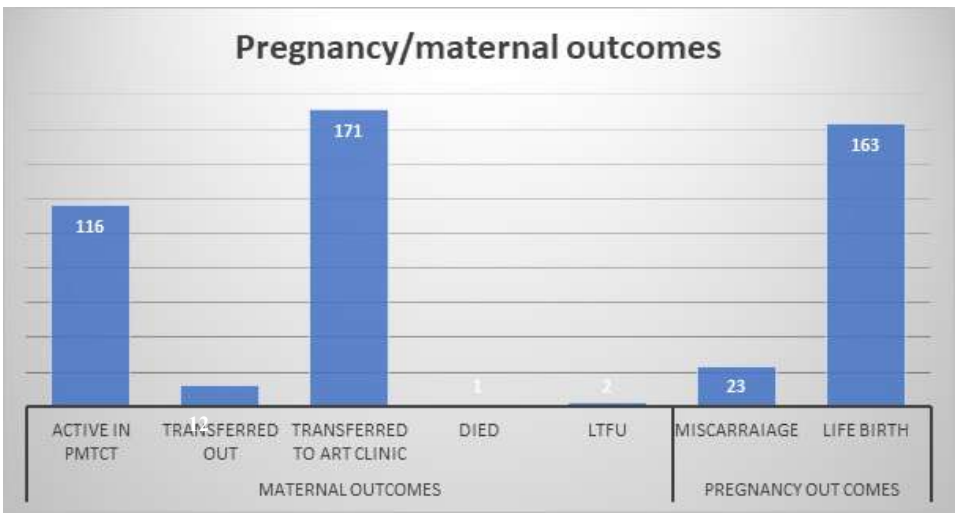

Figure 2: Pregnancy/PMTCT maternal outcome

***Active in PMTCT means a total of 4 or more PMTCT visits. Sociodemographic characteristics of respondents**

Table 1: Sociodemographic characteristics

Age		Mean	N (%)
		28.8 ±5.6	
age range	20 and bellow	14 (7.5)	153(82.3)
	21-25	45 (24.2)	17(17.6)
	26-30	68(36.6)	
	31-35	37 (19.9)	
	36 and above	22 (11.8)	
point of entry	Antenatal		185(99.5)
	Post-natal		1(0.5)
ARV Regimen	1st line		184(99)
	2nd line		2(1)
GA in weeks		15.2weeks	
G A range (weeks)	0-12 weeks		120(64.5)
	13-26 weeks		63(33.9)
	27-40 weeks		3(1.6)
Art Start	within 1 year of ART enrolment		67(36.0)
	after 1 year of ART enrollment		119(64.0)
prior PMTCT experience	Yes		108(58.1)
	No		78(41.9)
Place of delivery	Facility		11(5.9)
	Out of facility		175(94.1)
total visit	≤3		70(37.6)
	4 and above		116(62.4)

Relationship between number of visits and place of delivery

The total number of visits significantly affected a woman's place of delivery. Over 70% of those who gave birth at the facility had more than four visits. This was statistically significant at $X^2 = 43.5$, $p = 0.00$.

Distribution of miscarriages per trimester

Most miscarriages 15/23 (65%) occurred during the 1st trimester(see Figure 3).

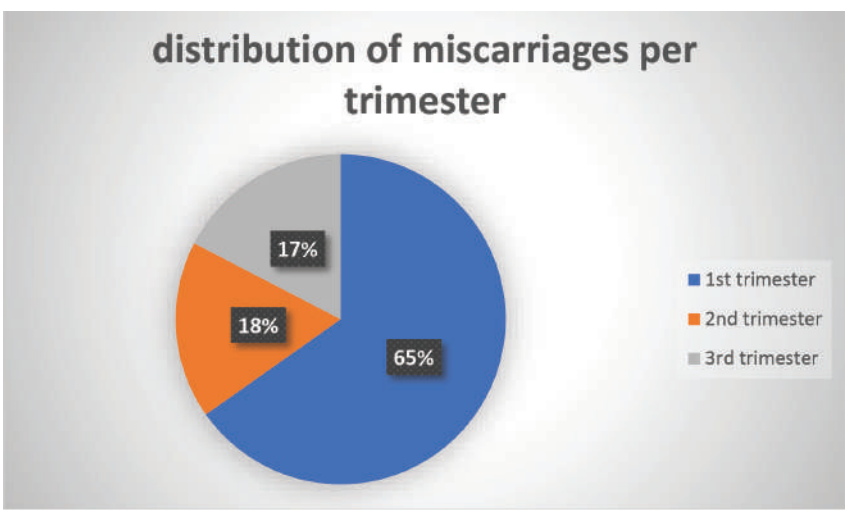

Figure 3: distribution of Miscarriages per trimester

Outcomes of PMTCT women who registered in the Maternal cohort.

