

# Khat (*Catha edulis*) chewing as a risk factor of low birth weight among full term Newborns: A systematic review

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## Abstract

**Introduction:** Chewing the leaves of Khat (*chata edulis*) plant has been a custom of people living in east Africa and the Arabian Peninsula dating back centuries. Khat has Cathinone, an amphetamine-like alkaloid which is responsible for most of documented physiologic effect. Vasoconstriction in the utero-placental vascular bed, reduction of placental blood and myo-endometrial blood flow were among noted reproductive assaults during pregnancy.

**Methods:** The objective of this systematic review was to synthesize the best available evidence on association of Khat chewing during pregnancy and birth weight. Databases searched were PubMed, CINAHL, PopLine, LILACS, MedNar and Embase. All papers selected for inclusion in the review were subjected to a rigorous appraisal using standardized critical appraisal. Review Manager Software (Revman 5.0) was used for meta-analysis and effect size and their 95% confidence intervals were calculated.

**Result:** On Meta-analysis, data of 1850 neonates and their maternal history were obtained, with Khat chewers to non-chewers ratio of 1.1:1. A mean birth weight of Khat chewing mothers was found lower than the non-chewers neonates, with the mean difference of -130.74 [-189.90, -71.59] grams,

Heterogeneity:  $\text{Tau}^2 = 0.00$ ;  $\text{Chi}^2 = 0.95$ ,  $\text{df} = 1$  ( $P = 0.33$ );  $I^2 = 0\%$ . In all assumptions tested, the finding of the Meta analysis has shown consistent direction, while a reduction of 130.74 grams is the best available estimate of the effect size.

**Conclusion:** Khat chewing during pregnancy is found to be a significant risk factor for reduction of birth weight which may contribute a lot to infant mortality.

**Key words:** Khat chewing, birth weight, systematic review

## Introduction

Khat (*Catha edulis*) is a plant which grows wild in countries bordering the Red Sea and along the east coast of Africa and the Arabian Peninsula (1). Chewing the leaves of this plant has been a custom of people living in these countries dating back centuries. Khat Chewing in this region has mixed regulatory legislation; legal in Ethiopia, Djibouti, Kenya, Yemen and Uganda and illegal in Tanzania and Eritrea (2, 3). Globalization, hammering its restrictions has helped Khat consumption spread across countries such as the USA and Western Europe (4, 5). Khat chewing is common among all segments of the population, as high as 15% in Ethiopia and 90% in Yemen (6, 7). According to an Ethiopian national demographic survey, nearly one in ten Ethiopian women chew Khat while the corresponding figure in Yemen is 50% (6, 7). Other studies reported 26% of Ethiopian pregnant women chew Khat, less compared to Yemenis 41.0% (7-8).

Khat has an active ingredient, Cathinone, an amphetamine-like alkaloid, responsible for most of its pharmacological action (10). Additionally, various phenylalkylamines and considerable amounts of tannins and flavonoids were also found in Khat leaves (10-11). Toennes et al., reported 100 grams of Khat leaves contain, 114 mg cathinone, 83 mg cathine and 44 mg norephedrine (12). These active chemicals induce wider physiological effects. El-Guindy demonstrated an increase in temperature and pulse rate as well as mydriasis in people chewing Khat (13). Urinary retention, increased sexual desire, impotence and nocturnal emission, which involves either ejaculation during sleep for a male or lubrication of the vagina for a female, are also common with chronic Khat chewing behavior (13-14). Other studies on effects associated with Khat chewing reported sleeplessness, nervousness, nightmares, anorexia, constipation and inhibition of lactation (13-17).

Effect of Khat on reproductive function is not optimal. Jansson and colleagues in 1987 noted vasoconstriction in the utero-placental vascular bed, impairing foetal growth through reduction of placental blood flow among pregnant guinea pigs fed Khat leaves (16). They also showed an increase in the pressure of uteroplacental blood by 25% and heart rate by 9% and contrarily a reduction of Myoendometrial blood flow by 31%. Other studies also reported association between Khat chewing during pregnancy and reduced daily food intake, anaemia, and disturbance of fetal growth, low birth weight, perinatal and infant death, and other obstetric health problems (17-22). All the above cocktailed physiologic effects of Khat are untoward considering the requirements of the fetus towards optimal maternal environment for proper growth and fetal development. Furthermore, the add-on physiologic effect of Khat on existing stress due to socioeconomic misfortunes of the region should not be ignored considering highest infant mortality.

