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Research Article

Effect Of Maternal Caffeine Consumption on Low Birth Weight in Butajira, Southerncentral Ethiopia: A Nested Cohort Study

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Abstract

Background: Caffeine consumption is common among people throughout the world, Africa and Ethiopia. The prevalence of the caffeine exposure during pregnancy was 69%-79% and excessive caffeine consumption during pregnancy was 14%-57% in most Western countries and in Ethiopia, the prevalence was 41%. The main source to caffeine is through coffee and tea in the world and African countries, including Ethiopia. Even though there were number of studies indicating caffeine intake has reported as a risk factor for low birth weight during pregnancy, the findings are not conclusive in western and no evidence in Ethiopia. Therefore, this study is designed to assess the effect of maternal caffeine consumption on low birth weight during late pregnancy.

Objective: The objective of this study was to determine effect of maternal caffeine consumption on low birth weight in Butajira Cohort, South central, Ethiopia.

Method: Population based Nested cohort study design was employed among 244 pregnant mothers from September 2018—May 2019 in Butajira. Beverages contain caffeine were collected by 24hour recall method. Birth weight was considered as outcome group. Pediatric weight scale was used for measurement of birth weight with in 72 hour after delivery. Pregnant mothers exposed to caffeine consumption greater than 200mg/day was considered as exposure group. The mean usual intake of caffeine was estimated by National cancer institute (NCI method). Finally the effect of Caffeine on low birth weight was analyzed by log binomial regression by STATA SE version 14.

Results: The study found that 26.2% of pregnant women had daily caffeine consumption more than or equal to 200mg/day. The risk of low birth weight was four times more likely to occur in exposed group than in unexposed group (ARR=3.72; 95%CI: 1.76, 7.87). In other hand, the risk of low birth weight was four, five and five times more likely to occur in middle, rich and richest wealth status at (ARR=4.61;95%CI (1.08,19.69),(ARR=5.39;95%CI (1.23,23.58),(ARR=4.54;95%CI(1.07,19.25) respectively than in poorest wealth status.

Conclusion and recommendation: In conclusion, excessive maternal caffeine consumption might results in low birth weight. Therefore, intervention that address caffeine exposure among pregnant mother should be designed to reduce the burden of low birth weight.

Keywords: Caffeine consumption, Caffeine intake, Low birth weight, Pregnancy, Effect.

Introduction

Caffeine is the most commonly used stimulant substance mainly found in coffee and tea [1]. Other sources of caffeine are chocolate/cocoa, and cola soft drinks. In addition to this, nearly 200 non prescribed drugs is estimated to contain caffeine and this may be an important source for a minority of people [2].

Caffeine clearance from the body is delayed during pregnancy, especially in the second and third trimesters and it decreases to one-half and to one-third of the normal rate, respectively [3]. Its half life is 2.5 to 4.5 hours in non pregnant women but doubled during late pregnancy especially during third trimester. Because, estrogen increases during pregnancy inhibits CYP1A2 enzyme function to metabolize caffeine [4-6]. until fetal blood levels are equal, maternal blood levels to caffeine crosses the placental barrier [7].

The principal enzymes, cytochrome CYP1A2, needed for caffeine metabolism, however, are absent both in placenta and even up to the eighth month after delivery in infants and prone to different neonatal infection like jaundice [8].

Caffeine consumption in pregnant women has been studied as a determinant factor for low birth weight [13]. There are studies which are done to find out the effect of caffeine consumption on low birth weight. But there are no similar results. Due to those conflicting conclusion from numerous studies the March of Dimes, food and drug administration, American college of obstetrician and gynecologists and American pregnancy association, cable news network's and American food safety states until more conclusive studies are done, pregnant women should be limit caffeine consumption <200mg/day. But recently world health organization guidelines recommend caffeine intake during pregnancy has also been suggested as risk factor for pregnancy outcome for greater than 300mg caffeine per/day [14].

Globally; from 127 million delivered neonates per year; more than 20 million (16%) infants are born with LBW. Of which 96.5% of them are in developing country especially Asia and Africa, including Ethiopia [15, 16], LBW babies are more likely to experience physical and developmental health problems or die during the first year of survival than infants of normal birth weight. Based on an observational studies that neonates weighing less than 2,500 g are approximately 20 times more likely to die than normal birth weight neonates [17]. Because of this birth weight is considered as the sole most essential factor influencing neonatal and early neonatal mortality.

The numbers of epidemiological studies have explored the association between caffeine consumption and low birth weight. Some of these studies showed that caffeine consumption is associated with an increased likelihood of being low birth weight, while others report no association. Yet the majority of the evidence on this topic is from wealthy nations, and remains poorly understood in developing

countries including Ethiopia. Furthermore, these studies suffer from methodological drawbacks. For example, the use of invalidated food frequency questionnaire to assess the caffeine consumption status of the study participants and failed to measure birth weight within three days. Our review suggests that studies that use objective measurement of caffeine consumption by 24 hour recall method for all study participants and repeated measurement was also considered to adjust usual caffeine consumption by National cancer institute (NCI) method.

Material and Methods

This study was embedded population based Prospective nested cohort study design

The cohort includes 244 mothers and their children lived in Butajira southern, central Ethiopia

All mothers were enrolled between February 2018 and November 2018, and all children were born between February 2018 and May 2019. Of all eligible children in the study area, 92% exposed and 98% unexposed group participated at birth in the study.

