Examining the Effect of Education on Dietary Calcium Intake in Reducing Blood Pressure Variability Among Pregnant Mothers in Tigray Region, Northern Ethiopia, Two Arm, Randomized Control Trail Parallel Design

Mulugeta Woldu Abrha (mulugetawoldu425@gmail.com)
Tigray Health Research InstituteTigray Health Research Institute, Mekelle, Ethiopia
https://orcid.org/0000-0001-7990-8940

Alemnesh Abarha
Tigray Health Research Institute

Ataklty Gebretsadik
Tigray Health Research Institute

Brhane Ayele
Tigray Health Research Institute

Haylay Gebretensae
Tigray Health Research Institute

Equbay Gebre-egziabher
Tigray Health Research Institute

Tsegay Hadgu
Tigray Health Research Institute

Afework Mulugeta
Mekelle University College of Health Sciences

Research

Keywords: Calcium, education, pregnant mother, blood pressure variability, Ethiopia

Posted Date: September 14th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-71446/v1

Abstract

Background: Investigating effects of calcium diets on blood pressure can contribute to development of diet based recommendations for health. Epidemiologic data suggest contradicting evidence relationship between dietary calcium intake and pregnancy-induced hypertension. So, this study aimed to determine the effect of calcium nutrition education on blood pressure variability among pregnant mother.

Method: Single center, two-arm, main individual randomized trial parallel design; single blinded was conducted among 415 pregnant mothers. Bi-variable tabulations were computed to identify the distributions of the outcome variables by selected background characteristics. We estimated a multilevel model that assessed the relation of individual and community level factors (fixed effects) as well as community level random effects. All analysis was conducted using STATA 14 software.

Result: Blood pressure variability during pregnancy after 28 gestational age was significantly associated with weekly calcium nutrition education [AOR=0.38; 95% CI: 0.19, 0.5], pregnant mothers who attained secondary school [AOR=0.21, 95%CI: 0.20, 0.70], employed pregnant women [AOR=9.05; 95% CI: 1.95, 14.02] , Antenatal Care [AOR=1.82; 95% CI: 1.01, 2.22], supplemented iron/folic acid [AOR=6.32; 95% CI: 1.09, 36.59], food craving [AOR=0.78; 95% CI: 0.20, 0.98], reading newspaper [AOR=9.05; 95% CI: 1.95, 14.02], place of residence [AOR=2.11; 95% CI: 1.36, 3.26].

Conclusion: Individual level factors (Calcium nutrition education, maternal educational status, maternal occupation, Antenatal care during last pregnancy and current pregnancy, iron/folic acid supplementation, food craving, dietary calcium level and reading newspaper) and community level factors (place of residence) were significant predictors of blood pressure variability. During antenatal visits, pregnant women should be made aware of some dietary practices which are harmful during pregnancy, and increase education regarding the benefit of adequate nutrition.

Trail Registration: PACTR, PACTR202009693949631 and Registered 02 September 2020- Retrospectively registered

Background

Calcium is the most abundant mineral in the body and essential for bone formation, muscle contraction, enzyme and hormone functioning, most of the body's calcium found in bone [1, 2]. Calcium has potential to reduce adverse gestational outcomes by decreasing the risk of developing hypertensive disorders during pregnancy, which are associated with a significant number of maternal deaths and considerable risk of preterm birth [3, 4].

Globally Over half a million women die each year from pregnancy related causes. Pregnancy related hypertensions are the second leading cause of maternal death; it accounts 27.1% of maternal death [5]. In Low and middle income countries maternal death accounts 99% of the total death at global level and

about one out of every 10 maternal deaths in Africa and Asia have been attributed to pre eclampsia and eclampsia [6].

WHO recommended Calcium supplementation during early pregnancy for population with poor dietary calcium intake to prevent pregnancy related hypertension [2, 4]. In Ethiopia dietary calcium intake is too law, which accounts 88.4% women have inadequate dietary calcium intake and also in Tigray the average mean intake of women of child bearing age was estimated 296.67 ± 1.04 mg/day, which is below the recommended EAR for women [7].

However, in poor counters availability and affordability of calcium are the main challenge to implement the recommendation [2, 4]. Due to this other studies recommend that healthy dietary intake can meet micronutrient needs of pregnant women in developing countries [8, 9]. Thus, this trail aimed to determine the effect of education on dietary calcium intake in decreasing variability of blood pressure in pregnant mothers.

Methodology

Study Area, period and Trail design

Single center, two-arm, main individual randomized trial parallel design, single blinded including 12-16 weeks follow up was conducted in selected district of Tigray Region from June to September 2019. Tigray is one of the 9 Regional states of Ethiopia and Mekelle is the capital city of the Region which is located 783 km North of Addis Ababa which is capital city of Ethiopia. Tigray Region, which has about one million hectares of arable land in total, is also successfully expanding its agriculture extension program. In Tigray, bread is one of the main foods. Two of the more common varieties are thin, pancake-like bread preferred by most people and a dense, disk-shaped loaf of baked whole wheat bread and is made from many kinds of cereal grains (wheat, barley, etc.). A variety of tsebhi (spicy stews) are eaten with the bread.

Population

All greater than 28 weeks gestational age pregnant mothers in Tigray region were the source population and all randomly selected pregnant mothers from the selected districts were study population.

Eligibility criteria

Pregnant women who had a mean systolic BP from 120 to 140 mmHg and a diastolic BP from 80 to 90 mmHg, based on six readings at two screening visits were included to the study and Mothers with a systolic BP ≥140 mmHg or a diastolic BP ≥90 mmHg or that were taking antihypertensive medications was excluded. In addition, persons with a self-reported history of clinical cardiovascular disease (CVD), cancer, chronic kidney disease, body mass index (BMI) ≥30 kg/m2 were excluded from the study.

