COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

Title: - Early pregnancy mean arterial pressure and maternal risk factors for prediction of preeclampsia among women who delivered at three teaching hospitals in AA, Ethiopia: a case control study.

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A research thesis submitted to the department of obstetrics and gynecology, college of health sciences, Addis Ababa University in partial fulfillment of the requirements for the specialty in obstetrics and gynecology.

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Title of research	Early pregnancy mean arterial pressure and maternal risk factors for prediction of preeclampsia among women who delivered at three teaching hospitals in AA, Ethiopia: a case control study.
Duration of research	7 months
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Student declaration

I declare that this thesis titled "Early pregnancy mean arterial pressure and maternal risk factors for prediction of preeclampsia among women who delivered at three teaching hospitals in AA, Ethiopia: a case control study." was conducted completely by me under the supervision of my advisor. I affirm that I have cited all sources of information used in this thesis to the best of my knowledge and effort. Additionally, I confirm that this thesis has not been submitted to any other institution for the purpose of obtaining any degree, certificate, master's, or diploma.

Name of Student: Masreshaw Bogale Legesse

Signature……..

Date: October 10, 2024

Supervisors' Declaration

I hereby confirm that I have read and assessed this research thesis on "Early pregnancy mean arterial pressure and maternal risk factors for prediction of preeclampsia among women who delivered at three teaching hospitals in AA, Ethiopia: a case control study." I have provided guidance throughout its development up to the present format, and I believe it is ready for submission for final approval in partial fulfillment of the Degree of Specialty in Obstetrics & Gynecology

Advisor:

Dr. Seid Arage (MD, Assistant Professor of Obstetrics and Gynecology,, fetomaternal medicine subspecialist, School of Medicine, College of Health Sciences, Addis Ababa University)

Signature……..

Date: October 16, 2024

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Acronym and Abbreviation

ACOG ……..American College of Obstetricians and Gynecologist

APS……Antiphospholipid syndrome

ART ……..Assisted reproductive technologies

ASPRE…….Combined multimarker screening and randomized patient treatment with aspirin for evidence-based pre-eclampsia prevention

AUROC……..……Areas Under Receiver Operating Characteristic Curve Analysis

BP……..…..Blood Pressure

CEMACH……...Confidential Enquiry into Maternal and Child Health

CI……Confidence Interval

dBP…….Diastolic blood pressure

DR……..Detection Rate

ETB…….Ethiopian Birr

FPR…….False Positive Rate

FGR……Fetal Growth Restriction

FIGO……..International Federation of Gynecology and Obstetrics

GH…….…….Gestational Hypertension

GMH…….……Gandhi Memorial Hospital

TASH ……..……...Tikur Anbessa Specialized Hospital

HELLP……..…….Hemolysis elevated liver enzyme, low platelet

ISSHP……...…..International Society for the Study of Hypertension in Pregnancy

IUFD ……..Intrauterine Fetal Death

IVF …….In Vitro Fertilization

MAP …….. Mean Arterial Pressure

MOM …….Multiples of the Median

NHBPEP ……..…….National High Blood Pressure Education Program

NICE ……..……...National Institute for Health and Care Excellence

NICU ……..……..Neonatal intensive care unit

PE …….Preeclampsia

PMBI ……Pre-Pregnancy Body Mass Index

OR ……Odds Ratio

PE …….Pre-Eclampsia

RR ……Relative Risk

sBP ……..……Systolic Blood Pressure

SD …….…...…….....Standard Deviation

SGA ……Small for Gestational Age

SLE …….Systemic Lupus Erythematosus

ZMH ……Zewditu Memorial Hospital

Abstract

Background: -The diagnosis of PE is made based on high blood pressure and proteinuria after 20 weeks of gestation of pregnancy in previously normotensive women. The best combined first-trimester screening studies for PE is one that includes maternal risk factors, measurements of mean arterial pressure (MAP), serum placental growth factor (PLGF), and uterine artery pulsatility index (UTPI).