## Method

The objective of this review was to systematically identify, appraise and synthesize the best available evidence on association of Khat chewing during pregnancy and birth weight of the new born. Studies which include newborns of mothers who are adults (18 years old or older) regardless of race, country of residence, Khat dose, frequency, duration of chewing or other characteristics of Khat exposure and co-presence of other drug use were included. A three staged search strategy was used to identify all relevant published literature in English language. Databases searched were PubMed, CINAHL, PopLine, LILACS, MedNar and Embase. Secondary search were carried out from cross references and finally gray literature were sought from institutions and government websites. The search strategy used or modified for the various databases and search engines was with initial keywords/search terms: ["*Catha edulis*" or "Khat" or "Mairungi" or "Miraa" or "Qat"] and ["birth weight" or "low birth weight"]. All papers selected for inclusion in the review were subjected to a rigorous, independent appraisal by the investigator prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute (23). Quantitative papers were pooled in statistical meta-analysis using the Review Manager Software (Rev Man 5). Odds ratios and their 95% confidence intervals were calculated for analysis. Papers of optimal quality which were selected for inclusion but without optimal data set for meta-analysis were subjected to narrative synthesis.

## Result

A total of 254 relevant papers were identified in the literature search and 84 of them were retrieved for examination. Following review of titles and abstracts against the review objectives and inclusion criteria, 69 titles were excluded. The full texts of the remaining 16 studies were retrieved for detailed evaluation, after which, 11 of these were excluded. The remaining 7 studies were assessed for methodological quality using the JBI-MAStARI critical appraisal tool and, subsequently 3 were excluded; four of them were included in the review for meta-analysis.

On Meta-analysis, data of 1850 neonates and their mothers were obtained, with Khat chewers to non-chewers ratio of 1.1:1. Khat chewing mothers had a mean birth weight lower than the non-chewers with the mean difference of -346.97 [-670.29, -23.64].

The summary effect of the Meta analysis was found to be -346.97 [-670.29, -23.64] (Heterogeneity:  $\tau^2 = 103914.69$ ;  $\chi^2 = 191.95$ ,  $df = 3$  ( $P < 0.00001$ );  $I^2 = 98\%$ ). The observed heterogeneity in the meta-analysis may not be substantial as the researchers passed their critical appraisal and all have uniform direction of effect measure. However for the statistical fidelity sensitivity analysis yields a better summary of effect, tested by removing each study and analyzing the effect, accordingly, removing the study of Abdurehman and Kaima, 2009, gives a summary effect with less heterogeneity (Heterogeneity:  $\tau^2 = 19075.18$ ;

Figure 1: Forest Plot including all available relevant studies, 2015.

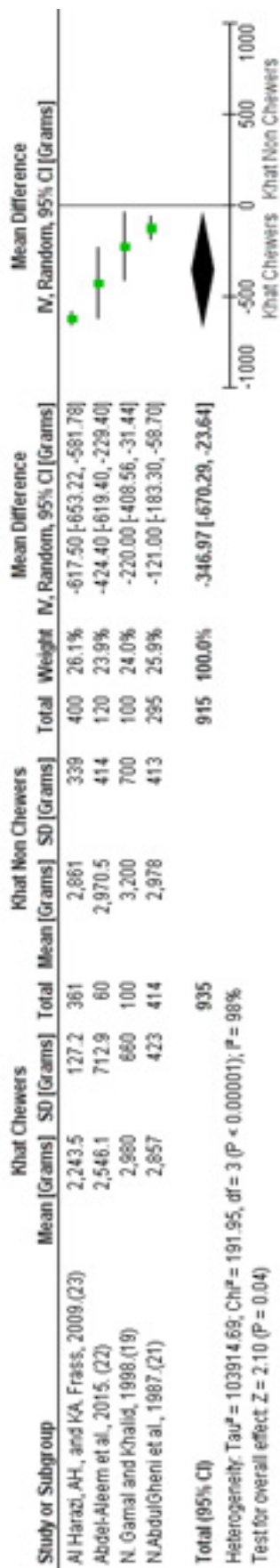


Figure 2: Forest Plot of the Meta analysis while removing a study of 'Abdurrahman and Keima' including all available relevant studies, 2015