Sample size determination

The sample size for the study was calculated from a study which indicates maternal death due to hypertensive disorder was 20%. Sample size was computed to detect minimum of 10% additional reduction in intervention as compared to the control arm with the following assumptions: level of significance 5%; Power 80%, lost to follow up 10%. The required sample size was 415 subjects in all groups. The total duration of the intervention was 12-16 weeks.

Trail intervention

Dietary intake was assessed at baseline and in every weekly visit to household using an interactive 24-hour recall method. After completing the baseline assessments (described further in study assessments) mothers were randomly assigned to either the education on dietary intake of calcium containing foods or the control group. The randomization was 1:1 for the 2 groups and was performed using simple randomization computer generated codes for each individual. For pregnant mothers in the calcium nutritional education intake group, a target calcium intake was calculated on the basis of 1200 milligram per day baseline, and the importance of meeting this target intake was explained to mothers. An estimate of current dietary intake was made from an interactive 24-h food recall; education was provided about the intake in relation to the target intake, and mothers were given a dietary plan to meet the target intake. Pregnant mothers were instructed to consume these foods per serving required to meet the target. Pregnant mothers were contacted house to house 3 times per week to assess progress and to provide the necessary feedback. Blood pressure was measured every month until the end of the intervention period. For pregnant mothers randomly assigned to the control group, general advice was given to address any major dietary imbalance identified from the interactive 24-h food recall at baseline. They were instructed to increase their food intake as they felt able but were not given a specific plan for dietary intake.

Measurement of Blood Pressure

Blood pressure was measured once per week per subject using an aneroid sphygmomanometer (Marshall Electronics, Inc., Clayton Division, Skokie, Ill.). Readings was recorded three times with 1 min between each reading. Participants was allowed a 10-min rest period before readings taken. All participants maintained a sitting position while blood pressure was measured in the non-dominant arm. A measurement was made at the same time of day by the same investigator, who was trained and experienced in the recording of blood pressure.

Randomization and Blinding

Each participating centre was assigned a special code generated by the computer using the simple randomization. The randomization was kept by the PI. The assessor for clinical outcomes was blinded to the randomization status. The research assistants who perform the intervention did not know the assessment result. After the eligibility assessment, blood pressure and dietary recall was conducted at the baseline (after completion of informed consent), at 4th, 8th and 12th weeks and every visit respectively.

Study outcome

The primary outcome of interest was the BP variability between the study groups and Incidence of pregnancy induced hypertension were secondary outcome.

Explanatory variables: such as age, marital status, religion, educational level, occupation, monthly house hold income, family size, ANC visit, housing characteristics, household food insecurity, diversity of diet.

Data collection procedures and quality Assurance

The survey was community based structured and semi-structured, pre-tested, interviewer administered questionnaire mainly with closed ended questions was interviewed to pregnant mothers. The questionnaire was used to collect data through face-to-face interview on socio-demographic and dietary calcium intake. The questionnaires have adapted from different studies considering the local situation of the study area and contextualized to the study based on the relevant variables to be used. Data collectors provided a four days training on the data collection process. The research tool was first developed in English and then translated to the local language Tigrigna. The final version of the questionnaire was both in Tigrigna and English. Tigrigna version of the questionnaire was used for data collection to ensure clear understanding of the interviewee and respondents. To maintain quality and to estimate the time required collecting data, a pre-test was done on 21 individuals in nearby community to the intervention area to check the feasibility of the data collection process. Questionnaires were revised, as necessary, based on the pre-test and time required to fill one questionnaire was determined. During the study data collection, questionnaires were checked for its completeness and consistency by supervisors and principal investigators. Data that have entered in Epi data version 3.7 was checked for its accuracy by the principal investigators.

Data management and analysis

Blood pressure variability was compared between the intervention groups. Bi variable tabulations were computed to identify the distributions of the outcome variables by selected background characteristics. We estimated a multilevel model that assessed the relation of individual and community level factors (fixed effects) as well as community level random effects. Facility and community variables were considered as ‘community level’ variables in the study. Multilevel analysis was used to account for the hierarchical nature of the data. A two-level multilevel logistic regression model was estimated. The model consisted of two sub models at level 1 and level 2 (i.e., individuals (level 1) were nested within communities (level 2). A two-level multilevel model for a dichotomous outcome uses a binomial sampling and a logit link. We estimated four models. The first model was an empty model containing no covariates, but decomposed the total variance into individual and community components. The second model included individual characteristics. The third model contained only the community characteristics and this allowed the assessment of the relation of the community variables to the outcome variable. The final model contained explanatory variables at both the individual and community levels and allowed the assessment of the net effect of community variables over and above the individual variables. The

variables were retained in each of the models if the variance component was significant ($p<0.05$) or if they were important demographic variables. In all the estimated models, fixed effects were expressed as odds ratios (OR), while the random effects were expressed as variance partition coefficient (VPC) and proportional change in variance (PCV). Data was analysis using STATA 14.

Ethical consideration

Ethical clearance was obtained from Tigray health research institute, and an official support and permission letter was obtained from Tigray Regional Health Bureau. Written informed consent was assuring from the study participants, after explaining the purpose and significance of the study and they was assured that they had the right to withdraw from the study at any stage. Interview was conducted after receiving their consent. Confidentiality of the data/information was secured by assigning unique code to each of the participants and will not be used for other purpose.

Result

Demographic and socio-economic characteristics

A total of 415 early third trimester pregnant mothers were recruited. Of these, 203 were in the intervention group and another 212 in the control group with 100 % response rate. The mean ages (±SD) of the mothers were 39(±15) years. Out of the total mothers interviewed, three fourth 305 (73.5%) belongs to the age group of 20-34 years. Most of the mothers 393(94.7%) were currently in marital union and 395(95.2) them were orthodox religion believer. Six out of ten 254 (61.2%) of the mothers were rural residence, greater than three-fourth of them had less 5 family members 320(77.1%). More than one third 320 (41.9%) of the mothers and almost half of the husbands 196 (47.2%) were illiterate. Majority of the maternal occupational 333(80.2%) were housewife and more than half paternal occupation 234 (56.4%) were farmers. One fifth of the mothers 86(20.72%) had middle wealth quintile [**Table 1**].