The ethical clearance was obtained from Addis Ababa University School of Public health after approval of by research ethical committee.

Caffeine Intake Measurement

Caffeine measurement was done for all study participants in second trimester and repeated for 51(21%) study participants in third trimester by using 24 hr recall methods for collect beverages like tea, coffee, soft drinks to know amount of caffeine consumption of individuals. All days of the week were considered in the sample to make the selection representative for both first and repeated measurement. If the material was not available at home, the picture of calibrated serving size would be shown to the mother to estimate the amount consumed. Then, the participant was asked to indicate how many of each size of the beverages consumed in the last 24-hour. The daily 24-hour recall consumption amount of caffeine was changed in to a standard unit (mg).

The amount of caffeine collected by milliliter (ml) was converted to milligram (mg) by multiplied with average content of caffeine per unit of each caffeine source. The average amount of caffeine from coffee (0.533 mg/ml) was obtained from a study conducted in Ethiopia [82]. The caffeine concentration for tea (0.359 mg/ml) and coca cola (0.113mg/ml) was obtained from the International Food Information Council Foundation (IFICF) critical review on clarifying the controversies of caffeine and health [83]. To obtain the caffeine amount from coffee with milk was estimated. The estimated proportion of coffee in coffee served with milk was 0.7365[84]. Then the caffeine level was calculated based on

the caffeine level in coffee as shown above. Finally Caffeine was categorized using scales ranging 0) normal (caffeine consumption less than 200mg/day), 1) excessive (caffeine consumption greater than or equal to 200mg/day).

Birth Weight Measurement

Birth weights of the neonates were measured by digital weight scale after delivery within three days following standard procedure and techniques. Birth weight was categorized using scales ranging 0) Low birth weight (weight less than 2500gram, 1) normal (birth weight greater than 2500gram). To ensure measurement accuracy the scale was checked for 0.00 reading and calibrated before each data collection.

Covariate Variables Measurements

Socio demographic characteristics such as age, sex, occupation, educational status and marital status which were adapted from Ethiopian Demographic Health Survey (EDHS) were included. Age was categorized using scales ranging: 1) 15-24, 2) 25-34, 3) 35 and above years old. Occupation was categorized using scales ranging: 1) Farmer and housewife, 2) Housewife, 3) employee/private, 4) Student, 5) Merchant, 6) Local drink seller, 7) Commercial sex worker, 8) Maid servant, 9) Daily laborer, 10) Unemployed, 11) Farmer and merchant, 99) Other (specify). Educational status was categorized using scales ranging: 1) Primary (1-8), 2) Secondary (9-12), 3) College/university, 4) Read and write, 5) can't read and write wealth index was assessed by principal component analysis using scales ranging: 1) poorest, 2) poor, 3) middle, 4) rich, 5) richest.

Obstetric factors like ANC follow up was categorized using scale ranging: 0) yes, 1) no. Gravity was categorized using scale ranging 0) primigravida, 1) Multigravida. Parity was categorized using scale ranging: 0) Null Para, 1) Para I, 3) Multipara. Pregnancy interval was categorized using scale ranging: 0) less than 18month, 2) 18-33month, 3) 33 month and above. Pregnancy plan was categorized using scale ranging: 0) planned 1) unplanned.

Participants' toxic exposure use was assessed using questions adapted from EDHS. Participants were asked whether or not they use the substances with a response category of „yes" or „no" and the frequency (number of days) and amount (for cigarette) of their consumption, Placental factors (placenta abruption, placenta previa, and hydramnious) and infant congenital anomaly were using ultrasound (yes/no).

Anthropometric Measurements

Height of the mothers was measured by portable stadiometer and categorized using scale ranging: 0) normal height (≥ 150 cm), 1) short stature (< 150 cm).

MUAC was categorized using scale 0) normal (MUAC ≥ 22 cm and above), 1) malnourished as (MUAC < 22 cm), Blood pressure categorized using scale ranging 0) not hyper-

tensive ($< 140/90$ mmhg) 1) hypertensive ($> 140/90$ mmhg).

Biochemical Measurement

Hemoglobin level of the mothers categorized using scale ranging: 0) anemia (less than 11mg/dl, 1) not anemia (greater than 11mg/dl).

Maternal Disease like Hypertension was measured as (yes/no) and toxic exposure (cigarette smoking, alcohol consumption) was not included in this analysis because no pregnant mother faced to those factors.

Data Quality Managements

Data quality control was done before, during and after data collection. Five days onsite training was given for the experienced and fluent in local language, five local data collectors and two supervisors by the principal investigator while data collection on weight measurement of newborn. Data collection takes a total of eight month duration which was conducted from September, 2018-May, 2019.

Measurement scales were checked whether the scales were at 0.00 reading before each measurement. Technical error of measurement for height, weight and MUAC should be checked for acceptable range. Less than 0.5kg for weight, 0.5cm for mid arm circumference, and < 1 cm for height. Five milliliter of blood sample was taken from left brachial vein of pregnant mother to detect anemia by using hem cue following standard procedure by experience laboratory technicians.