After assigning scores to maternal and pregnancy outcome variables, over 80% of the women had a good outcome as seen in figure 4.

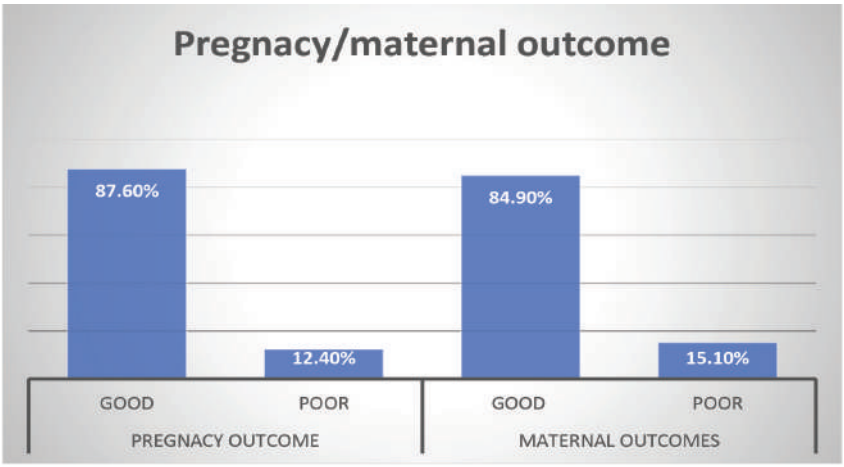

Figure 4: proportion of women with good/poor outcomes

While 87.6% had good pregnancy outcomes, 84.9% had good maternal PMTCT outcomes.

Association between sociodemographic characteristics and pregnancy /maternal outcome

In table 3, aside the age of the respondents, same factors that affected maternal PMTCT outcomes affected pregnancy outcomes. A woman on ART Prior to PMTCT experience, maternal age and total number of visits significantly affected maternal outcome. Most women with good outcome had prior PMTCT experience. This was statistically significant ($\chi 2$ = 14.8.; p = 0.00 and $\chi 2$ = 11.02; p = 0.001) for maternal and pregnancy outcomes respectively. Most women with facility delivery had a good outcomes ($\chi 2$ = 148.43; p = 0.00 and $\chi 2$ = 151.59; p = 0.00 for maternal and pregnancy outcomes respectively) . also women with over 4 PMTCT visits had good outcomes($\chi 2$ = 32.47; p = 0.00 and $\chi 2$ = 32.21; p = 0.00 for maternal and pregnancy outcomes respectively) . the age of the respondent significantly affected only maternal outcome $\chi 2$ = 11.46, p = 0.022.

Table 2: Relationship between number of visits and place of delivery

		Place of delivering Facility	chi-square Out of facility	P value
total visit	≤3visits	3(27.3)	67(38.2)	43.5.000
	4 and above	8(72.7)	103(61.8)	
Total	11(100)	175(100)		

*The Chi-square statistic is significant at the .05 level.

Table 3: Bivariate association between sociodemographic characteristics and pregnancy /maternal outcome

Outcome		Maternal Outcome		Pregnancy	
		Test statistic	P value	Test statistic	P value
Age range	20 and bellow	11.46**	.022*	6.44**	.169
	21-25				
	26-30				
	31-35				
	36 and above				
Regime	1st line	.358**	.55	.29**	.593
	2nd line				
Art start	within 1 year of PMTCT enrolment	2.795	.095	1.59	.208
	after 1 year of PMTCT enrolment				
G A range (weeks)	0-13 weeks	.69**	.73	.62**	.734
	14-26 weeks				
	27-40 weeks				
Place of delivery	Facility	148.43**	.000*	151.59**	.000*
	Out of facility				
prior PMTCT experience	yes	14.80	.000*	11.02	.001*
	No				
total visit	less than 4 visits	32.47**	.000*	32.21**	.000*
	4 and above				

*. The test statistic is significant at the .05 level..