Table 1: Demographic and socio-economic characteristics of pregnant mother, Tigray Region, Northern Ethiopia, 2019 (N=415)

Characteristics	Number	Percent
Maternal Age		
< 20 years	68	16.39
20-34 years	305	73.49
35-49 years	42	10.12
Marital status		
Marred	393	94.70
Single	15	3.61
Divorced	7	1.69
Religion		
Orthodox	395	95.18
Muslim	20	4.82
Place of Residence		
Rural	254	61.20
Urban	161	38.80
Family members		
< 5 members	320	77.11
>5 members	95	22.89
Maternal highest Grade		
No formal education	174	41.93
Elementary School	134	32.29
Above Secondary School	107	25.8
Paternal highest grade		
No formal education	196	47.23
Elementary School completed	107	25.78
Above secondary School	112	27.0
Maternal occupation		
Housewife	333	80.24
Daily-laborer	25	6.0

Employed	57	13.7
Husband occupation		
Farmer	234	56.39
Employed government	56	13.49
Employed non-government	25	6.0
Daily-laborer	47	11.33
Self-employed non farming	53	12.77
Wealth Quantiles		
Lowest	82	19.76
Second	84	20.24
Middle	86	20.72
Fourth	91	21.93
Highest	72	17.35

Environmental characteristics

Around four out of ten 182(43.9%) households did not possess toilet and out of the owners of toilet 112(48.1%) were pit latrine without slab [**Table 2**].

Table 2: Environmental characteristics of pregnant mothers, Tigray Region, Northern Ethiopia, 2019 (N=415)

Characteristics	Number	Percent
Have toilet		
Yes	233	56.1
No	182	43.9
Kind of toilet		
Pit latrine without slab	112	48.1
Pit latrine with slab cover	86	36.9
Ventilated improved pit latrine	20	8.6
Flush toilet	15	6.4

Obstetric and reproductive health characteristics

Three-fourth 326 (78.5%) of the mothers were willing to get pregnant and two third of the mothers 278 (66.99%) were multi gravid and 150 (36.1%) of them had 1-2 parity. Majority of 409(98.5%) of mothers did not have history gestational diabetes, gestational hypertension or postpartum depression previously. Sixty one percent (n=257) of mothers had received antenatal care during their last pregnancy. Around four percent (n=15), 246(59.3%) and 27(6.5%) were examined for ANC by Doctor/IEOS, Nurse/midwifery and Health extension workers respectively. Majority of the mothers 216(52%) receive ANC for their last delivery in public health centers. Ninety-five percent (n=395) of the mothers receive ANC for their current pregnancy and 313(75.4%) of mothers receive ANC in public health center. Most of them 382(92%) took supplements (Iron/folic acid Iodine, or other) during the current pregnancy [**Table 3**].

Table 3: Obstetric and reproductive health characteristics of pregnant mother, Tigray Region, Northern Ethiopia, 2019 (N=415)

Characteristics	Number	Percent
When you got pregnant, did you want to get pregnant		
Yes	326	78.55
No	89	21.45
Gravidity		
Primi-gravida	137	33.01
Multi gravid	278	66.99
Parity		
1-2	150	36.1
3-4	82	19.8
>5	46	11.1
Gestational diabetes, high blood pressure, depression, or postpartum depression in your last pregnancy		
No history of the mentioned	409	98.55
History Gestational Diabetes	2	0.48
History of Gestational Hypertension	2	0.48
History postpartum depression	2	0.48
Receive antenatal care during you last pregnancy		
Yes	257	61.93
No	158	38.07
Examined by Doctor/IEOS during ANC		
Yes	15	3.6
No	400	96.4
Examined by Nurse/midwife during ANC		
Yes	246	59.3
No	169	40.7
Examined by Health extension worker during ANC		
Yes	27	6.5

No	388	93.5
Receive antenatal care for your last child in Governmental Hospital		
Yes	15	3.6
No	400	96.4
Receive antenatal care for your last child in public hospital		
Yes	84	20.2
No	331	79.8
Receive antenatal care for your last child in public health center		
Yes	216	52.0
No	199	48.0
Receive antenatal care for your last child in Health post		
Yes	23	5.5
No	392	94.5
Did you see anyone for antenatal care for this pregnancy		
Yes	395	95.2
No	20	4.8
Place receive antenatal care for current pregnancy		
Government hospital	30	7.2
Public hospital	72	17.3
Public health center	313	75.4
Did you take any supplements (Iron/folic acid Iodine, or other) during this pregnancy		
Yes	382	92.0
No	33	8.0

Dietary and nutritional characteristics

Most of the pregnant mothers 392 (94%) were supplemented iron folic acid less than 90 days. More than one third 138(33.3) of the household resources were managed by husband and 145(34.9%) of the participants feel little weight gain since they become pregnant. Around quarter 61(14.7) of the mothers

were physically threatened by their husband and 34(8.2%) of them felt down depressed or hopeless. Almost nine out of ten mothers 366(88.5%) had no food taboos during this pregnancy and 359(86.5%) of them had no food cravings during this pregnancy. Average calcium level at base line was mean (±SD) 410±208 gm [**Table 4**].

