Khat Chewing During Pregnancy: an Insight on an Ancient Problem. Impact of Chewing Khat on Maternal and Fetal Outcome among Yemeni Pregnant Women

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Abstract
This study was conducted to clarify the impact of Khat chewing on maternal and fetal outcomes during pregnancy of Yemeni women.

Khat chewing during pregnancy can affect maternal health with a damaging effect on the baby’s health and wellbeing. This study was conducted to clarify the impact of Khat chewing on maternal and fetal outcomes during pregnancy of Yemeni women.

This prospective study enrolled 60 regular Khat chewing pregnant women and 120 non-Khat chewing pregnant women, selected from those attended with singleton pregnancy in their first or second trimester from the ANC unit of AL-Gamhouri Teaching Hospital in Taiz (Republic of Yemen).

Khat chewer pregnant women were having statistically significant risk of 6 times for preterm labor, 3.83 times for labor induction and statistically insignificant risk of 4.10 times for preeclampsia, 2.05 for PROM, 2.03 for PPH and perineal tears and 2.02 for IUFD. There is significant lower mean hemoglobin concentration at delivery when compared with the control.

Khat chewer pregnant women were having statistically significant risk of 6.56 times for breech presentation; 8.94 times to deliver fetuses with low birth weight (<2500 gm); 6.0 times for neonatal admission to the ICU and statistically insignificant risk of 3.54 times for perinatal mortality and 2.02 times for congenital malformations.

This study concluded that Khat chewing is globally associated with a negative impact on maternal and fetal wellbeing.

Keywords: Khat; Pregnancy; Maternal; Fetal; Outcome

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Introduction
Pregnancy is an important event during a woman’s reproductive life and her health as well as that of her fetus’s become sensitive to outside stimuli like tobacco smoking. Khat chewing during pregnancy can have a damaging effect on the baby’s health and wellbeing[1,2].

During pregnancy, several studies documented a number of negative reproductive health consequences and adverse pregnancy outcomes of Khat chewing, including lower lipoid, sexual impotence, and inhibition of utero-placental blood flow, leading to a teratogenic effect and the impairment of fetal growth[3].

Studies showed that the oral administration of cathinone, caffeine and their combinations for 15 days increased the arousal (motivation) in male rats as evidenced by increased mounting performance (sex drive) and anogenital investigatory behavior. However, erectile and ejaculatory responses, measured in the study, showed no stimulant effect[4]. On the other hand, a deleterious effects of Khat addiction were found on semen parameters in general and sperm morphology in particular, these parameters include semen volume, sperm count, sperm motility, index and percentage of normal spermatozoa[5].

Khat chewing during pregnancy is thought to influence fetal development. In an experiment to determine the genotoxic potential of Khat, a methanolic Khat extract was tested on male germ cells using a lethal assay procedure in Swiss albino mice[6,7]. The results showed that Khat reduces the percentage of pregnancy rates and increased the mean post-implantation losses in the treated groups while there was no change in the controls which received the vehicle (saline) only[6].

Lower birth weight was also found to be associated with Khat chewing[1,3,8]. However, there is no significant association between chewing Khat and stillbirth or congenital malformations[2].

Because the studies dealing with pregnancy outcome among Khat chewers pregnant women are few and the results are contradicting[9], it was decided to conduct this study among Yemeni women who are Khat chewers, in
order to reassess the outcome of pregnancy in regard to maternal health and fetal outcome.

Materials and methods

This case-control prospective study was conducted in the period between June 2013 and February 2014. It included 60 regular Khat-chewer pregnant women attending the antenatal care clinic of AL-Gamhouri Teaching Hospital in Taiz (Republic of Yemen). All of them had singleton pregnancy in their first or second trimester. We excluded those women who were smokers, having pre-existing medical disorders such as: hypertension, cardiac disease, diabetes mellitus, chronic nephritis, autoimmune diseases or Rh isoimmunisation. History of recurrent abortion, cervical incompetence, uterine tumor or anomaly or antepartum hemorrhage (placenta previa) was also an exclusion criterion.