Objective: -To look the relationship of early pregnancy mean arterial pressure and maternal risk factors for prediction of preeclampsia among women who delivered at three teaching hospitals in AA, Ethiopia:

Method: -The research design was a case control study and all women having early antenatal visit and recording blood pressure in the study area were included. Sample size is calculated by using double population proportion formula and with the case to control ratio will be 1:2.

Result: - In this study the prediction of preeclampsia using MAP by AUC and ROC MAP=0.698, 95% CI=0.637, 0.759). The sensitivity of MAP in predicting PE was 51.8%, and specificity of 78.6%. Positive predictive value of MAP was 54.18% and negative predictive value was 76.5%. Other determinates of preeclampsia were study participant whose age of ≥35 years compared to those of age 18-24 years, having a history of preeclampsia and mean arterial pressure of ≥90.

Recommendation: - Given the moderate predictive performance of MAP, SBP, and DBP in early pregnancy, these measures should be routinely monitored and used as part of a comprehensive preeclampsia screening strategy.

Keyword: - preeclampsia, mean arterial pressure, pregnant women

1. Introduction

1.1 Background

Preeclampsia (PE), diagnosed as the onset of hypertension and proteinuria during pregnancy, has been recognized and studied for centuries (1). Plenty previous studies assesed blood pressure in mid pregnancy as a screening tool in preeclampsia prediction (2-5). However, there has been insufficient evaluation of first-trimester blood pressure (6). As pre-eclampsia is a major cause of maternal and fetal mortality and morbidity (7-8).

The incidence of pre-eclampsia is 2-10%, depending on the population studied and definitions of pre-eclampsia (9).Risk factors associated with pre-eclampsia include maternal diabetes, chronic hypertension, renal disease, thrombophilias, and autoimmune disorders. Obstetric factors associated with PE are multiple pregnancies, previous pre-eclampsia, and molar or hydropic pregnancies. Other risk factors are first pregnancy, and extremes of age and obesity. A family history of pre-eclampsia may suggest a genetic predisposition (10).

An accurate prediction of PE using clinically accessible risk factors in the early second trimester is crucial to the prevention of PE progression. At present, many studies have assessed the predictive ability of various factors for predicting PE, including clinical features, biomarkers, and ultrasound markers (11-13).

Evidences suggests that PE can be subdivided into early onset PE, requiring delivery before 34 weeks' gestation and late onset PE, with delivery at or after 34 weeks, because the former is associated with a higher incidence of adverse outcome. A major challenge in modern obstetrics is early identification of pregnancies at high-risk of early onset PE and undertaking the necessary measures to improve placentaion and reduce the prevalence of the disease (14-17)

Pregnancies complicated by pre-eclampsia, chronic hypertension, or both, are at significantly increased risk of adverse outcomes. For most women, the assessment of blood pressure and urinalysis is the mainstay of routine antenatal care. Published report by the Confidential Enquiry into Maternal and Child Health (CEMACH), pre-eclampsia or eclampsia was the second most common cause of direct maternal mortality in the United Kingdom between 2003 and 2005 (18).

The diagnosis of PE is based on the demonstration of high blood pressure (BP) and significant proteinuria during the second half of pregnancy in previously normotensive women. There are 2 first-trimester screening studies for PE. The first study used an automated device to measure BP at 9 to 13 weeks and reported that, with a cutoff of 90 mm Hg in mean arterialpressure (MAP), the detection rate (DR) of PE was 62%, for a false positive rate (FPR) of 38% (19).The second study was a retrospective one in which the medical charts of pregnant women attending for routine prenatal care were examined to identify the BP measurements taken by mercury sphygmomanometers before 20 weeks (mean: 13.7 weeks) from 1655women.At a cutoff of 92 mm Hg in MAP, the DR of PE was 25%, for an FPR of 10% (20).

