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Adverse pregnancy outcomes among pregnant mothers who chewed khat in Meru County, Kenya: A retrospective cohort study

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ABSTRACT

Background: Khat (Catha edulis) is a green leafy plant containing psychoactive alkaloids, such as cathine and cathinone. Khat use in pregnancy affects maternal and fetal well-being.

Objective: This study aimed to determine the risk of adverse pregnancy outcomes among pregnant women who chew khat compared with pregnant women who do not chew khat in Meru County in 2023.

Methods: A retrospective cohort study was employed at the Meru Teaching and Referral Hospital and Nyambene Level 4 Hospital that compared immediate postpartum mothers who chewed khat during pregnancy (exposed, n=150) and those who did not chew khat during pregnancy (unexposed, n=300). Data on khat chewing during pregnancy and various maternal, fetal, and early neonatal outcomes were collected using a questionnaire. Data were summarized as means, frequency, and percentages and compared using the Students t-test, Pearson's Chi-square, and Fischer's exact test. All statistical tests were considered significant if the p<0.05.

Results: There was a statistically significant increased risk of preterm birth (AOR 4.44, 3.31-10.92, p 0.001), low birth weight (AOR 2.95, 1.19-7.57, p 0.02), admission to neonatal intensive care unit or newborn unit (AOR 1.13, 1.03-4.10, p 0.01), and postpartum hemorrhage (AOR 12.85, 2.17 – 244.02, p 0.02). An increased risk of premature rupture of membranes was observed, but this was not statistically significant (OR 1.61, 0.9-2.85, p 0.11).

Conclusion: Women who used khat during pregnancy had an increased risk of adverse pregnancy outcomes, including preterm birth, low birth weight, admission to neonatal intensive unit, and postpartum hemorrhage.

Keywords: adverse pregnancy outcomes, khat, Meru

Introduction

Khat, or Catha edulis, is a green leafy plant that grows naturally in Eastern Africa and the Arabian Peninsula (1,2). In Kenya, it is commonly called Miraa and is grown for commercial purposes in the Nyambene Hills of Meru County (3). Khat leaves and stems contain psychoactive alkaloids, such as cathine and cathinone, which are primarily absorbed through the buccal mucosa when chewed (4). Khat use during pregnancy has adverse effects on both the mother and the fetus (5). Research has revealed that khat use is associated with a decrease in uteroplacental blood circulation (6,7), which can result in intrauterine growth restriction, fetal distress, preterm birth, low birth weight, and stillbirth (8–10). Moreover,

khat usage is linked to poor nutrition and anorexia, leading to poor pregnancy outcomes, such as anemia, and other adverse perinatal outcomes (11). Neonates born to khat users are more likely to require admission to the neonatal intensive care unit (12). The rate of khat chewing among pregnant women is increasing, and it is estimated that approximately 40% of Yemenite (13) and 20% of Ethiopian (8) pregnant women chew khat.

The prevalence of khat chewing during pregnancy in Kenya is not known. However, the prevalence of khat use among people aged 15 – 65 years is estimated to be 4.1% (14). Due to the inconsistency of studies, it is still difficult to establish the association between khat use and pregnancy outcomes. Studies have presented conflicting findings regarding the effects of khat on pregnancy outcomes. There is still a paucity of data on the effects of khat on pregnancy still exists; to the best of our knowledge, no such study has been conducted in Kenya.

In this retrospective cohort study, we evaluated the risk of adverse fetal, early neonatal, and maternal outcomes among pregnant women in Meru County, Kenya who used khat compared with those who did not use khat.

Methods

Study design

A hospital-based retrospective cohort study was employed to compare immediate postpartum mothers who chewed khat during pregnancy (exposed) and those who did not chew khat during pregnancy (unexposed).

Study setting

The study was conducted from February to March 2023 in 2 public hospitals within Meru County, namely Nyambene District Hospital, a level 4 hospital, and Meru County Teaching and Referral Hospital (MTRH), a level 5 hospital. Meru County is the largest khat-growing region, and the Ameru people are the largest khat consumers in Kenya.

Study population

The study participants were immediate postpartum mothers within 48 hours of delivery. Mothers were eligible if they were above 18 years of age, consented, had singleton pregnancies, and had delivered at a gestational age of 28-40^{+6} weeks. The gestational age was determined by the last normal menstrual period (LNMP) and a first-trimester obstetric ultrasound scan. Mothers who delivered before hospital arrival were ineligible.