Regular Khat chewer pregnant woman was defined as pregnant women who chew Khat at least twice a week, for at least one year including the time of current pregnancy.

To assess the impact of Khat chewing on maternal and fetal outcomes, a matched control group of 120 pregnant women was selected at the same time from non-Khat chewer pregnant women with the same exclusion criteria.

Data were collected directly from all pregnant women in a previously designed questionnaire with demographic data, clinical history, and clinical examination. Then blood and urine samples were sent to the laboratory for examination and the studied pregnant women were subjected to ultrasound examination, and followed till delivery. In some pregnant women, data of delivery were collected from the hospital records or by phone contact.

All women were followed regularly up to the end of pregnancy. They were observed in about 4-5 visits during the period of pregnancy, during delivery, and after delivery to report any maternal or fetal complications.

Ethical consideration: This study was approved by the ethical committee of the hospital and according to the scientific methodology in researches involving human been, this study took in consideration at the time of data collection, the right of women to participate or not to participate in this study. Verbal consent was obtained from each woman after simple explanation of the objectives of the study.

Data analysis: The collected data were reviewed and processed by the SPSS statistical program. We analyzed data for those only who completed the study. Lost-to-follow up cases were excluded from the analysis. For the impact of Khat chewing on maternal and fetal outcomes, the adjusted OR was calculated with its 95% CI. Other continuous variables were presented as mean values with standard deviations and tested by the student t-test. P-values of <0.05 were considered statistically significant.

Results

Evaluation of the maternal outcome showed that Khat chewer pregnant women were having a statistically significant risk of 6 times for preterm labor; 3.83 times for labor induction; and a significant lower mean hemoglobin concentration at delivery when compared with the control.

### Table 1: Maternal outcome in Khat chewer pregnant women compared to the control

| Maternal outcome            | Pregnant women | Statistics |
|-----------------------------|----------------|------------|
|                             | Khat-chewer (n=60) | Control (n=120) | P OR 95% CI |
| Induction of labor          | 7 11.7 4 3.3    | 0.028 3.83 1.07 - 13.65 |
| Pre-eclampsia               | 2 3.3 1 0.8     | 0.217 4.10 0.36 - 46.19 |
| Urinary tract infection     | 10 16.7 11 9.2  | 0.140 1.98 0.79 - 4.97 |
| PROM                        | 3 5.0 3 2.5     | 0.378 2.05 0.40 - 10.49 |
| Preterm labor              | 8 13.3 3 2.5    | 0.004 6.00 1.53 - 23.53 |
| Fetal distress             | 4 6.7 3 2.5     | 0.173 2.78 0.60 - 12.87 |
| IUFD                        | 1 1.7 1 0.8     | 0.615 2.02 0.12 - 32.82 |
| PPH                         | 2 3.3 2 1.7     | 0.475 2.03 0.28 - 14.81 |
| Perineal tear              | 2 3.3 2 1.7     | 0.475 2.03 0.28 - 14.81 |
| Blood transfusion          | 4 6.7 3 2.5     | 0.173 2.78 0.60 - 12.87 |
| Hb concentration (g/dl)     | 10.1 ± 1.07     | 10.6 ± 0.93 | (F = 10.44 , p = 0.001)† |

Percentages were calculated from the total of each column SD: standard deviation; OR: odds ratio; CI: confidence interval; Hb: Hemoglobin

*p-value of <0.05 is statistically significant

PROM: premature rupture of membranes; IUFD: intrauterine fetal death; PPH: postpartum hemorrhage

The reference groups for each row are those not develop such outcome

†Calculated by the student t-test for two means

Khat chewer pregnant women showed other risks when compared with the control such as a risk of 4.10 times for preeclampsia; 2.78 for blood transfusion; 2.78 for fetal distress; 2.05 for PROM; 2.03 for PPH and perineal tears; and 2.02 for IUFD. However, these risks were found statistically insignificant.