**. Fishers exact test

DISCUSSIONS

The goal of enrolling women in the PMTCT cohort registry and following them up throughout their pregnancies until 18 months after delivery is to prevent HIV transmission from the HIV-infected woman to her infant. The National Guidelines for HIV Care and Treatment recommend this as the third and fourth component of PMTCT care[16]. However, according to USAID, preventing vertical transmission, though crucial for the health of both the mother and her child, is faced with numerous challenges in Africa, especially in displaced communities. This challenge stems from among other things; gaps in program data reporting, inadequacies in service delivery, and low service uptake[17]

In this study,Only 83% of HIV-positive pregnant women were registered in the PMTCT-mother cohort during the study years, . It has been reported that in displaced communities, the number of health care practitioners available are often inadequate to serve the population in need[18]. In a review by Beek, Dawson and Whelan, (2017), while assessing factors that affect the transfer of sexual and reproductive health training skills into practice in humanitarian settings of low and lower-middle income country, it was highlighted that inadequacy in the health workforce was a major factor that affected delivery of services[19]. These same factors has been highlighted as reasons for substandard SRHR care in humanitarian settings[20]

The majority of the women in our study were between 26 and 30 years old. These findings are similar to those of other studies, which confirm that the majority of women who seek antenatal care in Nigeria are between the ages of 20 and 39[21].

Although most of the women in our study registered in their first trimester, the mean gestational age of PMTCT-maternal cohort registration was 15.2 weeks, with about three-fifths having a total of 4–8 PMTCT visits. The WHO recommends that women begin antenatal care within the first 14 weeks of gestation and take part in at least four-sessions to mitigate the risk of high-risk pregnancy[22]. For women with high-risk conditions, including HIV, more visits are required. However, studies in Nigeria have shown that most women begin ANC late[21,23]. In our setting, the reason for late registration may include poverty, inaccessibility to services, and limited knowledge about service benefits, which are common reasons that affect SRHR service provision in displaced settings[24]. Our findings were similar to those of Adebangbe and Mturi (2021), which showed that the majority of women in displaced settings in Northern Nigeria began ANC care during the second trimester[25]. In a retrospective study in Lesotho that assessed HIV status and antenatal care attendance among pregnant women in a rural setting, findings suggested that though the number of visits and GA at the first visit did not differ between HIV-positive and HIV-negative women, HIV-positive women who knew their status before ANC were more likely to present early than all other women[26]. However, these findings seemed to differ from that in our study, which focused on PMTCT visits.

About two-thirds 62.4% of the women had over 4 PMTCT visits. Other studies on number of ANC visitation are generally low, especially among internally displaced women[25,27]. The question that follows is whether HIV infection increases a woman's care-seeking behavior. Previous research reported that Nigerian women were making insufficient progress towards the WHO's goal of at least four ANC visits in the absence of complications[28].

The majority of the women in the study gave birth outside of the facility; however, the total number of visits significantly affected a woman's place of delivery. Over 70% of women who gave birth at the facility had more than four ANC visits. In many displaced settings, women have been reported to delivery at home or in the hands of traditional Birth attendants (TBA)[29,30]. A study by Ohihoin et al., (2021) among displaced women in Nigeria highlighted that more than 50percent of pregnancies occurred during displacement however only 20% of the women sought ANC while majority birthed at home[29]. According to the USAID, if a woman has not received at least one antenatal care visit, she is less likely to give birth in a health facility. Hence, the use of community workers including TBAs is essential to linking pregnant women to antenatal care and encouraging the use of a health facility for safe delivery[31].