Sample size

The sample size was calculated based on a 31% risk of adverse pregnancy outcomes in the exposed group versus an 18% risk in the unexposed group. We estimated that 450 participants (150 exposed vs 300 unexposed) would be required to detect the 13% difference in adverse pregnancy outcomes with 80% power and an alpha level of 0.05.

Study variables

The exposure variable was khat chewing during pregnancy, which was defined as any use of khat during pregnancy regardless of the amount, duration, or frequency. Outcome variables included adverse maternal, fetal, and neonatal outcomes. Adverse fetal and neonatal outcomes included non-reassuring fetal status (NRFS), preterm birth, stillbirth, congenital malformations, low birth weight, birth asphyxia, and admission to the newborn unit (NBU) or neonatal intensive care unit (NICU). Adverse maternal outcomes were preterm labor, prelabor rupture of membranes (PROM), and postpartum hemorrhage (PPH). The confounding variables included hypertensive disorders in pregnancy (HDP), diabetes mellitus (DM), cigarette smoking, and alcohol consumption during pregnancy.

Data collection and management

Postpartum women who delivered within 24 hours were recruited, screened, and consecutively sampled. The participants were asked for a history of khat chewing during the current pregnancy, and if they answered yes, they were enrolled in the exposed group. For every participant enrolled in the exposed group, we enrolled the next two who reported no history of khat chewing during the current pregnancy. Data were collected using a questionnaire developed and pretested in Nyambene Level 4 Hospital. Consecutive sampling was employed until 150 eligible mothers were recruited in the exposed group and 300 in the unexposed group. A total of 298 participants were recruited from Meru Teaching and Referral Hospital, while 152 were recruited from Nyambene Level 4 Hospital. Sociodemographic data were retrieved or corroborated from both the files and patients. Previous medical history, parity, gestational age at delivery, mode of delivery, and the various

pregnancy outcome data were retrieved from the patients' files while data
on the history of cigarette smoking and alcohol consumption during pregnancy were corroborated directly by the patients.

Data analysis

Continuous variables were summarized as means (SD) and compared using Students t-test. Categorical variables were summarized using frequency and percentages and compared using Pearson's Chi-square test and Fischer's exact test. The outcomes associated with khat usage were evaluated using univariate and multivariate logistic regression. The potential confounders were adjusted for. The relative Risks of the adverse fetal, early neonatal, and maternal outcomes were calculated. The crude odds and adjusted odds ratios with their 95% confidence intervals were reported. All statistical tests were considered significant if the $p<0.05$.

Ethical consideration

This study was approved by the KNH-UoN Ethics and Research Committee (P749/09/2022). Administrative approval was granted by the County Government of Meru Department of Health (MRU/MED/GEN/R.14). The National Commission for Science, Technology and Innovation (NACOSTI) research license was also granted (NACOSTI/P/23/23677). Written informed consent was obtained from each participant.

Results

From February to March 2023, 598 of 1862 postpartum mothers were screened, and 450 were enrolled. Of these, 148 were excluded (97 from Meru Teaching and Referral Hospital and 51 from Nyambene Level 4 Hospital) due to discrepancies between LNMP and ultrasound estimated gestational age (GA), irregular menstrual bleeding, and lack of first-trimester obstetric ultrasound. One hundred and fifty (33%) mothers reported the use of khat (exposed), while 300 (67%) did not use khat during pregnancy (unexposed). 298 (66%) participants were recruited from Meru Teaching and Referral Hospital, while 152 (34%) were recruited from Nyambene Level 4 Hospital (**Figure 1**).