1.2 Statement of the problem

Blood pressure measurement is part of routine surveillance during antenatal care. High blood pressure may be the first sign of a hypertensive disorder and is a diagnostic tool. Oscillations in BP measurements in a pregnant woman may reflect a trend for hypertensive disorder, and is a predictive test (21).

Various clinical and biophysical tests have been proposed to predict PE, but no predictive test has been shown to be useful for isolated use to adjust pre-existing maternal risk of PE with enough specificity and sensitivity for clinical use. Consequently, the best results are obtained from tests involving the combination of multiple parameters (22).From those parameters, the 1st trimester has been considered ideal for PE screening because of the evidence of effectiveness of low-dose aspirin use by pregnant women risk initiated less than or equal to16 weeks of gestation (23).

MAP is an easy, non-invasive, and cost-effective test than can be conducted in all women from the 1st trimester. So, this study has assessed the predictive effect of mean arterial pressure of early pregnancy, for mothers having preeclampsia and no preeclampsia at the after 20 weeks of gestational age using a case control study.

1.3 Significance of the study

Predicting PE by early pregnancy mean arterial blood pressure is a crucial role for prevention of PE and PE related complications. Identifying the risked MAP is an instrument to use preventive drugs like aspirin. This study was designed with the specific focus of assessing the detection rate of MAP on PE among women having PE and non-PE using a case control study.

2. Literature review

The impact which any given blood pressure has on circulatory dynamics is best expressed by utilizing the mean arterial pressure (MAP). This also has the benefit of working with a single

figure which may be readily derived from the systolic and diastolic. readings. The most commonly used formula is chat advocated by Burton (24).

$$MAP=\frac{S+2D}{3}$$

Study done on First-Trimester Mean Arterial Pressure and Risk of Preeclampsia showed that, 3.0% of women developed preeclampsia according to the American College of Obstetricians and Gynecologist (ACOG) criteria. The risk of preeclampsia increased across increasing quartiles of average first-trimester MAP. Preeclampsia was related to MAP after adjustment for maternal age, ethnicity, parity, and pre-pregnancy body mass index (BMI) (P =0.003). Women with MAP ≥89 mm Hg had a three-times increased risk of preeclampsia compared with women with MAP <79 mmHg (ARR, 3.0; 95% CI, 1.2–7.4). According to the ACOG criteria (1996), adjusted associations with first-trimester MAP were weak and not statistically significant. After adjustment, preeclampsia RRs among women in the highest quartiles of systolic and diastolic blood pressures relative to the lowest quartiles were 3.3 (95% CI, 1.2– 8.8) and 2.1 (95% CI, 0.9 –5.0), respectively. The adjusted high-quartile RR was 1.1 (95% CI, 0.5–2.7. MAP cutoff of ≥88 mm Hg provided an estimated sensitivity of 0.78 (95% CI, 0.76 – 0.80), specificity of 0.63(95% CI, 0.61– 0.65), positive predictive value of 0.06(95% CI, 0.05– 0.07), and negative predictive value of0.99 (95% CI, 0.98 –1.00). The area under the curve was 0.71 (95% CI, 0.69 – 0.73). The ROC curves for average first-trimester systolic and diastolic blood pressures were similar; areas under both curves were 0.68 (95% CI, 0.66 – 0.70). Pulse pressure was less predictive, with an area under the curve of 0.56 (95% CI, 0.54 – 0.58) (25).