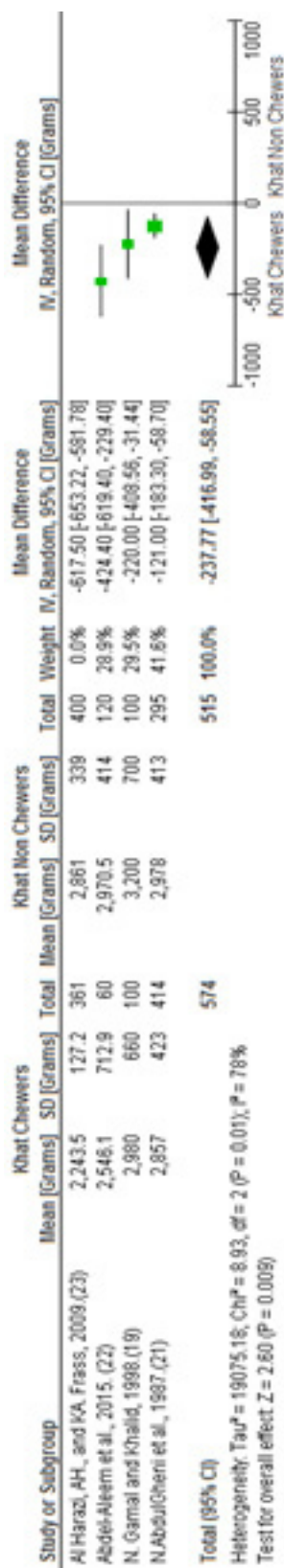


Figure 3: Subgroup analysis considering studies before millennium development, 2015



Chi<sup>2</sup> = 8.93, df = 2 (P = 0.01); I<sup>2</sup> = 78%) of -237.77 [-416.99, -58.55].

Furthermore, subgroup analysis by year of study (considering studies done before millennium development goal) gives a best summary effect with heterogeneity test equal to zero, (Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.95, df = 1 (P = 0.33); I<sup>2</sup> = 0%). The summary effect of the Meta analysis became -130.74 [-189.90, -71.59].

With all the assumptions tested, the finding of the Meta analysis was consistent, neonates of Khat chewing mothers had a reduced birth weight than non-chewers ranging from 130.74 to 346 grams. However considering heterogeneity, a reduction of 130.74 grams is the best available estimate of the effect size when heterogeneity is zero.

## Discussion

According to WHO, low birth weight contributes to 60% to 80% of all neonatal deaths. The global prevalence of LBW is 15.5%, which amounts to about 20 million Low birth weight infants born each year, 96.5% of them in developing countries, and most in sub-Saharan countries where Khat chewing is also a social custom (24). Conventional risk factors of low birth weight were well identified and interventions have made lots of progress across countries, however, studies on setting specific substances like Khat chewing were not studied well or interventions were not yet popular or done at all.

The finding of the Meta analysis is very crucial considering every gram which accounts for immediate and longer-term health and well-being of the individual infant and has a significant impact on neonatal and infant mortality at a population level. Furthermore, the harm which is induced on the fetus reflects the physiologic stress on the mother which may hamper the capability of post-natal care, more specifically feeding. Studies have shown Khat caused reduction in breast milk production and its active substances passed through breast milk to the infant (14-17).

The finding of this review is consistent with studies done on animal experiments intended to establish cause and effect relationship by Jansson et al., who has shown a reduced maternal daily food intake and maternal weight gain among Khat fed pregnant guinea pigs than their controls (16). The study also showed, Khat feeding of the mother significantly reduced the mean birth weight of the offspring by 7% (16). Another study done by the same authors to study the Effect of Khat on utero-placental blood flow in awake, chronically catheterized, late-pregnant guinea pigs showed a reduction of blood flow by 10% at 75 min and 24% at 180 min after Khat feeding (25). Since randomized controlled trials of such studies on human subjects are questionable, such findings of animal studies are helpful in postulating cause and effect relationship, rather than epidemiologic conclusions.