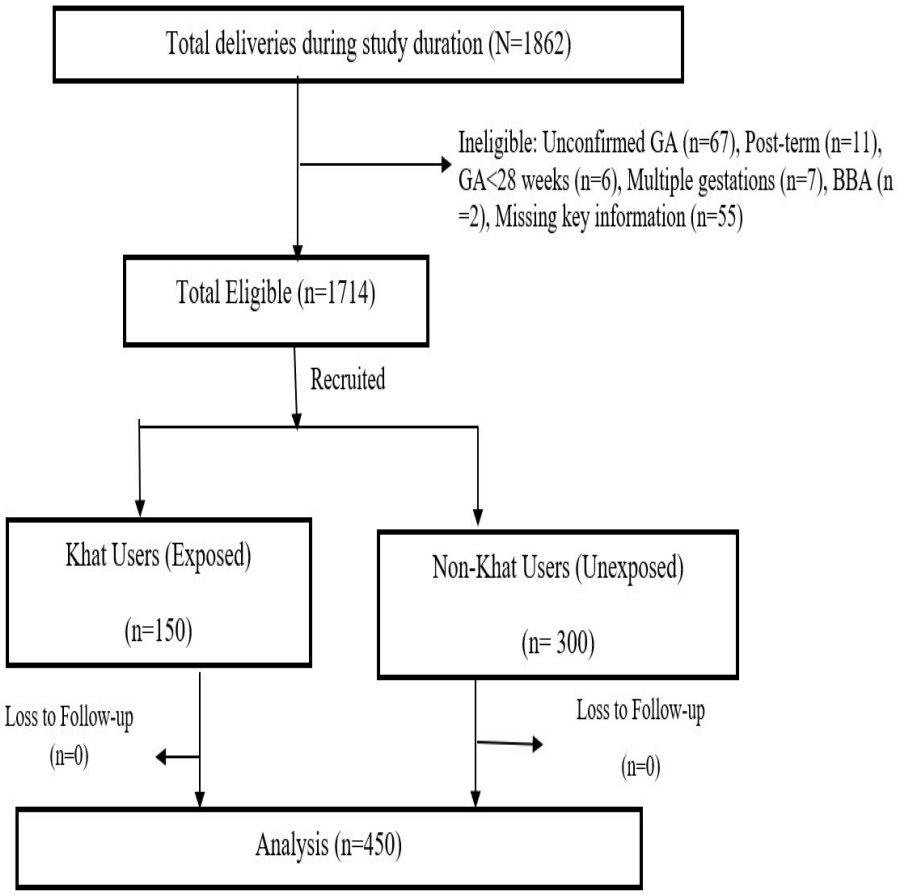

Figure 1: Recruitment of khat and nonkhat chewers during pregnancy in Meru County, Kenya

BBA: birth before arrival; GA: gestational age

Sociodemographic and clinical characteristics of khat and nonkhat users in pregnancy

The sociodemographic and clinical characteristics were similar between khat and nonkhat users. Most mothers of both khat and nonkhat users and nonusers were aged between 18 and 24 years. Approximately 40% of khat users (n=60) and nonusers (n=118) were

primiparous, and 42% (n=63) and 46.7% (n=140) had four or more ANC visits, respectively. Seventy-eight percent (n=117) of khat users and 80.7% (n=242) of nonkhat users delivered vaginally. Notably, 6% (n=6) of khat users reported alcohol consumption during pregnancy compared with 0.7% (n=2) of nonkhat users. Hypertensive disorders in pregnancy were diagnosed in 3.3% (n=5) of khat users compared with 2% (n=6) of nonkhat users (**Table 1**).

Table 1: Sociodemographic, obstetrics, and clinical characteristics of khat and nonkhat users during pregnancy in Meru County, Kenya

Variable	Exposed to khat, n (%)	Unexposed to khat, n (%)
Maternal age		
18 -24	80 (53.3)	178 (59.3)
25-29	25 (16.6)	59 (19.7)
30-34	30 (20.0)	30 (10)
35 and above	15 (10)	33(11.0)
Education level		
None	4 (2.7)	2 (0.7)
Primary	75 (50.0)	91 (30.3)
Secondary	52 (34.7)	150 (50.0)
College/University	19 (12.6)	57 (19)
Occupation		
Casual worker	12 (8)	15 (5.0)
Formal employment	-	2 (0.7)
Self/business	65 (43.3)	137 (45.7)
Student	12 (8)	41 (13.7)
Unemployed	61 (40.7)	105 (35.0)
Marital status		
Married	123 (82.0)	243 (81.0)
Single	23 (15.3)	55 (18.3)
Divorced	3 (2)	2 (0.7)
Widowed	1 (0.7)	-
Religion		
Christian	148 (98.7)	299 (99.7)
Muslim	2 (1.3)	1 (0.3)
Alcohol consumption	9 (6.0)	2 (0.7)
Cigarette smoking	1 (0.7)	-
BMI		
Normal	93 (62.0)	159 (53.0)
Underweight	4 (2.6)	8 (2.7)
Overweight	44 (29.3)	112 (37.3)
Obese class II	7 (4.6)	20 (6.7)
Obese class II	2 (1.3)	1 (0.3)
HIV status		
Positive	1 (0.7)	2 (0.7)
Negative	149 (99.3)	298 (99.3)
Parity		
Primiparous	60 (40.0)	118 (39.3)
ANC visits		
<4	87 (58.0)	160 (53.3)
≥4	63 (42.0)	140 (46.7)
HDP	5 (3.3)	6 (2.0)
Mode of delivery		
Vaginal	117 (78.0)	242 (80.7)
Cesarean birth	33 (22.0)	58 (19.3)