Table 4: Dietary and nutritional characteristics of pregnant mothers, Tigray Region, Northern Ethiopia, 2019 (N=415)

Characteristics	Number	Percent
Days Iron/folic acid supplemented		
< 90 days	392	94
>90 days	23	5.5
In the past month, have there been days when you did not have enough food or money to buy food?		
Yes	81	19.5
No	334	80.5
Household resources are managed by whom?		
Partner	138	33.3
Mother	54	13.0
Both of them	223	53.7
How do you feel about your weight change since you became pregnant?		
Gaining too much	95	22.9
Gaining too little	145	34.9
It's okay	116	28.0
Not sure	37	8.9
Weight has not changed	22	5.3
In the last month, has your partner physically threatened or tried to hurt you		
Yes	61	14.7
No	354	85.3
In the last month, have you felt down, depressed, or hopeless		
Yes	34	8.2
No	381	91.8
Any change in feeding habit		
Yes	64	15.4
No	351	84.6
Food taboos during this pregnancy		

Yes	49	11.8
No	366	88.2
Food cravings during this pregnancy		
Yes	56	13.5
No	359	86.5
Food averted during this pregnancy		
Yes	54	13.0
No	361	87.0
Average calcium intake	410±208 gm	

Communication related characteristics

Majority of the mothers did not read a newspaper or magazine 275(66.3%) and More than half 249(59.8%) of the mothers did not listen radio and more than one third 284(68.4%) did not watch television [**Table 5**].

Table 5: Communication related characteristics of pregnant mothers, Tigray Region, Northern Ethiopia, 2019(N=415)

Characteristics	Number	Percent
Read a newspaper or magazine		
At least once a week	49	11.8
Less than once a week	91	21.9
Not at all	275	66.3
Do you listen Radio		
At least once a week	102	24.6
Less than once a week	65	15.7
Not at all	248	59.8
Watch television		
At least once a week	82	19.8
Less than once a week	49	11.8
Not at all	284	68.4

Factors affecting Blood pressure variability among groups

Table 6 shows the results of mixed effect logistic regression analyses examining the effect of calcium nutrition education among pregnant women's individual characteristics and community-level factors in pregnant women in blood pressure fluctuation. Model 1, the empty model, includes only random intercept to capture between-cluster variability. In this model, 16% of the total variance in the odds of in blood pressure fluctuation was accounted for by between-cluster variation (ICC=0.12, The ICC was computed in each successive model to understand the relative effects of individual-level and community level factors on women in blood pressure fluctuation. Similarly, the ICC was computed in each successive model to understand the relative effects of individual-level and community level factors on calcium nutrition education to in blood pressure fluctuation. The between-cluster variability over successive models, from 12% in the empty model, to 9.7% in the individual-level only model, 8.9% in the community-level only model, and 8.3% in the combined model [**Table 6**]. Showing that variation in the blood pressure variability was explained best by the inclusion of both individual level characteristics.

The proportional of change in model in variance indicated the addition of predicators to the empty model better explained pregnant women calcium nutrition education change in blood pressure fluctuation.

Individual level effect

Model 2 contained only the individual level variables. Results showed that nutrition education on calcium for pregnant mothers was significantly associated with blood pressure variability, those mothers who got education had 62% lower blood pressure variability when compared with the control groups [AOR=0.38; 95% CI: 0.19, 0.5]. Concerning maternal highest grade, Pregnant mothers who attained secondary school had 79% less likely blood pressure variability than mothers who were with no formal education [AOR=0.21, 95%CI: 0.20,0.70]. Employed pregnant women [AOR=9.05; 95% CI: 1.95, 14.02] had higher likelihood of blood pressure variability when compared to the reference category. Pregnant mothers who did not visit health facility for ANC had higher likely of blood pressure variability than those visited for ANC [AOR=1.82; 95% CI: 1.01, 2.22]. Women supplemented iron/folic acid less than 90 days had 6 times greater odds of blood pressure variability than women supplemented iron/folic greater than 90 days. Women who were not craving were 22 % less likely blood pressure variability than those who were craving [AOR=0.78; 95% CI: 0.20, 0.98]. The odds of blood pressure variability among women who read newspaper less than a week was 99.3% less likely than mother who did not read at all [AOR=9.05; 95% CI: 1.95, 14.02]. As the average calcium intake increased by 1 unit the blood pressure variability decreases by 0.99 unit [AOR= -0.99; 95% CI:0.993-0.998].Compared to the empty model, the variation in health facility delivery was significant across communities (τ = 0.81, $p<0.001$). The intra-community correlation was 9.7% indicating the variability in the outcome variable.

Community level effect

We examined the effects of community level factors on the likelihood of blood pressure variability in model 3. As shown in the model, women living in urban area had 2.11 times higher odds of blood pressure variability than rural residents [AOR=2.11; 95% CI: 1.36, 3.26]. The intra individual correlation in the model increased, whereas that of the community decreased further suggesting that the proportional change in variance of odds of blood pressure across individuals and communities was explained by individual level characteristics. In other words this indicates that the differences in the likelihood of blood pressure variability were partly as a result of composition of communities by community level characteristics.

Finally we included both the individual and community variables in model 4. For the individual level variables, the relationship was consistent with that observed in model 1. Nutrition education on calcium for pregnant mothers was significantly associated with blood pressure variability, those mothers who got education had 71% lower blood pressure variability when compared with the control groups [AOR=0.29; 95% CI: 0.19, 0.50]. Concerning maternal highest grade, Pregnant mothers who attained secondary school had 80% less likely blood pressure variability than mothers who were with no formal education [AOR=0.20, 95%CI: 0.04,0.97]. Employed pregnant women [AOR=10.17; 95% CI: 1.96, 15.28] had 9 times higher likelihood of blood pressure variability when compared to the reference category. Pregnant mothers who did not visit health facility for ANC had 1.4 times higher likely of blood pressure variability than those visited for ANC [AOR=1.39; 95% CI: 1.05, 1.83]. Women supplemented iron/folic acid less than 90 days had 6 times greater odds of blood pressure variability than women supplemented iron/folic greater than 90 days. Women who were not craving were 23 % less likely blood pressure variability than

those who were craving [AOR=0.77; 95% CI: 0.18, 0.0.93]. The odds of blood pressure variability among women who read newspaper less than a week was 99.3% less likely than mother who did not read at all [AOR=0.07; 95% CI: 0.01,0.40]. As the average calcium intake increased by 1 unit the blood pressure variability decreases by 0.99 units [AOR= -0.99; 95% CI: 0.993-0.998]. However there are no significant community factors on the combined model 4. The community level variance was significant (τ =0.12, $p<0.001$). The intra-community correlation decreased to 8.3% suggesting that the inclusion of the community variables improved the overall explained variance in the use of delivery care compared with model 3. Moreover, the smaller values of AIC and BIC indicated that model 4 was a better explanatory model.