The retention rate among the participants in our study was about 98%, with 87% of the women having a good PMTCT or pregnancy outcome. This can be attributed to the fact that the study assessed only women who were registered in the PMTCT maternal cohort. Studies among internally displace women highlighted poor maternal and neonatal outcomes[25,32]. Adebangbe and Mturi, (2021) echoed that these outcomes are poorer than that in non-humanitarian settings[25]. However, this was majorly because most of the women failed to seek care or are not properly followed up by a health care practitioner during the antenatal or postnatal period[25,32]. Also, Prior PMTCT experience, maternal age and total number of visits had a significant impact on maternal outcome. According to UNICEF, in a 2019 report concerning sub-Saharan Africa, it was noted that only 70% of HIV positive women were placed on ART, and 64% of HIV-exposed infants (HEIs) were tested for HIV at six weeks, however, only 55% of these infants received a definitive diagnosis at 18 months[33]. Following analysis of data from the INSPIRE project in Malawi, Nigeria, and Zimbabwe, retention-in-care rates among 5107 women ranged from 30% to 76%(6). our findings thus demonstrates that PMTCT maternal follow-up is an effective quality improvement intervention for increasing retention in programs aimed at preventing mother-to-child

HIV transmission. Thus, HIV programmers must continuer to place a greater emphasis on PMTCT follow-up in order to ensure high quality of care for pregnant women living with HIV.

CONCLUSION

This study analyzed the data of 186 women who had enrolled in the PMTCT program in displaced setting. Findings suggested that following up pregnant women living with HIV during pregnancy has the possibility of improving maternal outcomes. The study also note a very high rate of out-of-facility delivery by HIV-positive women in the displace setting. However, women who participate in PMTCT are more likely to give birth in the facility. Also, maternal prior PMTCT experience, total number of visits, and place of delivery significantly affected the maternal and pregnancy outcomes of the women. Hence, we can conclude that the active involvement (visitation as scheduled and retention throughout pregnancy) of an HIV-positive pregnant woman in care can improve their health outcomes in times of displacement. We thus suggest that health care programmers should include lay community health workers, TBAs , and mentor mothers in PMTCT care programs to improve patient follow-up and linkage to a health facility for birthing. Leveraging mother-to-mother support group activities to improve awareness of the importance of PMTCT care and follow-up can improve program outcomes. In addition, it is also necessary for PMTCT providers to increase efforts to ensure women have appropriate PMTCT follow-up visits at the facilities. This will go a long way toward improving the quality of life of pregnant HIV-positive women in displaced settings.

LIMITATION

Our study was limited to women enrolled in the PMTCT cohort register; hence, data on women who were not registered in the program were un available. The study employed a retrospective approach, hence only data available in the record was used for the study. Cases of missing data were noted in some folders and in the registers while ANC uptake was not recorded along PMTCT service uptake, although having more information about ANC services uptake by the women would have been useful for this study, however, there was no unified record system whereby women's data could be traced and linked at the facility.

Conflict of Interest: The authors declare no conflict of interest.

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COJOINED TWINS: SAFE TERMINATION OF PREGNANCY THROUGH DILATION AND EVACUATION AT LATER GESTATION: A CASE SERIES

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ABSTRACT

BACKGROUND: Currently, there is limited evidence on termination of pregnancy for cojoined twin documented with only 33 cases reports to-date. This study aimed to describe the clinical and procedure characteristics of second trimester dilation and evacuation(D&E) for cojoined twins at later gestation.

METHODS: This retrospective case series was conducted at a tertiary-level hospital in Ethiopia from February 2023- July 2023. Women who had a cojoined twin pregnancy in later gestation (≥20 weeks) and underwent second trimester D&E were retrospectively studied through chart review. Clinical presentation, D&E procedural description, and procedure outcomes of the cases were analyzed.

RESULTS: Three women who had a cojoined twin in later gestation (≥20 weeks) and underwent second trimester D&E were identified. In two of the cases, a two- day cervical preparation with laminaria was used to prepare the cervix while overnight Foley catheter (1-day preparation) was used for similar purpose in the third case. A cervical dilation of 3 cm was achieved in all cases and was deemed adequate to proceed with the procedure by the managing physicians. Intra-operative ultrasound guidance was utilized in all the cases and there were no complications encountered.

CONCLUSION: Our case series underscores the importance of achieving adequate cervical preparation, utilization of intra-operative ultrasound guidance, and handling the procedure by the most experienced provider, in increasing the safety and effectiveness of D&E procedures for conjoined twin at later gestation.