BMI: body mass index, HIV: human immunodeficiency virus, ANC: antenatal clinic, HDP: hypertensive disorders in pregnancy

Neonates of khat users had a statistically significant increased odds of the following: 4-fold risk of increased preterm birth (AOR 4.44, 3.31-10.92, p 0.001), 3-fold risk of increased risk of low birth weight (AOR 2.95, 1.19-7.57, p 0.02), and 1.1-fold increased risk of admission to NICU/NBU (AOR 1.13, 1.03-4.10, p 0.01). The fetuses of khat users had slightly increased odds of NRFS, but this finding was not statistically significant. Only one stillbirth and one congenital malformation (spina-bifida) were recorded in neonates born to nonkhat users. Analysis of maternal outcomes revealed a statistically significant increased risk of PPH (AOR 12.85, 2.17 – 244.02, p 0.02) and preterm labor (AOR 4.44, 3.31-10.92, p 0.001). An increased risk of PROM was observed, but this was not statistically significant (OR 1.61, 0.9-2.85, p 0.11). Khat usage was associated with reduced odds of both anemia and congenital malformations although these were not statistically significant (**Table 2**).

Table 2: Association between khat usage and adverse pregnancy outcomes in Meru County, Kenya

Variable	Exposed to khat, n (%)	Unexposed to khat, n (%)	COR (95% CI)	P value	AOR (95% CI)	P value
Stillbirth	-	1 (0.3)	0.03 (N/A-Inf)	1.00	-	0.99
Preterm birth	10 (6.7)	2 (0.7)	9.03 (3.91 – 13.42)	<0.001	4.44 (3.31 – 10.92)	0.001
Apgar score Low (≤3) Intermediate (4-6) Normal (7-10)	 - 3 (2.0) 147 (98.0)	 2 (0.7) 5 (1.7) 293 (97.7)	 Ref 1.007 (0.65 – 7.23) 1.21 (0.87 – 3.920)	0.68	-	
Low birth weight	11 (7.3)	7 (2.3)	3.27 (2.81 – 7.97)	<0.001	2.95 (1.19 – 7.57)	0.02
NICU/NBU admission	12 (8.0)	7 (2.3)	3.55 (1.35 – 10.40)	0.01	1.13 (1.03 – 4.10)	0.01
NRFS	10 (6.7)	18 (6.0)	1.13 (0.48 – 2.55)	0.78	-	
Preterm labor	6 (6.7)	2 (0.7)	9.03 (3.91 – 13.42)	<0.001	4.44 (3.31 – 10.92)	0.001
PROM	26 (17.3)	34 (11.3)	1.61 (0.90 – 2.85)	0.11	-	
PPH	7 (4.7)	1 (0.3)	12.26 (2.15 – 230.15)	0.02	12.85 (2.17 – 244.02)	0.02
Anemia	15 (10)	34 (11.3)	0.84 (0.42 – 1.60)	0.60	-	
Congenital malformation	-	1 (0.3)	0.03 (N/A-Inf)	1.00	-	0.99

NICU: neonatal intensive care unit, NBU: newborn unit, NRFS: non-reassuring fetal status, PROM: prelabor rupture of membranes, PPH: post-partum hemorrhage, COR: crude odds ratio, AOR: adjusted odds ratio

Neonates of khat users had a statistically significant increased odds of the following: 4-fold risk of increased preterm birth (AOR 4.44, 3.31-10.92, p 0.001), 3-fold risk of increased risk of low birth weight (AOR 2.95, 1.19-7.57, p 0.02), and 1.1-fold increased risk of admission to NICU/NBU (AOR 1.13, 1.03-4.10, p 0.01). Fetuses of khat users had slightly increased odds of NRFS, but this finding was not statistically significant. Only one stillbirth and one congenital malformation (spina-bifida) were recorded in neonates born to nonkhat users.