Five days before interview principal investigator visited 10 household to collect data on caffeine for pregnant mother's tool used to drink coffee and tea and photo of equipment commonly used were taken. The equipment/cup/ was graded in to 1-3 after making coffee or tea during baseline assessment based on their size one for small, two for middle and three for large. Accordingly the equipments cups from the pictures were purchased from local market and used to use while data collection for pregnant mothers household who study unit is reside in.

The amount of beverage which has caffeine was collected from second and third trimesters pregnant women house to house once by using 24 hour recall methods for all study participants. Additionally exposure measurement was repeated by data collectors for fifty one pregnant mothers which account for twenty one percent to reduce with in person variation. Then the amount of beverages collected was converted to caffeine concentration by using already published article done in Ethiopian coffee and for tea and soft drinks from international caffeine concentration level reference.

The Supervisors and the principal investigator gave close supervision during different phases of data collection (interview, anthropometric measurements and documentation). Questionnaires were checked by the supervisors and the principal investigator for completeness each day. Editing and cleaning of data was done before data analysis.

Sampling Procedure

Figure 2: shows the sampling procedure for this study. A simple random sampling technique was applied to select the study subjects. Addis Ababa University College of health science school of public health established pregnancy –child cohort to screen pregnant mother of 1419 from 2017 to 2020. The aim of this cohort was to evaluate the effect of economic, psychological and quality aspect of food and nutrition on pregnancy outcome, child growth and development. For this study 776 eligible pregnant mother screened from February 2018 to November 2018 was the sampling frame. Only

second and third trimester was selected based on inclusion criteria. 258 of them had no caffeine data; 217 of them were first trimester pregnancy; two were multiple pregnancy. 299 eligible pregnant mothers were considered as sampling frame. 93 pregnant were exposed group 206 of them were unexposed group. By using simple random sampling 65 exposed and 196 unexposed pregnant mothers were selected. Both groups were followed for 8 month. At the end of 8 month 64 exposed and 180 unexposed completed follow up period and included in to analysis.

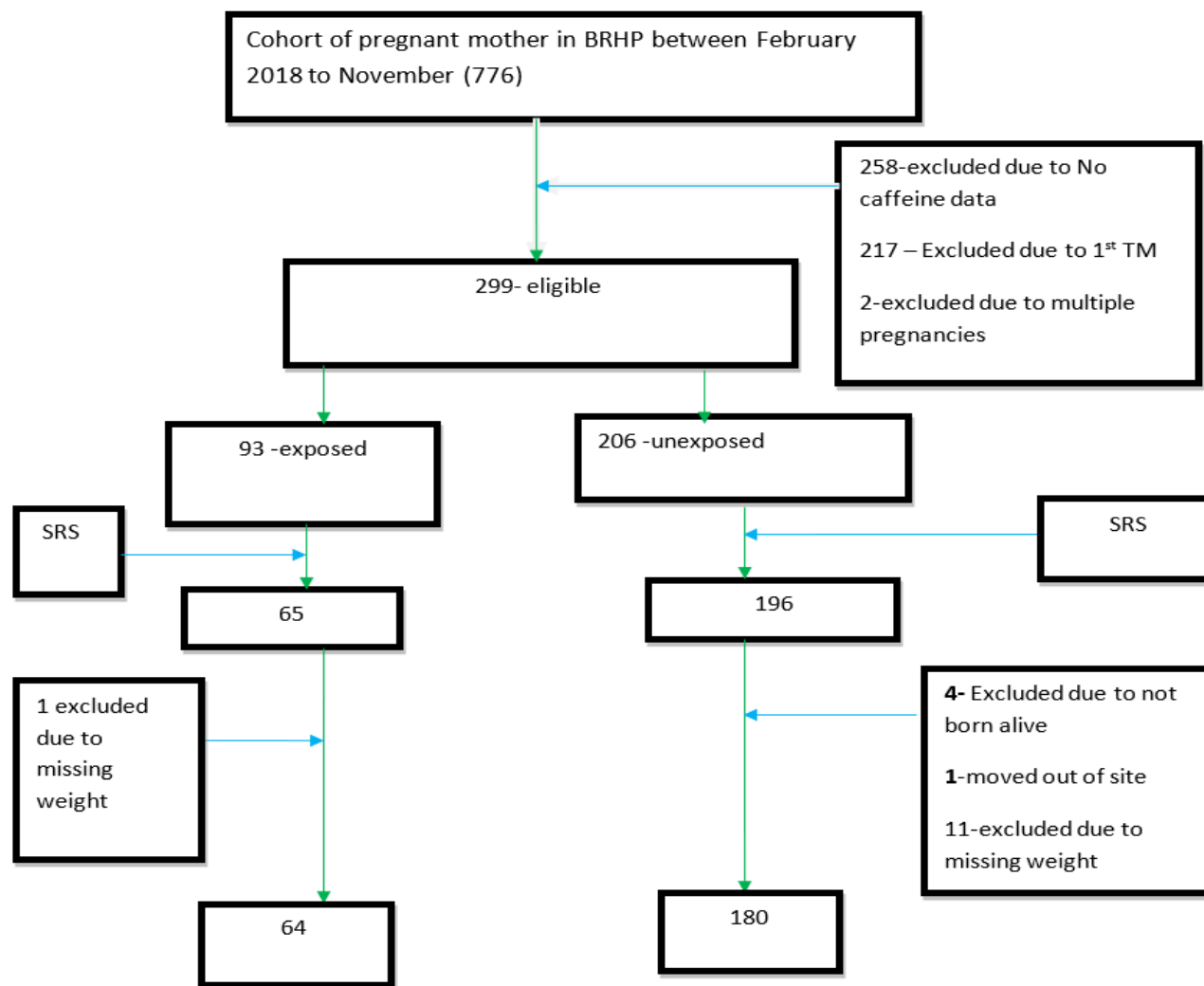


Figure 1: Diagrammatic presentation of sampling procedure

Results

Socio-Demographic and Economic Characteristics of the Respondents

Out of 261 pregnant mothers approached, 244 of them were interviewed, with attrition rate 92% and 98% for unexposed and exposed respectively. Table 1