Study done on Prediction of Preeclampsia by Mean Arterial Pressure at (MAP1=11–13) and (MAP1=20–24) Weeks' Gestation revealed that, the normal group, the median MAP-2 was 0.8 mm Hg (95% CI 0.6–1.0) and 0.9% (95% CI 0.1–6.0) lower than MAP-1 ($p < 0.0001$). In the PE group, compared to the normal group, the median MAP-1 and MAP-2, expressed as mm Hg or MoM, were significantly increased. In the prediction of early PE, the areas under receiver operating characteristic curve analysis (AUROC) for maternal characteristics with MAP-1, maternal characteristics with MAP-2 and the combination of all were significantly higher than the AUROC for maternal characteristics alone ($p = 0.001$;$p = 0.002$; $p = 0.001$). In the prediction of preterm PE, the AUROC for maternal characteristics with MAP-1, maternal characteristics with MAP-2 and the combination of all were significantly higher than the AUROC for maternal

characteristics alone ($p = 0.001$; $p < 0.001$; $p < 0.001$). In the prediction of total PE, the AUROC for maternal characteristics with MAP-1, maternal characteristics with MAP-2 and the combination of all were significantly higher than the AUROC for maternal characteristics ($p < 0.001$; $p < 0.001$; $p < 0.001$). The AUROC for the combination of all was significantly higher than the AUROC for maternal characteristics with MAP-1 ($p = 0.039$) and maternal characteristics with MAP-2 ($p = 0.021$) (26).

A case control study done on validation of the prediction models for Preeclampsia revealed that, compared with the non-PE group, the patients with PE had a longer duration of hypertension (0.6±2.0 vs. 0.1±0.6 years, P<0.001), higher frequencies of multiple gestations (9.6% vs. 5.1%, P=0.026), GDM (46.3% vs. 29.9%, P<0.001), chronic hypertension (23.9% vs. 2.4%, P<0.001), DM (4.8% vs. 1.8%, P=0.028), kidney diseases (2.7% vs. 0.4%, P=0.008), history of PE (8.5% vs. 0.4%, P<0.001), BP ≥130/80 mmHg (64.4% vs. 13.6%, P<0.001), family history of hypertension (75.5% vs. 19.7%, P<0.001), and higher pre-pregnancy body mass index (BMI) (27.4±5.4 vs. 22.9±3.5 kg/m2, P<0.001) (27)

Study done for mean arterial pressure for predicting preeclampsia in Asian women shows that from a total of 926 study participants 20 women developed preeclampsia, who had significantly lower levels of placental growth factor and MAP throughout pregnancy than women without preeclampsia. For predicting preeclampsia, MAP had AUCs of 0.86 (95% CI 0.78 to 0.95), 0.87 (95% CI 0.80 to 0.95) and 0.91 (95% CI 0.85 to 0.98) at 11–14, 18–22 and 28–32 weeks, respectively. (28).