KEYWORDS: cojoined twin, dilation and evacuation, D&E for conjoined twin, D&E for twin

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INTRODUCTION

Despite existence of significant limitation of epidemiological data, best estimates indicate up to 1% of monozygotic twins are conjoined twins[1]. Early diagnosis and thorough prenatal obstetric counselling (safe termination pregnancy versus continuing the pregnancy, expectant management) is the recommended management approach[2,3]. Some evidence show that 50–70% of patients with conjoined twin elect termination of pregnancy after comprehensive consultation[4]. However, there is limited evidence on termination of pregnancy for cojoined twin documented with only 33 cases reports to-date. Majority of the termination procedures in these reports were at ≥20 weeks through either labor induction or medication abortion or hysterotomy, with dilation and evacuation[5]. Our presents the first case series on dilation and evacuation procedure for conjoined twin at ≥20 weeks of gestation. We aimed to describe the clinical and procedure characteristics of second trimester dilation and evacuation(D&E) for cojoined twins at later gestation.

METHODS AND MATERIALS

We retrospectively studied three women with a diagnosis of cojoined twins at later gestation who were managed with a second trimester dilation and evacuation at St. Paul's Hospital Millennium Medical College, Ethiopia, Addis Ababa, from February 1, 2023 - July 24, 2023. Detailed anatomy scan with ultrasound was used to confirm the diagnosis in all the cases and it was performed by Maternal-fetal medicine (MFM) specialists. Counselling on safe termination as an option of management was also provided by the MFM unit. After patients consented for the D&E procedure, cervix was prepared adequately with combination of mechanical and medical methods. In this case series, we studied through chart review. Clinical presentation, D&E procedural description, and procedure outcomes of the cases were retrospectively analyzed through chart review. Formal ethical clearance was obtained from IRB of St. Paul's Hospital Millennium Medical College for this case series. Obtaining informed consent from study subjects was waived by this Ethics committee.

RESULTS

We identified three women who had a cojoined twin in later gestation (≥20 weeks) and underwent second trimester D&E were identified. Their age ranged from 25-32 years and the gestational age was ≥20 weeks (with one case being at 23 weeks). Two of the cases were parous while the third was a primigravid case. The two of the cojoined twins were pyopagus, while the third case was omphalopagus (Table-1). In case 1 and case 2, a two-day cervical preparation with laminaria was used to prepare the cervix while overnight Foley catheter (1-day preparation) used for similar purpose in case 3. Additionally, all cases received misoprostol 400mcg and mifepristone 200 mg oral as part of the cervical preparation in all cases. A cervical dilation of 3 cm was achieved in all cases and was deemed adequate to proceed with the procedure by the physicians, family planning specialists, who attended the procedures. Spinal anesthesia was utilized for pain control in two cases while conscious sedation with morphine plus paracervical block was used for the same purpose in third case (case 3). In all the cases the D&E procedures were performed under intra-operative ultrasound guidance and no complication was encountered. The duration of the procedure was 30-50 minutes.

Variable	Case 1	Case 1	Case 3
Maternal age(years)	25	32	25
Gestational age (weeks)	20	23	21
Parity	Nulliparous	Para-1	Para-3
Type of cojoined twin	pyopagus	pyopagus	omphalopagus
Cervical preparation method	2 days preparation with Laminaria	2 days preparation with laminaria	one day overnight transcervical Foley catheter
Cervical dilation before procedure Anesthesia	3 cm Spinal(bupivacaine)	3cm Spinal(bupivacaine)	3 cm Conscious sediation with morphine + paracervical block
Level of provided who attended the D&E	Family planning specialist	Family planning specialist	Family planning specialist
Procedure time(minutes)	40	50	30
Complication encountered	None	None	None

Table-I Reproductive characteristics and D&E procedure characteristics and outcomes of conjoined twins, Ethiopia 2023

DISCUSSION

In the present series, 3 conjoined twin cases had a second trimester dilation and evacuation at gestational age of 20-23 weeks. When it comes to the types; 2 cases were pyopagus conjoined twin and the third case was an omphalopagus conjoined twin. Two days of cervical preparation with laminaria was used in two of the case while an overnight transcervical Foley catheter placement (one-day preparation) was utilized in the third case for a similar purpose. Adequate cervical preparation (3 cm as objectively measured by the attending physicians-family planning attendings) was declared before starting the procedures. All the procedures were performed under intra-operative ultrasound guidance with spinal anesthesia used as a mode of pain control in two of the case while conscious sedation was utilized in the third case.