Evaluation of fetal presentation by ultrasound before delivery of the studied groups showed that Khat chewer pregnant women when compared with the control were having a significant risk of 6.56 times for breech presentation.

### Table 2: Fetal outcome in Khat chewer pregnant women compared to the control

| Fetal outcome                | Pregnant women | Statistics |
|------------------------------|----------------|------------|
|                              | Khat-chewer (n=60) | Control (n=120) | P OR 95% CI |
| Birthweight of the delivered fetus (gm): | | | |
| 1500 – 2499                  | 8 13.3 2 1.7 | 0.001 8.94 1.83 - 43.59 |
| 2599 – 3999                  | 51 85.0 114 95.0 | 1 | |
| ≥ 4000                      | 1 1.7 4 3.3 | 0.602 0.56 0.06 – 5.12 |
| Mean ± SD (gm)              | 2546.1 ± 712.9 | 2970.5 ± 414 | (F = 25.45, p = 0.0001)† |
| Congenital malformations     | 1 1.7 1 0.8  | 0.615 2.02 0.12 – 32.82 |
| Admission to neonatal ICU   | 8 13.3 3 2.5 | 0.004 6.0 1.53 - 23.53 |
| Stillbirth                   | 2 3.3 3 2.5 | 0.748 1.34 0.22 to 8.27 |
| Early neonatal death        | 3 5.0 0 0.0 | 0.014 - |
| Perinatal mortality         | 5 8.3 3 2.5 | 0.073 3.54 0.81 – 15.37 |

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Fetal outcome among the studied groups showed that Khat chewer pregnant women when compared with the control were having a significant risk of 8.94 times to deliver fetuses with low birth weight (<2500 gm); and a significant risk of 6.0 times for neonatal admission to the ICU.

They showed other risks of 3.54 times for perinatal mortality and 2.02 times for congenital malformations. However, these risks were found statistically insignificant.

**Discussion**

The impact of Khat chewing on maternal and fetal outcomes is a matter of debate. Khat chewing is a wide spread practice among Yemenis and it is part of the social and cultural fabric of Yemeni society (WHO, 2006).

Khat chewer pregnant women in this study showed other risks when compared with the control such as a risk of 4.10 times for preecclampsia; 2.78 for fetal distress; 2.05 for PROM; 2.03 for PPH and perineal tears; and 2.02 for IUFD. However, these risks were found statistically insignificant. These risks may be of significant association to Khat chewing during pregnancy but our sample size was small and not enough to elucidate such significant risks.

During delivery of Khat chewer pregnant women in this study, they showed a significant risk of 3.83 times for labor induction. It may be attributed to the premature rupture of membranes, where the amniotic fluid has ruptured but labor has not started within 24 to 48 hours.

It may also be explained by the hormonal effects on uterine contraction, where the constituents of Khat have been shown to exert their effects on two main neurochemical pathways: dopamine and noradrenalin. Cathinone has a releasing effect on adrenalin storage sites, which supports the conclusion that cathinone facilitates adrenalin transmission. Drake (1988) also proposed that cathinone and cathine cause inhibition of adrenalin uptake.

Normally, later in labor, a burst of adrenaline can give the laboring woman the extra energy she needs to push her baby out during a time when she would otherwise be feeling taxed and exhausted, and can trigger the involuntary expulsive reflex.

It may be due to the inhibitory effect of Khat on the uptake of adrenaline, in some Khat chewer pregnant women in this study, they needed labor induction to complete their labor successfully.

Blood transfusion to Khat chewer pregnant women in this study was higher than to non-Khat chewer pregnant women (33.2% vs 19.6%). Khat by itself was found to cause anorexia and decreased absorption of food in the gastrointestinal tract (WHO, 2006). These factors in addition to the preexisting bad nutritional habits among Yemeni pregnant women explained by the National Nutrition Strategy for Yemen which included inadequate dietary intake quantitatively and qualitatively, less access of nutrition screening and counseling services, early and frequent pregnancies, heavy work load, high prevalence of parasitic infestation and inappropriate life habits like chewing Khat (The National Nutrition Strategy for Yemen, 2009).