Studies on human subjects with primary outcome of assessing effect of Khat on birth weight and or low birth weight among human subjects are too few or date back decades considering the very high custom of Khat chewing habits across residents of east Africa and the Arabian peninsula. However, almost all available studies describe the negative effect of Khat on fetal outcome. A study by Eriksson et al., has shown non-users of Khat, had significantly fewer low birth-weight babies (less than 2,500 gram) compared to occasional users and regular users; Khat-chewing mothers had more surviving children than the non-chewers; more children of Khat-chewers had concomitant diseases than non-chewers (26). Similarly, another study reported, mothers who chew Khat during pregnancy four times per week were twice likely to have fetal death compared to non-chewers and mothers who chewed Khat during pregnancy every day were found four times more likely to have fetal death history compared to non-chewers (27).

Experience has clearly shown that appropriate care of low birth weight infants, including their feeding, temperature maintenance, hygienic cord and skin care, and early detection and treatment of infections and complications can substantially reduce mortality (24). However, such interventions are costly compared to primary prevention options.

## Conclusion and Recommendation

In this systematic review, Khat chewing during pregnancy is found to be a significant risk factor for reduction of birth weight which may contribute high for neonatal mortality. Thus, comprehensive setting specific primary prevention of low birth weight should include novel risk factors such as Khat chewing during pregnancy. Contemporary interventions targeting Khat chewing habit, incorporating a continuum of care including prevention, treatment, and maintenance of pregnant mothers should be delivered at all levels of health care. Prevention measures designed for the general population as well as selectively for future mothers and pregnant women are important in deterring the harmful effect of Khat on fetal birth weight.

## References

1. Hassen, Kalkidan, et al. "Khat as risk factor for hypertension: A systematic review." *The JBI Database of Systematic Reviews and Implementation Reports*. 2012; 10.28; Suppl 53-64.
2. Beckerleg, S. What harm? Kenyan and Ugandan perspectives on khat. *African Affairs*. 2006; 105(419): 219-241.
3. Beckerleg, S. Khat Special Edition Introduction. *Substance Use & Misuse*, 2008; 43(6): 749-761.
4. Al-Motarreb A, Briancon S, Al-Jaber N, Al-Adhi B, Al-Jailani F, Salek MS, Broadley KJ: Khat chewing is a risk factor for acute myocardial infarction: a case-control study. *British Journal of clinical pharmacology*. 2005; 59(5):574-581.