shows the socio-demographic and economic characteristics of the respondents. The median age in unexposed was 28(IQR=5) whereas in exposed was 26.5(IQR=7). All unexposed and exposed (100%) of the respondents were married.

Variables	Caffeine intake (<200mg/day)		Caffeine intake (>=200mg/day)	
	Number(n)	Percent (%)	Number(n)	Percent (%)
Age group				
15-24	43	23.89	23	35.94
25-34	114	63.33	36	56.25
35 and above	23	12.78	5	7.81
Education status mothers				
No formal education	79	43.89	29	45.31
Primary level	92	51.1	27	42.19
>=Secondary level	9	5	8	12.50
Religion				
Orthodox Christian	37	20.56	6	9.38
Muslim	132	73.33	53	82.81
Protestant and other	11	6.11	5	7.81
Mothers occupation				
Farmer and housewife	28	15.56	9	14.06
Housewife	151	83.89	53	82.81
Merchant	1	0.56	2	3.13
Wealth status				
Poorest	32	17.78	18	28.13
Poor	35	19.44	13	20.31
Middle	37	20.56	12	18.75
Rich	39	21.67	10	15.63
Richest	37	20.56	11	17.19
Partners Educations status.				
No formal education	69	38.3	26	40.63
Primary level	81	45.00	28	43.75
>=Secondary level	30	15.67	10	15.63
Occupation partner				
Farmer	115	63.89	39	60.94
Merchant	32	17.78	12	18.75
Other*	33	18.33	13	20.31

*Daily laborer, employee/unemployed

Table 1: Shows the socio-demographic and economic characteristics of sampled pregnant mothers who lived at BRHP, Gurage, Zone, SNNPR, Ethiopia, 2019

Maternal and Pregnancy Related Characteristics of the Respondents

Figure-2 shows maternal and pregnancy related characteristics of the exposed and unexposed respondents. Only 4(3%)

of unexposed 1(2%) exposed pregnant mothers had history of low birth weight. Regarding gravidity, about 146 (81.1%) unexposed pregnant mothers were multigravida and 47(73.4%) of exposed pregnant women were multigravida.

Less than half 62 (34.4) unexposed and 29(45.31) wanted current pregnancy (Fig 2).

