

ASSOCIATION BETWEEN CAFFEINE INTAKE DURING PREGNANCY AND PREGNANCY OUTCOME AMONG SAUDI WOMEN LIVING IN ALMADINA ALMONAWARA CITY: A PROSPECTIVE COHORT STUDY

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ABSTRACT

Caffeine is considered as the most consumed beverage all over the world, it has the ability to pass the placental barrier freely. Fetal exposure to caffeine might lead to fetoplacental vasoconstriction and hypoxia and eventually affect fetal birth weight and development here's our study aims to examine the association between maternal caffeine intake during pregnancy and pregnancy outcome in a Prospective cohort study. 1180 native healthy Saudi pregnant women were randomly chosen from those attending the antenatal care clinics of Taibah University, and 20 primary health care centers in Almadina Almonawara city. Full history, clinical examination were done to all subjects. Dietary intake of caffeine was assessed using food frequency questionnaire. The cut of point of low and high caffeine intake was determined as < 300 mg/day (equivalent to 2 cups/day) and ≥ 300 mg/day respectively. It was observed that Women who consumed caffeine ≥300 mg/day throughout pregnancy had more prevalence of low birth weight, congenital malformation, and decreased pregnancy duration, compared with women who consumed <300 mg/day. However statistical analysis showed no significant differences between the two groups (P<0.05).

Key words:Caffeine, Low birth weight, gestational length, birth weight, congenital malformation

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INTRODUCTION

Caffeine is considered as the most consumed beverage daily all over the world (Food and Agricultural Organization). Health benefits of caffeine have been attributed solely to caffeine, but increasing studies suggests that other compounds may contribute to the health benefits of caffeine consumption (Butt, 2011). In fact, caffeine contain more than a thousand of active compounds attributed to its physiological effects, among the most important compounds is caffeine. Caffeine is a xanthine alkaloid compound contained in caffeine, tea, cocoa and carbonated drinks (Spiller 1998). The World Health Organization (WHO) recommend a caffeine intake less than 300 mg/day during gestation (World Health Organization 2002), while the American College of Obstetricians and Gynecologists and the Norwegian Food Safety Authority and the Nordic Nutrition guidelines recommending a total intake of caffeine below than 200 mg/day ACOG (Committee Opinion, 2010). In 2005, a Scandinavian expert committee concluded that high caffeine intake may harm the fetus (Andersson et al., 2004). Caffeine has the ability to pass the placental barrier freely; and the principal enzyme, cytochrome CYP1A2, which is the responsible for caffeine metabolism, is not present in the placenta and thus the fetus (Oesterheld, 1998 and Andersson et al., 2004). Fetal exposure to caffeine increases catecholamine concentrations in the blood, which might lead to fetoplacental vasoconstriction and hypoxia and

eventually affect fetal birth weight and development (Mcmillen, 2005). It has been estimated that 15.5% of all babies are born with low birth weight, defined as birth weight less than 2,500 g (Wardlaw 2004). Low birth weight is not only adversely affect the new born babies but also considered as an important causal factor for death Wardlaw, 2004 and Lawn et al., 2005). , it also associated with a higher risk of chronic diseases such as type 2 diabetes and cardiovascular diseases in the later life (Wardlaw, 2004): Most epidemiological studies showed that Caffeine intake of ≥ 300 mg/day has been associated with fetal growth restriction (Peck et al., 2010). Many observational studies have examined the relationship of maternal Caffeine intake > 300 mg/day with low birth weight and spontaneous abortion, with unmatched results (Peacock et al., 1991 and Chen et al., 2014).

Objectives: The objectives of our study was to examine the association between maternal caffeine intake during pregnancy and pregnancy outcome (abortion, birth weight, pregnancy duration and congenital malformation)

Methodology

Study design: a prospective Cohort study. This study was a part of a larger study with the objective of finding an association between occurrence of birth defects in infants and the presence of

some preventable risk factors among Saudi pregnant women.

Settings: Outpatient clinics of Ohoud hospital, the medical directory of Taibah University (girls section), Al-Safa hospital and 20 primary health care centers at Al-Mainah Al-Monawara city.

Subjects: 1180 native Saudi pregnant women were randomly chosen from those attending the antenatal care clinics.