Table 6: Two level mixed effect logistic regression of individual and community factors on Blood Pressure variability during pregnancy, Tigray Region, 2019

Characteristics	Model I Empty model	Model II Individual factors OR (95%CI)	Model III Community/HH factors OR (95%CI)	Model IV Individual and community factors OR (95%CI)
Fixed effect (individual factors)				
Study arm (Calcium nutrition education)				
Intervention arm	-	0.38* (0.20-0.70)		0.29*(0.19-0.50)
Control arm	-	1.00		1
Maternal Age	-			
< 20 years	-	1.00		1
20-34 years	-	0.33(0.51-2.19)		0.43(0.12-1.48)
35-49 years	-	0.35(0.12-1.18)		0.42(0.06-2.90)
Family members	--			
< 5 members	-	0.35(0.12-1.09)		0.32(0.10-0.9)
>5 members	-	1.00		1.00
Maternal highest Grade	-			
No formal education	-	1		1
Elementary School	-	0.75(0.23-2.42)		0.77(0.24-2.53)
Above Secondary School	-	0.21*(0.05-0.95)		0.20*(0.04-0.97)
Paternal highest grade	-			
No formal education	-	1		1
Elementary School completed	-	1.68(0.41-6.82)		2.02(0.66-6.17)
Above secondary School	-	2.45(0.84-7.15)		1.73(0.41-7.31)
Maternal occupation	-			
Housewife	-	1		1

Daily-laborer	-	0.35(0.06-1.96)	
Employed	-	9.05*(1.95-14.02)	10.17*(1.96-15.28)
Husband occupation	-		
Farmer	-	1	1
Employed government	-	1.06(0.20-5.56)	0.90(0.16-5.20)
Employed non-government	-	1.67(0.32-8.79)	1.52(0.27-8.57)
Daily-laborer	-	2.01(0.41-9.86)	1.89()0.36-9.82
Self-employed non farming	-	1.55(0.38-6.18)	1.38(0.31-6.15)
Wealth Quantilles	-		
Lowest	-	1	1
Second	-	1.44(0.41-5.12)	1.38(0.38-5.04)
Middle	-	2.01(0.41-9.78)	1.93(0.36-10.24)
Fourth	-	0.27(0.06-1.26)	0.27(0.06-1.27)
Highest	-	0.86(0.17-4.35)	0.98(0.18-5.44)
Have toilet	-		
Yes	-	1	1
No	-	0.59(0.23-1.52)	0.63(0.23-1.69)
When you got pregnant, did you want to get pregnant			
Yes	-	1.00	1
No	-	1.36(0.45-4.13)	1.56(0.49-4.94)
Gravidity	-		
Primi gravid	-	1.00	1
Multi gravid	-	0.65(0.24-1.73)	0.67(0.25-1.82)

Receive antenatal care during you last pregnancy			
Yes	-	1	1
No	-	1.82*(1.01-2.22)	1.39*(1.05-1.83)
Did you see anyone for antenatal care for this pregnancy			
Yes	-	1.00	1
No	-	1.65*(1.24-1.73)	1.78*(0.33-0.99)
Place receive antenatal care for current pregnancy			
Government hospital	-	1	1
Public hospital	-	6.51 (057-73.97)	2.26(0.16-30.93)
Public health center	-	2.09 (0.17-25.98)	8.66(0.57-13.10)
Did you take any supplements (Iron/folic acid Iodine, or other) during this pregnancy			
Yes	-	1	1
No	-	2.16(0.52-8.97)	1.69(0.39-7.33)
Days Iron/folic acid supplemented			
> 90 days	-	1	1
< 90 days	-	6.32*(1.09-36.59)	7.88*(1.29-48.08)
In the past month, have there been days when you did not have enough food or money to buy food			
Yes	-	1	1
No	-	0.67(0.25-1.86)	0.61(0.21-1.76)
Household resources are managed			
Partner	-	1	1
Mother	-	0.77(0.20-2.99)	0.94(0.22-3.98)
Both of them	-	1.21(0.44-3.34)	1.37(1.08-3.86)
How do you feel about your weight change since you became pregnant			

Gaining too much	-	1	1
Gaining too little	-	0.87(0.29-2.60)	0.89(0.29-2.71)
It's okay	-	0.57(0.16-2.06)	0.62(0.16-2.38)
Not sure	-	0.19(0.02-1.73)	0.15(0.01-1.65)
Weight has not changed	-	3.96(0.64-24.43)	3.39(0.49-23.67)
In the last month, has your partner physically threatened or tried to hurt you			
Yes	-	1	1
No	-	0.63(0.11-3.52)	0.88(0.14-5.40)
In the last month, have you felt down, depressed, or hopeless			
Yes	-	1	1
No	-	0.81(0.07-9.36)	0.67(0.05-8.45)
Any change in feeding habit			
Yes	-	1	1
No	-	1.25(0.35-4.50)	1.27(0.34-4.75)
Food taboos during this pregnancy			
Yes	-	1	1
No	-	0.86 (0.21-3.59)	0.96(0.22-4.26)
Food cravings during this pregnancy			
Yes	-	1	1
No	-	0.78*(0.20-0.98)	0.77*(0.18-0.93)
Food averted during this pregnancy			
Yes	-	1	1
No	-	3.45(0.88-13.57)	3.27(0.78-13.59)