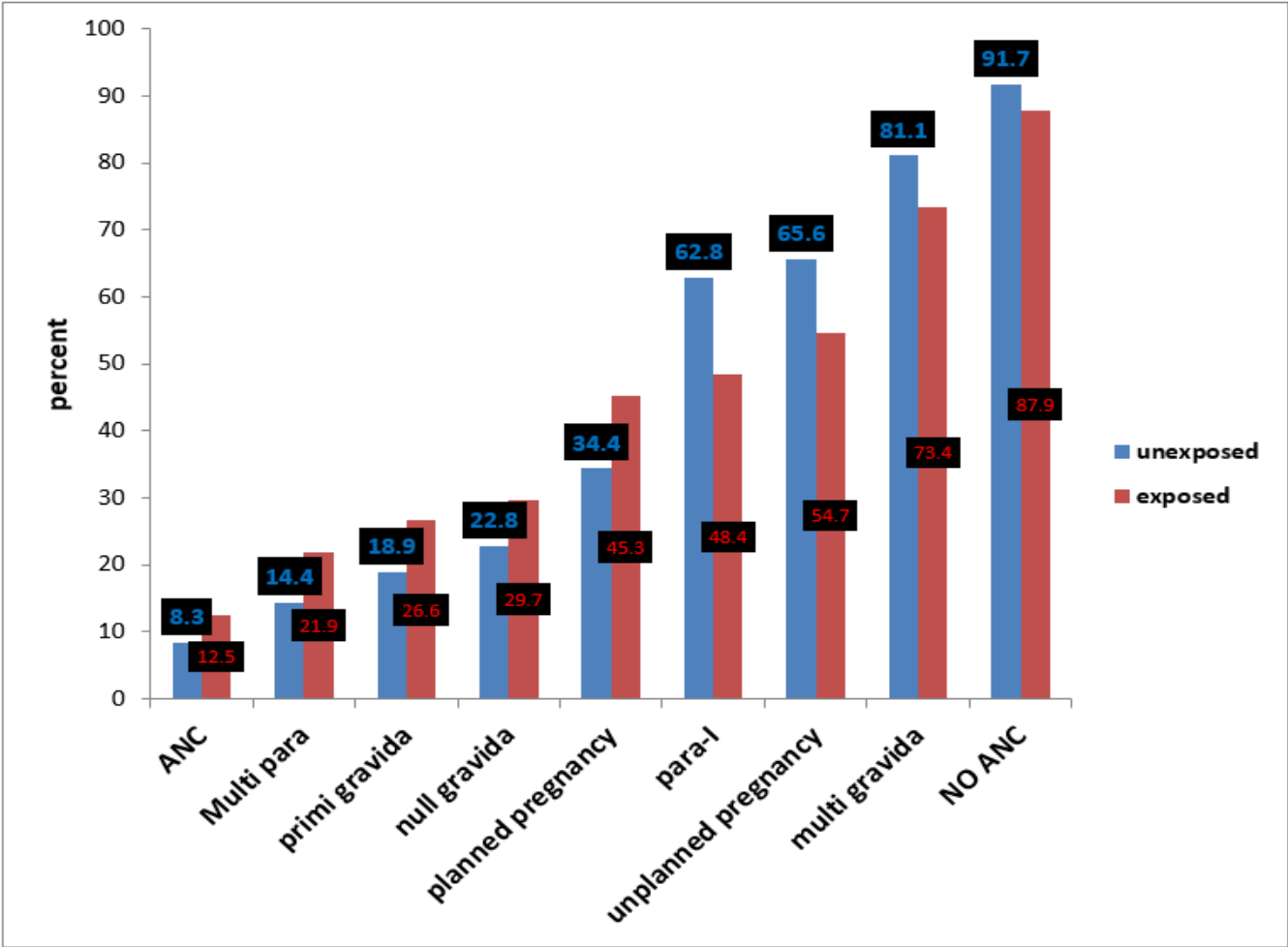


Figure 2: Maternal and pregnancy related characteristics of the sampled pregnant women who lived at BRHP, Gurage Zone, SNNPR, Ethiopia, 2019.

Maternal Exposure to Caffeine Consumption

statistics	Unexposed(in mg/day)	Exposed(in mg/day)
Median	79	307
IQR	86	102
Minimum	0	201
Maximum	199	478

Table 2: Summary of descriptive statistic among pregnant mothers by exposure status BRHP, Gurage Zone, SNNPR, Ethiopia 2019

As shown in figure four, Ninety three percent, 223(92.6%) were exposed to caffeine. Pertaining the sources of their caffeine consumption, 165 (67.6%) used to drink black coffee, about 41(21.5%) consumed coffee with milk and around 20(10.5%) of the pregnant women consumed black tea (Figure 3). None of the pregnant mothers was drinking Pepsi, coca -cola, coffee with tea and tea with lemon.

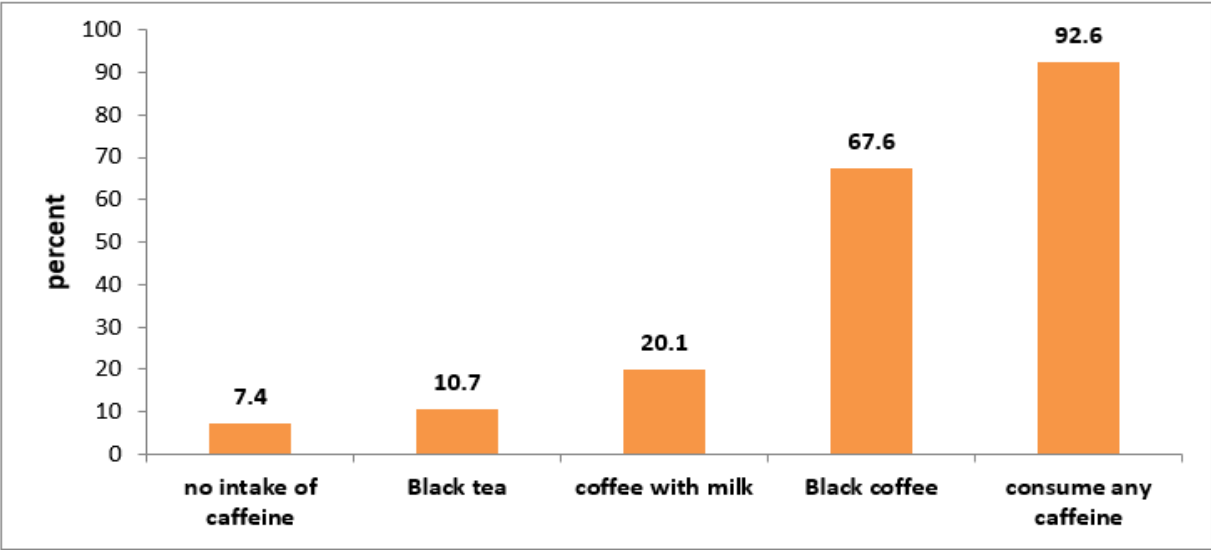


Figure 3: Source of caffeine consumption in percentage among pregnant mothers in BHRP, Gurage Zone, SNNPR, Ethiopia, 2019

Birth Weight of the Neonate

Figure 4: shows percentage of low birth weight. Of total delivered neonates about 31(12.7%) of them were low birth weight 25(10.2%) was small for gestational age (Figure 4).