Inclusion criteria included:

- Willing to participate and attend for follow up
- In the first trimester
- Absence of systemic diseases that are known to cause poor pregnancy outcome such as diabetes, epilepsy, heart diseases,.....etc

The followings were done:

- Full history and clinical examination for criteria of inclusion and exclusion.
- **Caffeine intake assessment:** Daily caffeine consumption was estimated by using a validated questionnaire, to estimate habitual caffeine intake. Data in the questionnaire contained estimates of caffeine intake from all potential food sources and beverages. We used a cut of points of < 300 mg/day equivalent to 2 cups as low caffeine intake and ≥ 300 mg/day as high caffeine intake.
- Follow up until delivery and examination of the newborn
- Statistical analysis:

- Descriptive analysis (mean, standard deviation and Student's t test) was done using Statistical Package for Social Sciences (SPSS17) including frequency distribution and cross tabulation. The comparative outcome of pregnancy in relation to the level of caffeine intake were analyzed by using the chi-square test for categorizing data & T-test for paired samples for continuous data. The minimal level of significance will set at $P < 0.05$.

RESULTS

- Seventy four cases (6.3%) were missed during follow up, mostly because their phones were changed or out of service and they did not attend the antenatal care. Few cases traveled from Al-Madinah before giving birth and 6 cases refused to continue in the study. Those who changed their pattern of caffeine consumption pattern during pregnancy were excluded. All these cases were considered as drop out.
- Follow up of 1106 pregnancies resulted in 961 apparently normal infants, 83 pregnancies ended by abortions, additional 14 cases ended in still birth, neonatal death or intrauterine fetal deaths (IUFD). Forty eight (48) cases were diagnosed with congenital malformations. Only 1030 mothers gave valid detailed estimation of the amounts of food and beverages consumed and portion sizes and they were included in the analysis.

In this study, most mothers (65.35% n=671) consumed less than 300 mg/day equivalent to 2 cups/day of caffeine and were classified as low caffeine consumers, while only (34.85% n=359) consumed \geq 300 mg/day equivalent to more than 2

cups/day and were classified as high caffeine consumers.

There was small increase (although none significant) in the duration of pregnancy and birth weight among the low caffeine consumers (table 1)

Table (1) Statistical comparison of (age, duration of pregnancy, & birth weight between mothers with low and high caffeine intake.

	*High caffeine intake	**Low caffeine intake	P (P \leq 0.05)
Age (years)	28.20 \pm 5.99	27.667 \pm 6.35	0.194
Duration of pregnancy(weeks)	37.07 \pm 8.00	37.28 \pm 7.318	0.676
***Birth Weight of infants (KG)	3.03 \pm .59 (n=320)	3.10 \pm .53 (n=616)	0.090

* High caffeine intake** \geq 300mg/day.

**Low caffeine intake<300 mg/day

***Birth weight is included for live born infants only.

Although abortion was more prevalent among high caffeine consumers (8.9% v.s. 7.5%), yet results were insignificant (table 2).

Table (2) Statistical comparison in the prevalence of abortion and full pregnancy among mothers with low and high caffeine intake.

Caffeine intake (n=1014)	Full pregnancy (n=933)	Abortion n=81
*High caffeine intake (n=349)	318 (91.1%)	31(8.9%)
**Low caffeine intake (n=665)	615(92.5%)	50(7.5%)

* High caffeine intake** \geq 300mg/day.
 **Low caffeine intake<300 mg/day
 Pearson Chi-Square=.579
 P=0.259

We found no significant difference in occurrence of congenital malformations between both groups (table 3). An important observation is that two cases of the congenital group reported daily intake

of 1 liter of caffeine throughout all months of pregnancy (1500mg/day); one delivered an infant with congenital heart disease and the other delivered an infant with blind esophagus.

Table (3): Caffeine consumption and occurrence of congenital malformation.

Amount of caffeine/day (all types)	Normal infants N=901	Congenital*** N=42
*High caffeine intake	308 (34.2%)	18 (42.9%)
**Low caffeine intake	593 (65.8%)	24 (57.1%)

* High caffeine intake**≥300mg/day.