Conjoined twin gestation is a rare event with a peculiar and complex obstetric management approach[6]. Management starts with early detection with thorough prenatal imaging including ultrasound, fetal echocardiogram and fetal MRI, which may be a useful adjunct to clarify fetal anatomy that is incompletely defined sonographically, as well as to enhance details regarding brain, abdominal, and thoracic structures. Based on findings of these imaginings, conjoined twins can be categorized into the proper anatomic subgroup according to the most prominent site of connection (thoracopagus, omphalopagus, parapagus, ischiopagus, pygopagus, and craniopagus)[6,7]. Of conjoined twin types, thoracopagus is the most common one and also have the highest associated mortality rate due to the likelihood of shared vital cardiac structures[8,9]. In the present series three of the cases had different types of cojoined twins, one was pypagus, one was omphalopagus, while the third one was craniopagus. For families faced with a conjoined twin diagnosis, obstetric counseling must explore the expectant parents' values while providing realistic and detailed expectations for the postnatal course. Options for pregnancy management including termination of pregnancy and expectant management should be thoroughly reviewed[2,3]. In our case series, both the women and their husbands were counselled about the prognosis their conditions and the available options of management of the cojoined twin safe termination versus continuing the pregnancy by maternal fetal medicine specialists and safe termination of pregnancy was preferred by the couples in all the cases.

All options of pregnancy termination, including dilation and evacuation (D&E) has been described in the literature, although few case have been reported on this so far[10,11]. The option of termination depends on the site of connection (type of conjoined twin) and gestational age with the goal of minimizing maternal complications[6]. Induced termination at later gestation carries increased maternal risk, and the utility of induced fetal demise prior to the induction, as well as use of laminaria, mifepristone, and misoprostol with the purpose of promoting adequate cervical effacement and dilation should well considered before the procedure. Pre-procedure counseling for women undergoing such procedure should include potential risk for hemorrhage and need for hysterotomy or urgent D&E if such complication occurs. Although gestational age and clinician's experience will affect the availability of D&E as a safe option for conjoined twins in the later gestations (≥20 weeks), it is much preferred over hysterotomy, which has historically been employed for surgical termination including conjoined twins[11,12]. Considering the availability of family planning specialists with ample second trimester D&E experience, including those at advanced gestation of 22-24 weeks and after discussing the benefits and risks of surgical versus medication abortion with the patients, D&E was the preferred method termination of pregnancy.

If D&E is selected as option of termination of pregnancy for such patients, assessment of fetal size, fetal presentation, fetal width, and fusion site to determine the extent of indicated cervical preparation (i.e., number of millimeters of laminaria) and use of adjuvant medications including

mifepristone or misoprostol should be made[13]. Taking into account the advanced gestational age of the cases and the type of the cojoined twins, a clear plan of achieving adequate cervical preparation was put before the procedures in our case. To attain this, a 2-day preparation with laminaria was required in 2 of the cases while one-day preparation with Foley sufficed in the third case on the top of administering mifepristone and misoprostol in all cases. Moreover, it has been suggested to utilize intra-operative ultrasound guidance during the procedure for safe passages of D&E instruments in and out of the uterine cavity[5]. This suggestion was well utilized in all the procedures in the present series, with assistant surgeons holding the ultrasound prove and scanning the uterus in the directions as desired by the handling surgeons.

In summary, being the first case series on second trimester dilation and evacuation for cojoined twin at later gestation (≥20 weeks), our case series supports the previously reported suggestion of adequate cervical preparation, using intra-operative ultrasound guidance, and procedure attendance by the most experienced D&E provider, in order to have a safe termination of pregnancy with less complication through this procedure.

DECLARATION

Conflicts of Interest

The authors report no conflicts of interest.

Ethical Clearance

Formal ethical clearance was obtained from IRB of St. Paul's Hospital Millennium Medical College for this case series. The IRB waived the requirement for informed consent from participants.

Author contributions

AFS and LBT developed the concept and design of the project. AFS, LBT, TD, and DB contributed data collection and case analysis. AFS, DB, and LBT contributed manuscript write-up. All authors checked the manuscript for intellectual contents. The final manuscript is approved for submission by all authors.

Data Availability Statement

Data are available from authors up on reasonable request.

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INSTRUCTION TO AUTHORS

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