Average calcium intake	-	0.996* (0.993-0.998)		0.996*(0.993-0.998)
Read a newspaper or magazine				
Not at all	-	1		1
Less than once a week	-	0.07*(0.01-0.43)		0.07*(0.01-0.40)
At least once a week	-	0.35(0.09-1.40)		0.29 (0.07-1.28)
Do you listen radio				
Not at all	-	1		1
Less than once a week	-	0.86(0.20-3.68)		1.03(0.23-4.56)
At least once a week	-	0.79(0.25-2.48)		0.86(0.26-2.82)
Watch television				
Not at all	-	1		1
Less than once a week	-	0.64(0.10-3.96)		0.55(0.08-3.58)
At least once a week	-	0.74(0.17-3.10)		0.99(0.22-4.53)
Fixed effect (Community/facility factors)				
Place of Residence	-			
Rural	-		1	1
Urban	-		2.11*(1.36-3.26)	1.39(0.44-4.44)
Examined by Doctor/IEOS during ANC				
Yes	-		1	1
No	-		0.53(0.17-1.64)	0.68(0.11-3.99)
Examined by Nurse/midwife during ANC				
Yes	-		1	1
No	-		1.09(0.71-1.67)	2.96(0.49-17.80)
Examined by Health				

extension worker during ANC				
Yes	-		1	1
No	-		0.71(0.29-1.72)	0.63(0.08-4.69)
Random effects	**Empty**	**Individual**	**Community/facility**	**Individual and community**
Variance (SE)	0.16* (0.609)	0.81*(0.5)	0.36*(0.07)	0.12*(0.53)
(VPC)= ICC (%)	12%	9.7%	8.9%	8.3%
PCV	Reference	35	22	12
Log-likelihood	-276.68484	-117.81133	-269.68537	-116.30423
Model fit statistics				
AIC	557.3697	291.6227	551.3707	296.6085
BIC	565.4262	384.2542	575.5404	402.473

*NB: * indicates significant variable in its respective model, the empty model contains no variables, SE = Standard error, VPC= Partition variance coefficient AIC=Akaike Information Criteria. PCV was calculated for successive models with reference to null model to look at relative contribution of each model to explain BP variability*

Discussion

The primary objective of this research was to examine the effect of calcium nutrition education on blood pressure variability among pregnant mothers, and accordingly pregnant mother who got nutrition calcium education had decreased blood pressure variability. And other significant factors that affect blood pressure variability among pregnant mothers were individual level factors (maternal educational status, maternal occupation, ANC during their last and current pregnancy, iron/folic acid supplementation, food craving, calcium intake and reading news paper) and community factors (place of residence).

Calcium nutrition education showed significant association with blood pressure variability among pregnant mothers. This result indicates that mothers who had knowledge regarding what to feed that have effect on blood pressure variability had less likely of blood pressure variability. A study done in Ethiopia in support of this showed that pregnant mothers who has no awareness on risk hypertension were more likely develop PIH as compared to their counter parts [10]. This result indicates that if pregnant mother are educated regarding calcium nutrition from previous evidence which has been proposed that low-calcium intake may increase blood pressure by stimulating either parathyroid hormone or renin release, increasing intracellular calcium in vascular smooth muscle and leading to vasoconstriction. Calcium supplementation may reduce parathyroid release and could reduce smooth muscle contractility. It could also reduce uterine smooth muscle contractility or increase serum magnesium levels and thus

prevent preterm labour and delivery [11]. And also other meta-analysis result conducted in United Kingdom showed that among interventions, those based mainly on diet showed a significant reduction in pre-eclampsia by 33%, compared with the controls [12].

Other finding were maternal education has significant association with blood pressure variability specifically educated pregnant mothers had lower blood pressure variability. This result is similar with study done in Netherland that showed that women with relatively low levels of education had a higher risk of gestational hypertension than women with a high level [13]. This implies that if we educate mothers on nutrition there might decrease pregnancy induced hypertension.

The study revealed that maternal occupation was significantly affecting blood pressure variability among pregnant mothers. Previous studies have found mixed outcomes. This study was in line with study done in Bangladesh [14]. However this finding was inconsistent with study done in Taiwan [15]. Employed pregnant mothers are at risk of blood pressure variability this could be due to one of the suggested mechanism through which physically demanding work and psychological stress could lead to hypertensive disorders during pregnancy is an increased utero placental vascular resistance which follows physical exertion. Physically demanding work may cause an increase in catecholamine levels, which may lead to a decreased uterine blood flow and therefore may induce PIH and preeclampsia. It has also been suggested that part of the excess catecholamine release is due to an overactive sympathetic nervous system[16]. Whatever this could support the finding; however, further research is warranted to confirm these negative findings.

Another significant predictor for blood pressure variability was Antenatal care follow-up during the last pregnancy and current pregnancy. Antenatal care (ANC) is a care of women during pregnancy by skilled health care providers. The components of ANC include: early high risk screening, prevention and care of pregnancy-related complications, including PIH, and provision of health education and health promotion. With adequate ANC (≥ 4 times), pregnant women would be monitored and have better pregnancy outcomes and a reduction in complications. This study is supported by study done in Thailand [17], USA [18]. Pregnancy induced hypertension is not a totally preventable disease but maternal and foetal Complication due to PIH can be halted at mild stage by quality Antenatal care with good outcome through controlling blood pressure variability.

The other main exposure variable used in our study was self-reported consumption of iron and folic acid supplementation during pregnancy. Iron/folic supplementation had significant association with blood pressure variability among pregnant mothers. This finding is consistent with the study done in India which indicates the likelihood of reporting Preeclampsia or eclampsia symptoms was lower among those mothers who consumed iron and folic acid supplementation for at least 90 days during their last pregnancy [19]. Iron plays a significant role inter alia in: Oxygen transport, in the production of ATP, in the synthesis of DNA, in preserving the function of mitochondria and in protecting cell structures against oxidative damage, in the activity of numerous enzymes, as well as in cell growth and proliferation. Iron plays a catalyzing role in the production of reactive oxygen species in the Fenton and Haber-Weiss

reactions. The role of iron in the development of the placenta is not fully understood, but the discovery of the hypoxia-inducible factor (HIF) and its regulatory mechanisms also drew attention to the importance of iron. Another systematic review and Meta analysis done in china showed that iron deficiency correlates with some complications of pregnancy [20].