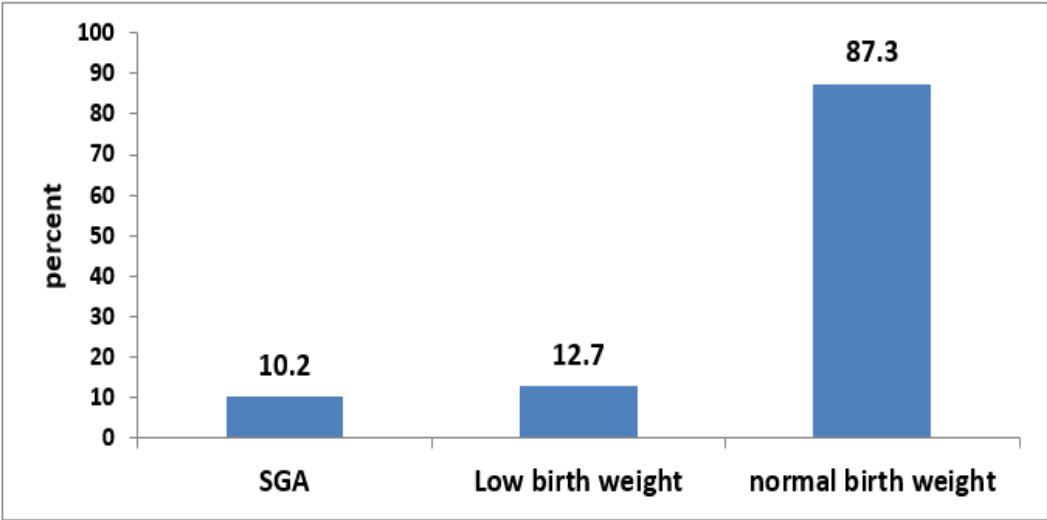


Figure 4: The incidence of low birth weight of neonate delivered at BRHP, Gurage Zone, SNNPR, Ethiopia, 2019.

From the total 244 pregnant mothers involved in this study, about 64(26.2%) pregnant consumed caffeine ($\geq 200\text{mg/day}$) and 33(13.5%) consumed caffeine ($\geq 300\text{mg/day}$) by using single 24-recall method and 64(20.11%) and 33(3.75%) respectively for caffeine consumer ($\geq 200\text{mg/day}$) and ($\geq 300\text{mg/day}$) by NCI method using SAS. The difference might be single 24 recall method overestimate daily caffeine consumption. Regarding hypertension, only 6(2.46%) of unexposed were hypertensive (Table2). Concerned about nutritional status of the mothers, based on mid upper arm circumference (MUAC) about 5(2.78%) of unexposed and 3(4.69%) of exposed pregnant mothers had chronic energy malnutrition

Variables	Unexposed mothers(<200mg/day)		Exposed mothers (>200mg/day)	
	Number	Percent (%)	number	Percent (%)
Caffeine	180	73.77	64	26.23

Hypertensive	6	2.46	0	0
Maternal height(<150cm)	21	11.67	12	5.00
Anemia	1	1.67	2	3.13
Nutritional status(MUAC<22cm)	5	2.78	3	4.69

Table 3: Frequency distribution of risk factors of low birth weight among pregnant mothers in BRHP, Gurage Zone, SNNPR, Ethiopia, 2019

Chi-square (cross tab result of associated factors of low birth weight)

From the total pregnant women who consume excessive

caffeine, sixty four about 17(7.0%) were delivered low birth weight neonate .This was shown (Table4).

Caffeine consumption	Birth weight		Total (%)	P-value
	Normal (%)	LBW (%)		
<200mg/day	166(68.)	14(5.7)	180(73.8)	
>=200mg/day	47 (19.3)	17(7.0)	64(26.2)	< 0.01
Total	213(87.3)	31(12.7)	244(100)	

Table 4: The cross tabulation of caffeine consumption with low birth weight among pregnant mothers in BRHP, Gurage Zone, SNNPR, Ethiopia 2019

Factors Associated With Low Birth Weight

Bivariate and multivariable log binomial regression

After bivariate and multivariable log binomial regression was run independently, caffeine consumption, maternal height and wealth index were declared variables as risk factors for low birth weight.

Table 4: Show the multivariable log binomial regression analysis fitted to identify associated factors for low birth weight.

After adjustment for possible confounder such as maternal height, sex of neonate, educational status of partner, wealth status, ANC, and chat chewing during pregnancy we found that pregnant mothers exposed to caffeine consumption, height of the mothers and wealth index were significantly associated with low birth weight. The risk of low birth weight was three times more likely to occur in exposed group than in unexposed group (ARR=3.72; 95%CI: 1.76, 7.87)

Variable	BW Count (n, %)						
Caffeine(mg/day)	Normal	LBW	CRR	95%CI	ARR	[95%CI]	Sig
<200	166(68.03)	14(5.7)	1	.	1	.	.
>=200	47(19.3)	17(7.0)	3.42	(1.79,6.52)**	3.72	(1.76,7.87)	***
Maternal height(cm)							
>=150	190(77.9)	21(8.60)	1	.	1	.	.
<150	23(9.43)	10(4.1)	3.04	(1.58,5.88)**	2.45	(1.11,5.41)	***
ANC4							
Yes	22(9.02)	1(0.4)	1	.	1	.	.
NO	191(78.3)	30(12.30)	3.12	(.44, 21.84)	3.07	(0.40,23.62)	
Wealth status							
poorest	46(18.85)	4(1.64)	1	.	1	.	.
Poor	44(18.03)	4(1.640)	1.04	(.28,3.93)	3.19	(.63,16.17)	
Middle	42(17.21)	7(2.87)	1.79	(.56 , 5.72)	4.61	(1.08,19.69)	**
Rich	41(16.80)	8(3.28)	2.04	(0.66, 6.34)	5.39	(1.23,23.58)	**
richest	40(16.39)	8(3.28)	2.08	(.67 , 6.47)	4.54	(1.07,19.25)	**
Partner Education							
No formal	81(33.2)	14(5.74)	.84	(.37,1.93)	.39	(.13, 1.23)	