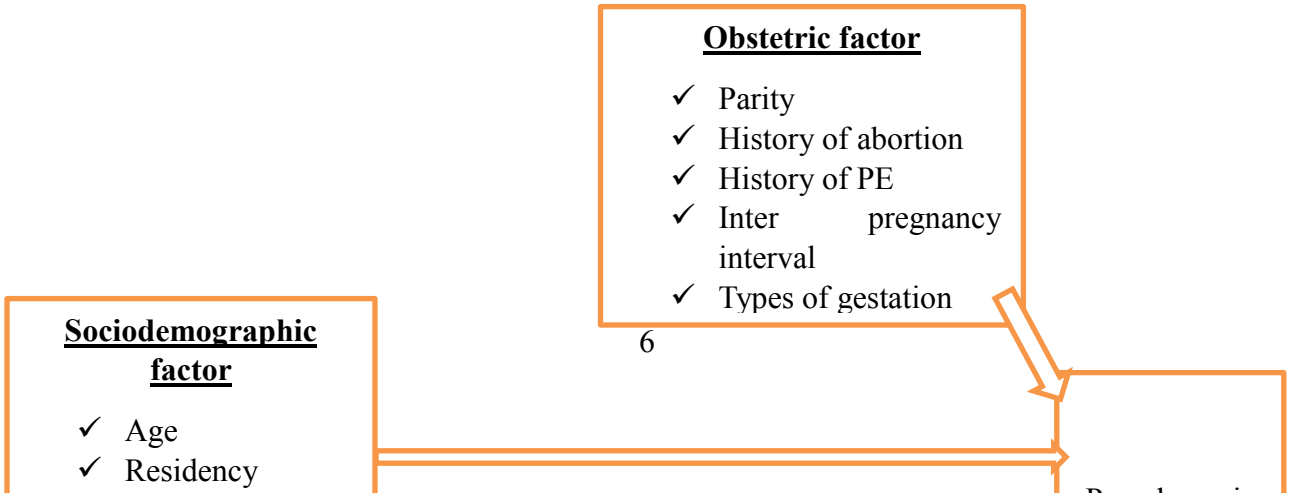
A study on Prediction of Preeclampsia by mean Arterial Pressure at 11^{+0} to 13^{+6} Weeks indicates that the mean (95% CI of the mean) multiples of the Median (MoM) MAP were 1.0(1.0008 to 1.0055) MoM in the unaffected group, 1.0840(1.0649 to 1.1032) MoM in the PE group, and 1.0646 (1.0452to 1.0839) MoM in the GH group. The areas under the AROCs for the detection of PE were significantly higher with the combined model (AROC: 0.852) than with either history alone (AROC:0.801; P=0.017) or MAP alone (AROC: 0.734; P=0.001). The detection of GH, the AROC for the combined model was significantly higher (AROC: 0.743) than with either history alone (AROC: 0.682; P=0.030) or MAP alone (AROC: 0.680; P=0.006). At a 10% FPR, the DR of PE was 43.3% for history alone, 37.5% for MAP alone, and 62.5% for combined testing, and the respective values for GH were 27.8%, 32.0%, and 41.2% (29).

A study done on Risk Factor Assessment for Pre-eclampsia showed that, age >30 years, Pre-obese (BMI=25-29.9), obese (BMI≥30 Kg/m2), Primiparity, age of menarche at 12 years and rural residence were found to be independent risk factors associated with Preeclampsia (30).

Study done on mean arterial pressure for the prediction of preeclampsia in the first trimester of pregnancy shows that from 733 pregnant women; 55 developed PE, 21 of those developed preterm PE and 34 term PE. detection rate of 67% cases of preterm PE, with a false-positive rate of 10%, positive predictive value of 17% and negative predictive value of 99% (31).

A study on potential predictive tool for preeclampsia by MAP revealed that women with early-onset preeclampsia had higher mean arterial blood pressure levels at 20 weeks of gestation, compared to the normotensive group. Women with late-onset preeclampsia had higher mean arterial blood pressure levels at 37 weeks of gestation, than the normotensive groups and higher increases in this marker between 20 and 37 weeks of gestation. Based on ROC curves, the predictive performance of mean arterial bloodpressure was higher at 37 weeks of gestation, with an area under the curve of 0.771 (32).

Conceptual framework



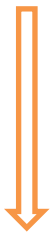


Figure 1. The conceptual framework

3. Objective

3.1 General objective

To compare the occurrence of PE based on early pregnancy mean arterial pressure and maternal risk factors among women who delivered at three teaching hospitals in AA, Ethiopia:

3.2 Specific objective

I. To assess early pregnancy mean arterial pressure as a contributing factor for screening PE

II. To compare the level of mean arterial pressure between the case and the control group

III. To assess the maternal risk factor contributed for incidence of preeclampsia

4. Methodology

4.1 study design and period

The research design was a case control study and it was conducted from November, 2023 up to May 2024.

4.2 Population and Study Sample

The study population is all pregnant women having early Antenatal visit with recorded blood pressure during GA of 11-16 weeks and recording blood pressure in the study area who delivered

at Department of Obstetrics and Gynecology at the three teaching hospitals in Addis Ababa, Ethiopi**a.**

These women were grouped into two groups [case and control groups]. The case groups are those women that have preeclampsia. The control groups are those women who haven't preeclampsia in the specified time frame.