5. Griffiths, P., Gossop, M., Wickenden, S., Dunworth, J., Harris, K., Lloyd, C. A transcultural patterned drug use: Qat (khat) in the UK. *British Journal of Psychiatry*, 1997; 170: 281-284.
6. Haile, Demewoz, and Yihunie Lakew. "Khat Chewing Practice and Associated Factors among Adults in Ethiopia: Further Analysis Using the 2011 Demographic and Health Survey." *PloS one* 10.6 (2015): e0130460.
7. Al-Mugahed, Leen. "Khat Chewing in Yemen: Turning over a New Leaf: Khat Chewing Is on the Rise in Yemen, Raising Concerns about the Health and Social Consequences." *Bulletin of the World Health Organization* 86.10 (2008): 741.
8. Nakajima, M., Jebena, M., Tesfaye, M. & Hoffman, R. (2014). Correlates of Khat use During Pregnancy: A Cross sectional Investigation. *Africa & Middle East Congress on Addiction*, Rabat, Morocco, November 14-16, PAPER 3-4
9. Khawaja, Marwan, Mohannad Al-Nsour, and Ghada Saad. "Khat (*Catha edulis*) chewing during pregnancy in Yemen: findings from a national population survey." *Maternal and Child Health Journal* 12.3 (2008): 308-312.
10. Kalix P. Pharmacological properties of the stimulant khat. *Pharmacol Ther* 1990; 48:397-416.
11. Geissshusler S, Brenneisen R. The content of psychoactive phenylpropyl and phenylpentenykhatamines in *Catha edulis* Forsk. Of different origin. *J Ethnopharmacol* 1987; 19:269-277.
12. Toennes SW, Harder S, Schramm M, Niess C, Kauert GF. Pharmacokinetics of cathinone, cathine and norephedrine after the chewing of khat leaves. *Br J Clin Pharmacol* 2003; 56:125-130.
13. El-Guindy, M. K. Effects of *Catha edulis* (khat) chewing on the human body. *Journal of the Egyptian Medical Association* 1971; 54, 230-234.
14. Halbach, H. Khat - the problem today. In *Problems of Drug Dependence, Proceedings of the 41st annual Scientific Meeting, National Institute of Drug Abuse*. US Government Printing Office, Washington, DC. Research Monograph. 1979; 27: 318-319
15. Kristiansson, Bengt, N. Abdul Ghani, M. Eriksson, M. Garle, and A. Qirbi. "Use of khat in lactating women: A pilot study on breast-milk secretion." *Journal of ethnopharmacology*. 1987; 21(1): 85-90.
16. Jansson, Thomas, Bengt Kristiansson, and Abubaker Qirbi. "Effect of khat on maternal food intake, maternal weight gain and fetal growth in the late-pregnant guinea pig." *Journal of ethnopharmacology*. 1988; 23.1: 11-17.
17. Bedada, Worku, and Ephrem Engidawork. "The neuropsychopharmacological effects of *Catha edulis* in mice offspring born to mothers exposed during pregnancy and lactation." *Phytotherapy Research* 2010; 24.2: 268-276.
18. H. Kedir, Y. Berhane, and A. Worku, "Khat chewing and restrictive dietary behaviors are associated with anemia among pregnant women in high prevalence rural communities in Eastern Ethiopia," *Plos ONE*, 2013;8,11, Article ID e78601,.
19. A. Gamal and A. Khalid, "Neonatal parameters and placental weight in khat chewing mothers in Jimma," *Ethiopian Journal of Health Science*, 1998; 8(1):39-45.
20. J. M. Mwenda, M. M. Arimi, M. C. Kyama, and D. K. Langat, "Effects of khat (*Catha edulis*) consumption on reproductive functions: a review" *East African Medical Journal*, 2003; 80(6):318.
21. N. Abdul Ghani, M. Eriksson, B. Kristiansson, and A. Qirbi, "The influence of khat-chewing on birth-weight in full-term infants," *Social Science & Medicine*, 1987; 24(7): 625-627,
22. Abdel-Aleem, M., et al. Khat chewing during pregnancy: An insight on an ancient problem. Impact of chewing Khat on maternal and fetal outcome among Yemeni pregnant women *JGynecol Neonatal Biol*, 2015;1(2): 1-04
23. Al Harazi, A. H., and K. A. Frass. "Persistent khat chewing habit during pregnancy may affect neonatal birth weight." *Middle East J. family med*. 2009; 7.5: 12-15.
24. The Joanna Briggs Institute. *Joanna Briggs Institute Reviewers' Manual*: 2008.
25. WHO. Care of the preterm and/or low-birth-weight newborn. 2015. Available at: [http://www.who.int/maternal\\_child\\_adolescent/topics/newborn/care\\_of\\_preterm/en/](http://www.who.int/maternal_child_adolescent/topics/newborn/care_of_preterm/en/)
26. Jansson, Thomas, Bengt Kristiansson, and Abubaker Qirbi. "Effect of khat on uteroplacental blood flow in awake, chronically catheterized, late-pregnant guinea pigs." *Journal of ethnopharmacology*, 1988; 23.1: 19-26.
27. Eriksson, M., N. A. Ghani, and B. Kristiansson. "Khat-chewing during pregnancy-effect upon the off-spring and some characteristics of the chewers." *East African medical journal*, 1991; 68.2: 106-111.
28. Muhammed S.A. Masood, Muhammed A.K. Al-Mansoob. The Impact of Chewing Khat during Pregnancy on Foetal Death History. *International Journal of Novel Research in Healthcare and Nursing* : 2015; 2:2.