These factors were evident by the finding of significantly lower mean hemoglobin concentration in the studied Khat chewer pregnant women when compared to non-Khat chewer pregnant women. All these factors increased the rate of blood transfusion during pregnancy and delivery.

Evaluation of fetal presentation by ultrasound before delivery of the studied groups showed that Khat chewer pregnant women were having a significant risk of 6.56 times for breech presentation. The higher risk for malpresentation among Khat chewer pregnant women may be attributed to the higher risk of preterm labors, where the studied Khat chewer pregnant women had a statistically significant risk of 6 times for preterm labor.

Fetal outcome in this study, showed that Khat chewer pregnant women were having a significant risk of 8.94 times to deliver fetuses with low birth weight (<2500 gm); and a significant risk of 6.0 times for neonatal admission to the ICU. The retardation of growth rate may be due to decreased absorption of food and not to decreased food consumption only.

A study on pregnancy outcome and Khat (included 1,141 consecutive deliveries at delivery centers in Yemen) showed a significantly increased incidence of low-birth-weight, full-term infants among the offspring of women who chewed Khat during pregnancy in comparison to those who were non-chewers during pregnancy.

The study of Abd-El-Aziz and Ahmed, in Ethiopia, showed that neonates of mothers who chewed Khat during pregnancy had a significant decrease in all neonatal parameters such as birth weight, length, head circumference and Apgar score at 1 and 5 minutes in comparison with those of mothers who did not chew Khat during pregnancy, this effect was found to increase in severity with the increased frequency and duration of Khat chewing during pregnancy.

The results obtained from the above-mentioned studies indicate that frequent use of Khat during pregnancy may impair intrauterine fetal growth. An experimental study in rats has recently proved that Khat can affect intrauterine fetal growth by reducing total fetal fat and weight and by inducing some changes in the chemical composition of fetal organs, particularly the liver, heart and kidneys. This effect was attributed to depletion of carbohydrate material and suppression of DNA and protein synthesis in the fetal organs.

Low birth weight is a contributing risk factor for both prenatal and infant mortality among Khat chewers during pregnancy. It can affect fetal growth during pregnancy through placental insufficiency, which could be explained by the high blood pressure registered among these women. In many experiments visceral and skeletal malformations have been reported but have not been proved yet in humans.

Jansson et al investigated the effects of Khat chewing on uteroplacental blood flow in animal model. Placental blood flow was reduced by 10% 75 minutes and by 24% 180 minutes after Khat ingestion. The authors concluded that Khat chewing in pregnancy might reduce placental blood flow, and impair fetal development.

In the current study, the delivered fetuses of regular Khat chewing mothers showed a risk of 3.54 times for perinatal...
mortality and 2.02 times for congenital malformations. Animal studies reported that Khat had a genotoxic effect and the study of female rats that given Khat extracts during pregnancy, in King Saud University reported an increased number of rats that died while still in the uterus, and in the smaller litter size. They observed also a retarded fetal growth and induced musculoskeletal abnormalities in a dose-dependent manner\(^{[16]}\). However, in the study on pregnancy outcome and Khat in Yemen in 1991, there was no difference in rates of stillbirth or congenital malformations\(^{[2]}\). While Mwenda et al, reported Khat as a genotoxic with teratogenic effects on the fetus if regularly consumed by pregnant mothers\(^{[3]}\).

It is supposed that not only the Khat leaves that have the risk on bad fetal outcome, but additional substances that were proved toxic and hazardous used for cultivation of Khat in Yemen play a role.

This study in addition to the previously available limited data revealed that Khat chewing during pregnancy has a negative impact on maternal and fetal wellbeing. Khat is also known to be excreted in breast milk, but no studies have been done so far on how this affects nursing babies.

**Conclusion**

Khat chewing is a wide spread practice among pregnant Yemeni women, with a negative impact on maternal and fetal wellbeing. It is recommended that a wide spread educational program illustrating these negative aspects of Khat chewing during pregnancy and implemented in all mass media to cover the whole population.

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