**Low caffeine intake<300 mg/day.

***The other six cases of congenital malformation are missing accurate data on caffeine consumption.

Chi-Square =1.334 P=.248

Discussion

According to our knowledge, this was the largest prospective cohort study that reported the effect of caffeine intake during pregnancy on birth outcome in Al-Madina Al-Monawara city. The majority of mothers in this study were classified as low caffeine consumers according to the WHO definition (World Health Organization, 2002). There was no significant difference in the duration of pregnancy between both groups. This was in agreement with Clausson et al., (2014). who found that both low caffeine intake <300 mg/d and high Caffeine intake ≥300 mg/d during pregnancy were not significantly associated with the duration of pregnancy Our results also revealed that high caffeine intake is slightly associated with

decreased birth weight; however, this association was not statistically significant. The present study is comparable with the Danish randomized controlled study which included a (1,207 pregnant women) a number which is much closer to our sampling size (1,180). The Danish study examined the association between the reduction of caffeine intake during pregnancy and birth weight and found no significant association (Chen et al., 2014). Our study also is consistent with some earlier studies, as (Grosso et al., 2001). who studied 2,714 women and revealed that there was no significant association between maternal caffeine consumption >300 mg/d and birth weight. This finding was supported by another prospective,

population-based cohort study conducted by (Beach et al., 2007). who reported no significant differences observed in birth outcome in relation to the mean daily caffeine consumption of >300 mg/d in each trimesters. Moreover (Santos et al., 2005). studied 1207 pregnant women who consume >300 mg/d and found no significant differences in the mean baby's birth weight.

On the other hand, evidence from the Norwegian Mother and Child Cohort Study conducted by the Norwegian Institute of Public Health (Sengpiel et al., 2013). Revealed that there is a significant associations between caffeine intake and decreased birth weight.

Our results also disagree with results from the meta-analysis conducted by (Chen et al., 2014). who showed that caffeine consumption during pregnancy is associated with a strong risk of giving a low birth weight infant. The risk increase with increase the level of caffeine intake.

Our results indicated an increased prevalence of abortion among mothers who consume ≥ 300 mg caffeine per day (8.9%vs 7.5 for low consumers), however, the difference was not statistically significant.

Our results are consistent with an earlier prospective cohort study which conducted by (Watkinson and Fried, 1985) on 284 mothers, levels of Caffeine intake was measured and grouped into <100, 100–300 and >300mg/day. And the Results revealed that no relation between

maternal caffeine intake and risk of abortion.

Another prospective cohort study conducted by (Dlugosz et al., 2003) confirmed our findings and reported that high caffeine intake (≥ 300 mg caffeine/day) was associated with an increased risk of abortions but this increase was not significant.

On the other hand some epidemiological studies indicated that there is no association between a caffeine intake of <300mg/day and an increased risk of abortion (Dlugosz, L. et al., 1996).

Possible reasons for these inconsistent findings of the effect of maternal caffeine intake on birth weight and abortion might be due to differences in study designs, including inaccurate methods of caffeine intake determination, because of the assumption that tea and caffeine are the only sources of caffeine (Linn et al., 1982). differences in sampling size, retrospective methods in estimating caffeine intake, also most studies focused on examining maternal trimesters caffeine intake rather than throughout all pregnancy duration (WACOG Committee Opinion, 2010, Khoury JC. et al., 2004 and Vik et al., 2003), and ignorance of the variations among individuals in caffeine metabolism (Mills et al., 1993).

Our findings indicated that there was no significant association between mothers with low caffeine intake or those with high caffeine intake at the level of 300 mg/d, in occurrence of congenital malformations.

Our results are in parallel with two early studies by (Linn et al., 1982 and Rosenberg et al., 1982). which did not show any

teratogenic risk for children of mothers who drank caffeine during pregnancy. Similar findings were reported in a pilot study in Finland with a conclusion of no association between maternal caffeine intake and the prevalence of congenital malformations in infants (Kurppa et al., 1982)

Another study confirmed our findings conducted by (Browne et al. 2011). Evaluating data from the National Birth Defects Prevention Study, which examined the relation between caffeine consumption during pregnancy and birth defects. This was a cohort study that included 3,346 caffeine consuming pregnant mother and 6,642 controls, they concluded that was no association between maternal caffeine intake and the birth defects (Chen et al. 2014).evaluated data from the National Birth Defects Prevention Study, assessed the relation between caffeine intake during pregnancy at the levels of (<100, 100 to <200, 200 to <300, and 300+ mg/day) and congenital limb deficiencies. This study included, 844 cases and 8069 controls and reported that Caffeine consumption during pregnancy was not associated with any limb deficiency subtype, and the risk did not vary by levels of caffeine intake.

However, we can't ignore the two cases of congenital malformation who consumed 1 litter (1500 mg/day) of caffeine daily (Borlee I, et al., 1997). found an increased risk of malformations in children born to mother with heavy caffeine consumption.

Conclusion

The present study showed that levels of caffeine intake recommended by the

world health organization during pregnancy are within a completely safe range. Some risks may be associated with very high caffeine intake and this needs further studies for proper estimation of a possible teratogenic effect with very high intake.

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