Primary	99(40.57)	10(4.09)	.52	(.21, 1.28)	.27	(.09, 1.85)	
>=secondary	33(13.52)	7(2.87)	1	.	1	.	.
Sex of neonate							
female	99(40.57)	18(7.34)	1.50	(.77,2.93)	1.55	(.73,3.28)	
Male	114(46.7)	13(5.34)	1	.	1	.	.
Chat chewing							
YES	205(85.4)	31(12.7)	1.32	(.55,3.19)	1.27	(.46,3.51)	
NO	8(3.3)	0(0)	1	.	1	.	.

*** p<0.01, ** p<0.05, CI: Confidence Interval, CRR: crude risk ratio, ARR: Adjusted Risk Ratio Adjusted for caffeine, maternal height, sex of neonate, educational status of partner, wealth status, ANC, and chat chewing during pregnancy

Table 5: Shows the multivariable log binomial regression analysis fitted to identify associated factor for low birth weight among sampled pregnant women who lived at BRHP, Gurage Zone, SNNPR, Ethiopia, 2019.

Discussion

A prospective nested cohort study was conducted to determine the effect of caffeine consumption during pregnancy on low birth weight. One-day nonconsecutive 24-hour recall was done to collect data related with caffeine for all pregnant mothers. In addition to this, 24-hour recall method was repeated for 21% pregnant mothers. The study found that 26.2% of pregnant women had a daily caffeine consumption more than or equal to 200 mg/day. The median caffeine consumption in unexposed was 79mg (IQR=86) per day with minimum zero and maximum of ninety nine. In addition to this, the median caffeine intake in exposed group was 307 mg (IQR=102) per day with minimum of two hundred one and maximum 478 mg/day.

After adjustment for possible confounder, caffeine consumption, height and wealth status were significant associated factors for low birth weight.

The risk of low birth weight was four times more likely to occur in exposed than unexposed group (<200 mg a day).

The postulated mechanism by which caffeine consumption result in low birth weight were, caffeine absorbed immediately (after 45minutes) from gastrointestinal and passes placenta across freely [9]. Additionally, fetuses don't metabolize it well [10] and caffeine has been increasing catecholamine [11] which may causes utero-placental vasoconstriction and then fetal hypoxia, which possibly cause fetal growth and increases cellular cyclic adenosine mono-phosphate which may affect cell development and result in low birth weight [12].

Based on Bradford hill criteria there were effect of caffeine consumption on low birth weight. It fulfills some of the criteria, causality like dose response relationship. The risk of low birth weight was three times more likely to occur in pregnant mothers who consumed caffeine 151-300mg/day than (0-150mg/day) (ARR=3.10; 95%CI: 1.12, 8.57). In similar manner, The risk of low birth weight was ten times more likely to occur in pregnant mothers who consumed caffeine greater

or equal to 300mg/day than (0-150mg/day) (ARR=9.52,95%-CI:- 3.68-24.58). From this dose response relationship, we can conclude that as the dose of caffeine consumption increase the probability to have low birth weight neonate also increase.

Concerning with temporality, the cause is caffeine, outcome is low birth weight. There were many studies with different study design and setting which had consistent finding. There was strong association between caffeine and low birth weight. The biological plausibility of caffeine effect on low birth weight was caffeine passes placenta and form vasoconstriction which limit nutrient passing from mother to fetus, then resulted in low birth weight. This study was not fulfilling the criteria of specificity, because there were other factors which result in low birth weight. Caffeine was not the sole risk factor to low birth weight.

Based on literatures, high levels of caffeine intake during pregnancy can result in miscarriage, low birth weight, growth restriction, stillbirth, and increases the risk of health problems in later life(85-90). According to a reports from literatures, a higher maternal caffeine intake (more than 50 mg per day) during pregnancy was associated with a higher risk of delivering low birth weight infants compared to no intake or very low intake (88, 90). This risk appears to increase linearly as caffeine intake increases [91, 92].

Other consistent reports from observational studies, the risk of having low birth weight was high for high caffeine consumption compared to moderate and low consumption. It has been established that each 100-mg/day increase in maternal caffeine intake (about one cup of coffee) was associated with 13%greater risk of having low birth weight [73].

Study done in united states shows, When comparison was made with women who had no caffeine exposure, the relative risks of low birth weight after adjustment for confounding factors were 2.3 (95% CI 1.1-5.2) for 151- 300 mg/day. Excessive daily caffeine intake(>=200 mg/day) has been asso-

ciated with an increased risk of birth to SGA or LBW (<2500 g) babies [25].

On the other hand, the recommendation of Marches of Dimes, American college of obstetrics and gynecology, American pregnancy association, Food and drug administration, cable news network's and American food safety which proposed greater than 200mg/day caffeine result in low birth weight so that caffeine should be limited to less than 200mg/day.