Analysis of maternal outcomes revealed a statistically significant increased risk of PPH (AOR 12.85, 2.17 – 244.02, p 0.02) and preterm labor (AOR 4.44, 3.31-10.92, p 0.001). An increased risk of PROM was observed, but this was not statistically significant (OR 1.61, 0.9-2.85, p 0.11). Khat usage was associated with reduced odds of both anemia and congenital malformations, although these differences were not statistically significant.

Discussion

In this retrospective cohort study, the effects of khat use during pregnancy were evaluated and found that it was associated with adverse pregnancy outcomes. Preterm birth and low birth weight were significantly associated with khat use during pregnancy. Preterm birth

was found to be four times more in pregnant khat users whose neonates had three times increased odds of low birth weight. Expectedly, these neonates were more likely to be admitted to the NICU or NBU. Postpartum hemorrhage was shown approximately ten times more likely to occur in khat users than in nonkhat users. However, this had a wide confidence interval, indicating that the sample size was inadequate to evaluate this outcome. Pregnancy outcomes like NRFS, birth asphyxia, stillbirth, congenital malformation, maternal anemia, and PROM were significantly associated with khat usage during pregnancy.

Our findings on preterm birth matched a case-control study that was conducted in Yemen looking at khat chewing during pregnancy, where they found that pregnant khat users had a statistically significant risk of 6 times for preterm birth (12). Their study also found statistically significantly higher odds (8 times) of low birth weight than ours (3 times). These notable higher odds could have been due to the fewer study participants (60 cases and 120 controls) and the difference in the study designs employed. Similar to their finding, another case-control study that looked at risk factors for low birth weight in Ethiopia in 2015 found six times increased odds of low birth weight among khat users during pregnancy (9). A recent meta-analysis that reviewed the effects of khat use during pregnancy on perinatal and maternal outcomes found the odds of low birth weight to be 2.5 times in khat users during pregnancy (5). This was more consistent with our finding of 3-fold odds of low birth weight. We hypothesize that the higher odds of low birth weight among pregnant khat users could be due to the higher odds of preterm birth. The low birth weight and preterm birth could be due to a reduction in uteroplacental blood circulation, which has been demonstrated in some experimental animal studies. In a 1987 study, pregnant guinea pigs were fed with khat leaves, and it was noted that vasoconstriction occurred in the uteroplacental vascular bed, leading to a 25% reduction in blood flow to the placenta (15). A 2021 experimental study on laboratory rats demonstrated disorganization of the vascular tree in the placental labyrinth layer with less vascular branching and certain degrees of dysmorphology in the decidua basalis in rats exposed to khat (16).

Similar to the Yemen study (12), there were significantly higher odds of admission to NICU/NBU of neonates born to khat users during pregnancy. This finding is predictable and in line with findings of higher odds of preterm birth and low birth weight, as these are the leading causes of neonatal admission. Our study failed to find any association between khat use during pregnancy and congenital malformations. However, several studies have found increased odds of congenital malformations in khat users (12,17). Our study design was not suited to evaluate relatively rare outcomes like congenital malformations compared with the case-control study design, which was employed in the two studies that showed increased odds of congenital malformations. In addition, we recorded only one congenital malformation (spina bifida) in a neonate born to a nonkhat user during pregnancy.

One limitation of our study was that the interviews were conducted in the immediate postpartum period. Mothers with adverse pregnancy outcomes could have strong social desirability and, therefore, withhold a history of khat, cigarette, or alcohol use during pregnancy. This was overcome by explaining that the information provided was confidential. Another limitation was that we could not assess khat use during pregnancy. In conclusion, khat use during pregnancy was associated with adverse pregnancy outcomes. Longitudinal studies with longer follow-up duration and assessment of the placentas of pregnant khat users for any abnormal changes are recommended.

Availability of data and materials

The data supporting the findings of this study are available within the article and its supplementary materials. Further inquiries should be directed to the corresponding author.

Author contributions

All authors made substantial contributions to the conception, design, acquisition, analysis, and interpretation of the data, and drafting or critically revising the article

Conflict of interest

The authors declare no conflicts of interest.

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