Food craving was another predictor for blood pressure variability at individual level. This was consistent with study done in Ghana which revealed that specifically geophagia was associated with pregnancy diastolic blood pressure variability [21]. Cravings in women have been shown to increase in frequency and intensity at two distinct times: during the perimenstrum (i.e., a period of about eight days around the onset of menstruation) and in pregnancy [22].

Dietary calcium intake was one of the significant factors associated with blood pressure variability. Low calcium intake has been hypothesized to cause increase in blood pressure by stimulating the release of parathyroid hormone and/or renin which leads to increased intracellular calcium concentration in vascular smooth muscle cells and causes vasoconstriction. Whatever different research finding [23,24] showed that calcium supplementation had significant effect on decreasing blood pressure variability and also this study indicates that if we educate mother on calcium nutrition there might be increase consumption of calcium so might lead to decreased blood pressure variability.

The other significant factor was reading newspaper, this might be due to if pregnant mother are reading newspaper they could get information concerning their pregnancy nutrition then after they may have knowledge what feed and regarding the complication during pregnancy. Health literacy is the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions. It comprises a complex set of reading, listening, analytical, decision-making skills, and the ability to apply these skills to health problems. Low health literacy during the perinatal period, and specifically about preeclampsia, may contribute not only to women's poor understanding of pregnancy and potential fetal health issues, but also to delayed care and poor health outcomes.

Regarding the community level factors place of residence was one of the significant factors affecting blood pressure variability. Urban residents were at risk of blood pressure variability. However a study done in Ethiopia, tigray showed that rural residents were at greater odds of suffering from hypertensive disorders [25]. The difference could be due to the study design used because they are different.

Conclusion

Individual level factors were significantly associated with blood pressure variability. Individual level factors (Calcium nutrition education, maternal educational status, maternal occupation, Antenatal care during last pregnancy and current pregnancy, iron/folic acid supplementation, food craving, dietary calcium level and reading newspaper) and community level factors (place of residence) were significant predictors of blood pressure variability among pregnant mother after 28 gestational age. During antenatal visits, pregnant women should be made aware of some dietary practices which are harmful

during pregnancy, and increase education regarding the benefit of adequate nutrition. Nutrient supplementation should be administered to pregnant women, especially those living in low socioeconomic areas to supplement dietary intakes. A prospective cohort study should have to be conducted using blood biomarkers of nutrients to properly determine the role of nutrients in the development of hypertension in pregnancy. Calcium nutrition education should have to be given through the health extension workers after developing guideline and Regional food composition table on how to counsel, type of foods found in tigray which have high calcium content.

List Of Abbreviations

ANC Antenatal Care

BMI Body Mass Index

Bp Blood pressure

CVD Cardio Vascular disease

Declarations

Ethics approval and consent to participate

Participation was voluntary for all participants. Before the interview, the interviewer explained in detail the content of the questionnaire, informed the participants on confidentiality of their responses and of their free choice to withdraw from the study during the interview or later. A written consent was obtained from all participants. The study was approved by the Institutional Review Board of the Tigray Health Research Institute (No: IRB145/2019).

Consent for publication

Not applicable

Availability data and material

The datasets used and/or analyzed during the current study is available from the corresponding author on request.

Competing interest

The authors' declare that they have no conflict of interest.

Funding

This research is not funded by any organization

Author Contributions

Conceptualization: Mulugeta Woldu, Alemnesh Abrha.

Formal analysis: Alemnesh Abrha, Ataklty Gebretsadik, Brhane Ayele, Equbay Gebreegziabher

Methodology: Afework Mulugeta, Haylay Gebretnsae,Tsegay Hadgu

Validation: Afework Mulugeta, Brhane Ayele

Writing – original draft: Mulugeta Woldu,Alemnesh Abrha, Ataklty Gebretsadik

Writing – review & editing: Brhane Ayele, Haylay Gebretensae, Equbay Gebre-egziabher, Tsegay Hadgu, Afework Mulugeta. All authors have read and approved the manuscript

Acknowledgment

Our heartfelt thanks go to the Tigray Health Research Institute for allowing us to undergoing this research.

References

1. Nutrient reference values for Australia and New Zealand. (2014). Retrieved from https://ascensionkitchen.com/calcium-on-a-plant-based-diet/.
2. WHO
   WHO. Guideline: Calcium supplementation in pregnant women. Geneva, World Health Organization, 2013.
3. Chotboon C, Soontrapa S, Buppasiri P, et al. Adequacy of calcium intake during pregnancy in a tertiary care center. International Journal of Women's Health 2018:10 523–527.
4. Van Mierlo LA, Arends LR, Streppel MT, Zeegers MP, Kok FJ, Grobbee DE, Geleijnse JM. Blood pressure response to calcium supplementation: a meta-analysis of randomized controlled trials. J Hum Hypertens. 2006;20:571–80. doi:10.1038/sj.jhh.1002038.
5. Getinet Ayele S. Factors Associated with Hypertension during Pregnancy in Derashie Woreda South Ethiopia, Case Control. Qual Prim Care. 2016.
6. Sammya Bezerra Maia e Holanda Moura
   Sammya Bezerra Maia e Holanda Moura. Lopes LM, Murthi P, Costa FS, "Prevention of Preeclampsia," Journal of Pregnancy, vol. 2012, Article ID 435090, 9 pages, 2012.
7. Tesfaye B, Wuehler S, Moges T, Samuel A, Kebede A, Zerfu A, Abera A, Mengistu G, Wodajo G, Katherine A, Jalal C, Kebede A. Making a Case for Calcium Supplementation for Prevention of Pregnancy Hypertension in Ethiopia. European Journal of Nutrition Food Safety. 2015;5(5):1187–8. Article no.EJNFS.2015.502 www.sciencedomain.org.