However, systematic review was done by WHO on effect of caffeine consumption on pregnancy outcome specifically on low birth weight. Based on this review, it developed context-specific recommendation guideline and generate three categories of certainty evidence level. These were very low, low and moderate certainty evidence level. Based on this certainty evidence level, very low certainty evidence level shows that less than 150mg per day of caffeine consumption during pregnancy may be associated with fewer low birth weights (5 none randomized studies). In similar manner low certainty evidence level indicated between 150-300mg/day caffeine consumption probably associated with low birth weight [7] (none randomized studies). On the other hand, moderate certainty evidence level revealed caffeine consumption greater than 300mg/day associated with low birth weight. The developed guideline revealed that greater than or equal to 300mg/day of caffeine consumption during pregnancy associated with low birth weight with moderate certainty evidence level. According to WHO recommendation, only moderate certainty evidence level is considered until high certainty evidence level will be updated. In accordance with this guideline development standards, this recommendation will be reviewed and updated following the identification of new evidence, with major reviews and updates at least every five years.

Furthermore, different studies which were done at different western country didn't find out any associations between caffeine consumption and low birth weight for daily caffeine consumption greater than 200mg/day, this may be due to studies measured birth weight at four week after delivery, this may be increase birth weight [77]. In addition to this study used food frequency questionnaire for caffeine consumption, this might be lead to recall bias.

Additionally, the risk of low birth weight was two times more likely to occur in short stature pregnant mothers than normal height. Maternal height might be associated with LBW even though it is not completely understood how. This may be contributed by both genetic and environmental factors. Short-statured women are more likely to pass on to their fetus a genetic predisposition for smaller growth [54]. Anatomical factors may also play a role in the risk, as short stature can be associated with a smaller uterus, and can therefore impose physical limitations [55] on the uterine, placenta and fetuses growth. Furthermore, height is correlated to pelvic size, and therefore, a short-statured woman may have a smaller pelvis, which may result in its earlier filling [54]. Maternal short stature may also be associated with a lack of

nutrients, resulting in decreased fetal growth or duration of gestation, [55].

Concerning about wealth status, the risk of developing low birth weight were four, five and five times more likely to occur in middle, rich and richest pregnant mothers than poorest wealth status respectively. As woman wealth status increases, the chance of buying coffee and consuming caffeinated beverages might increase. In other hand, developing countries, women of low socioeconomic status are likely to be shorter and thinner and to consume fewer calories and other nutrients during pregnancy and result in prematurity or IUGR and low birth weight [52].

Regarding the overall implication of this study, excessive caffeine (>200mg per day) consumption result in low birth weight. Caffeine in coffee alone would account for 4% of cases of low birth weight [72]. In Ethiopia neonatal death associated by low birth weight was high (3.63%) of all death [18]. Therefore, greater than two hundred milligram per day caffeine consumption could be addressed in order to prevent neonatal death associated with low birth weight.

Strengths

As strengths, since it was community based prospective cohort study, the finding of the study could detect cause-effect relationship for effect of caffeine consumption on low birth weight and also generalize able to all pregnant women living in the study area. All days of the week were considered in order to control days of the week effect. In addition, around twenty (21%) percent was repeated 24-hour recall which is the recommended methods for the assessment of exposure with in risk assessment processes was done to control within person variation of caffeine intake. Regarding data collection tools this study was used different methods like structured questionnaires, anthropometry measurement, and biochemical measurement. Fourthly, first trimester ultrasound was used to estimate gestational age which was appropriate than second and third trimester ultrasound.

Limitations

The study findings should be interpreted and utilized by considering the following limitations. First, the level of caffeine concentration was obtained from previously done researches. However, the concentration of caffeine may vary based on the roasting and brewing process. Due to these reasons it might not give a perfect estimation of daily caffeine intake. Second, substances use such as alcohol and tobacco use are considered as taboo in the study area. As a result, the respondent might not report their consumption and this might introduce social desirability bias and this might not be enables researcher to control confounder's effect of alcohol and tobacco on low birth weight. Third, physical activity and dietary Assessment of the pregnant women was not controlled for confounder.

Conclusion

Data obtained from 24-hour recall method for assessment of caffeine consumption during pregnancy, interview of general information, interview of birth weight, Measurement of maternal anthropometry and biochemical measurement was used. The finding of this study shows, excessive maternal caffeine consumption result in low birth weight.

Recommendations

Based on the study findings; the following recommendations were drawn:

Federal Ministry of health (FMOH) should give emphasis on substance use during pregnancy and align with this and should develop Guideline and manuals for social and behavioral change communication for community to prevent excessive caffeine consumption during pregnancy.

Health professionals should screen and counsel all pregnant women for substances use during ANC visit. Additionally, they should provide health education about the risk of substances use on the fetus.

Programmers working at maternal and child health shall plan an intervention program which aimed to increase the awareness of community and pregnant women about the harmful effects of excessive caffeine consumption during pregnancy with the ultimate goal of preventing adverse pregnancy outcomes related to excessive caffeine intake during pregnancy. Interested researchers shall determine the level of caffeine concentration from each caffeinated beverage for the accurate estimation of daily caffeine intake among pregnant woman and further research by using randomized controlled trial.

Data Availability

The data used to support the findings of this study may be released upon the request to the Principal investigator of this study who can be contacted at getacho2013@gmail.com

Conflicts of Interest

There is no conflict of interest among the Authors of this paper.

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