8. Schoenaker DAJM, Soedamah-Muthu SS, Mishra GD. The association between dietary factors and gestational hypertension and pre-eclampsia: a systematic review and meta-analysis of observational studies. BMC Med [Internet]. 2014 Sep;22:12:157.
9. Ndanuko RN, Tapsell LC, Charlton KE, Neale EP, Batterham MJ. Dietary Patterns and Blood Pressure in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Adv Nutr. 2016;7(1):76–89.
10. Getinet Ayele S. Factors Associated with Hypertension during Pregnancy in Derashie Woreda South Ethiopia, Case Control. Qual Prim Care. 2016;24:207–13.
11. Bezerra Maia e Holanda. Moura S, Marques Lopes L, Murthi P. Da Silva Costa F. Prevention of preeclampsia. J Pregnancy. 2012;2012.
12. Allen R, Rogozinska E, Sivarajasingam P, Khan KS, Thangaratinam S. Effect of diet- And lifestyle-based metabolic risk-modifying interventions on preeclampsia: A meta-analysis. Acta Obstet Gynecol Scand. 2014;93(10):973–85.
13. Silva L, Coolman M, Steegers E, et al. Maternal educational level and risk of gestational hypertension: the Generation R Study. J Hum Hypertens. 2008;22(7):483–92. doi:10.1038/jhh.2008.22.
14. Sultana N. Pregnancy Induced Hypertension and Associated Factors among Pregnant Women. J Gynecol Womens Heal. 2017;3(5).
15. Chang PJ, Chu LC, Hsieh WS, Chuang YL, Lin SJ, Chen PC. Working hours and risk of gestational hypertension and pre-eclampsia. Occup Med (Chic Ill). 2009;60(1):66–71.
16. Nugteren JJ, Snijder CA, Hofman A, Jaddoe VWV, Steegers EAP, et al. Work-Related Maternal Risk Factors and the Risk of Pregnancy Induced Hypertension and Preeclampsia during Pregnancy. The Generation R Study. PLoS ONE. 2012;7(6):e39263. doi:10.1371/journal.pone.0039263.
17. Phengsavanh A, Laohasiriwong W, Suwannaphant K, Assana S, Phajan T, Chaleunvong K. Antenatal care and its effect on risk of pregnancy induced hypertension in lao pdr: A case-control study [version 1; peer review: 1 approved, 1 approved with reservations]. F1000Research. 2018;7(May):1–11.
18. Sheng L, Christopher M, ä¹³é¼ å¿□è□□æ□□å□□ AM. HHS Public Access Physiol Behav. 2016;176(1):100–6.
19. Agrawal S, Fledderjohann J, Vellakkal S, Stuckler D. Adequately diversified dietary intake and iron and folic acid supplementation during pregnancy is associated with reduced occurrence of symptoms suggestive of pre-eclampsia or eclampsia in indian women. PLoS One. 2015;10(3):1–23.
20. Fu APA, Shimin MM, Li FMM, Zhou, Jianguo MM, Liu. Zhiping The Relationship Between Body Iron Status, Iron Intake And Gestational Diabetes, Medicine: January 2016 - Volume 95 - Issue 2 - p e2383 doi: 10.1097/MD.0000000000002383.
21. Sackey DS, Larbie C, Mensah FO. Geophagia, nutrition and health of women with pregnancy-induced hypertension. Afr Health Sci. 2018;18(4):1243–54.
22. Orloff NC, Hormes JM. Pickles and ice cream! Food cravings in pregnancy: hypotheses, preliminary evidence, and directions for future research [Internet]. Vol. 5, Frontiers in Psychology. 2014. p. 1076.

23. Imdad A, Jabeen A, Bhutta ZA. Role of calcium supplementation during pregnancy in reducing risk of developing gestational hypertensive disorders: a meta-analysis of studies from developing countries. BMC Public Health. 2011;11:18. https://doi.org/10.1186/1471-2458-11-S3-S18.
24. Lorrene D, Ritchie JC, King. Dietary calcium and pregnancy-induced hypertension: is there a relation?, *The American Journal of Clinical Nutrition*, Volume 71, Issue 5, May 2000, Pages 1371S–1374S, https://doi.org/10.1093/ajcn/71.5.1371s.
25. Kahsay HB, Gashe FE, Ayele WM. Risk factors for hypertensive disorders of pregnancy among mothers in Tigray region, Ethiopia: matched case-control study. BMC Pregnancy Childbirth. 2018;18(1):482. doi:10.1186/s12884-018-2106-5. Published 2018 Dec 6.

Figures

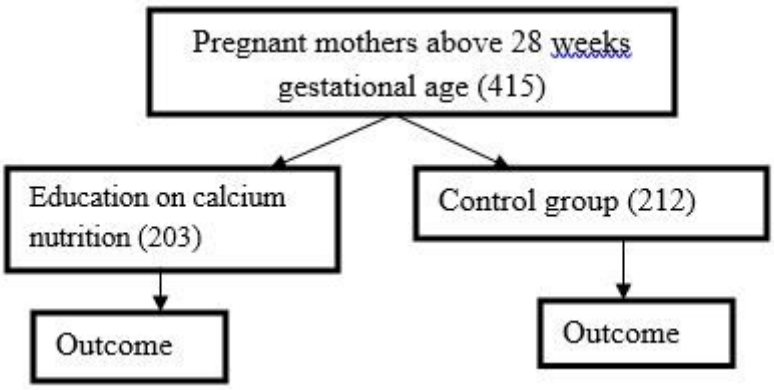

Figure 1

Schematic representation of randomization of pregnant mothers