4.3 Outcome

Primary outcome of the study is to know the association of MAP and preeclampsia

Secondary outcome of the study is to know the association other risk of preeclampsia when compared to the control group

4.4 Inclusion criteria

For the case definition

1. After late second trimester (>20 weeks of gestation)
2. Having preeclampsia/ severe gestational HTN
3. Having early pregnancy recorded BP

For the control definition

1. After late second trimester (>20 weeks of gestation)
2. Have not preeclampsia/ gestational hypertension
3. Having early pregnancy recorded BP
4. Not took Aspirin medication

4.5 Exclusion criteria

For the case group

1. Chronic HTN,
2. Having no early pregnancy recorded BP

For the control group

Any episode of recording high blood pressure

4.6 Sample Size and Selection of Sample

Sample size was calculated by using double population proportion formula using epi info software. Use as a variable with type 1 / 2 error rate alpha of 0.05 and a power of 80%. Two groups of patients used as a variable for sample size calculation. The case to control ratio was 1:2. The exposed and non-exposed group will be picked as case control study done on validation of the prediction models for Preeclampsia (27).

The sample size was calculated using Epi-info calc software.

Sample Size for Case-Control Study				
For:				
	Two-sided confidence level(1-alpha)			95
	Power(% chance of detecting)			80
	Ratio of Controls to Cases			2
	Hypothetical proportion of controls with exposure			29.9
	Hypothetical proportion of cases with exposure:			46.28
	Least extreme Odds Ratio to be detected:			2.02
	Kelsey	**Fleiss**	**Fleiss with CC**	
Sample Size – Cases	101	102	110	
Sample Size – Controls	201	203	220	
Total sample size:	302	305	**330**	

4.7 Study Variables

4.7.1 Dependent Variable

- Preeclampsia

4.7.2 Independent Variables

- Sociodemographic characteristics
  - ✓ Age
  - ✓ Residence
  - ✓ Marital status.
  - ✓ Educational status
  - ✓ Income

- Obstetric characteristics
- Mean arterial pressure
- Health related characteristics
- Substance utilization characteristics

4.8 Exposure Assessment

The exposures that are assessed as risk factors of Preeclampsia are assessed retrospectively after identifying the case groups.

4.9 Sources of Data

The data was collected from the three-teaching Hospital of Addis Ababa University after 20 weeks of gestation of both cases and controls. The data was collected directly from the patients and their charts using standardized structured questionnaire.

4.10 Data Quality Control Measures

Training was provided for data collectors and was supervised for data accuracy and completeness and an appropriate modification was made after discussing with the supervisor and data collectors before starting the actual data collection process. The questionnaire was tested on 5% of the total sample to ensure clarity of the questions. Closely, the filled questionnaires were reviewed before an interview. The principal investigator was controlling the data collection with a close supervision, honest communication and on spot decision in the data collection phase was implemented.

4.11 Data Collection

Data collection and patient consent was done by a data collector and the principal investigator who are undertaking the research. The data was collected from the three hospitals of Addis Ababa University: TASH, ZMH and GMH at the respective postnatal, labor, maternity and gynecology (those admitted for termination) wards of obstetric department after delivery/expulsion and before discharge. Patient consent was taken from the study participants. A separate paper was prepared together with the questionnaire for participants consent. The research assistants (data collectors) were read and inform the study participants about and obtain a written consent from them.

The calculated sample size was proportionally allocated to the hospitals on the basis of the number of deliveries for the past 6 months based on data from perinatal reports of the respective

hospitals. Based on this, ZMH shares 32% which is about 106, TASH shares 23.4% which is about 77, and GMH shares 44.6% of the sample size which is near to 147 making a total of 330). On the basis of this proportional allocation of samples were made for each facility. Then study participants were selected using simple random sampling method. Participants were selected as long as the eligibility criteria are met.

Diagram below shows how sample is proportionally allocated to the hospitals on the basis of the number of deliveries for the past 6 months based on data from perinatal reports of the respective hospitals.

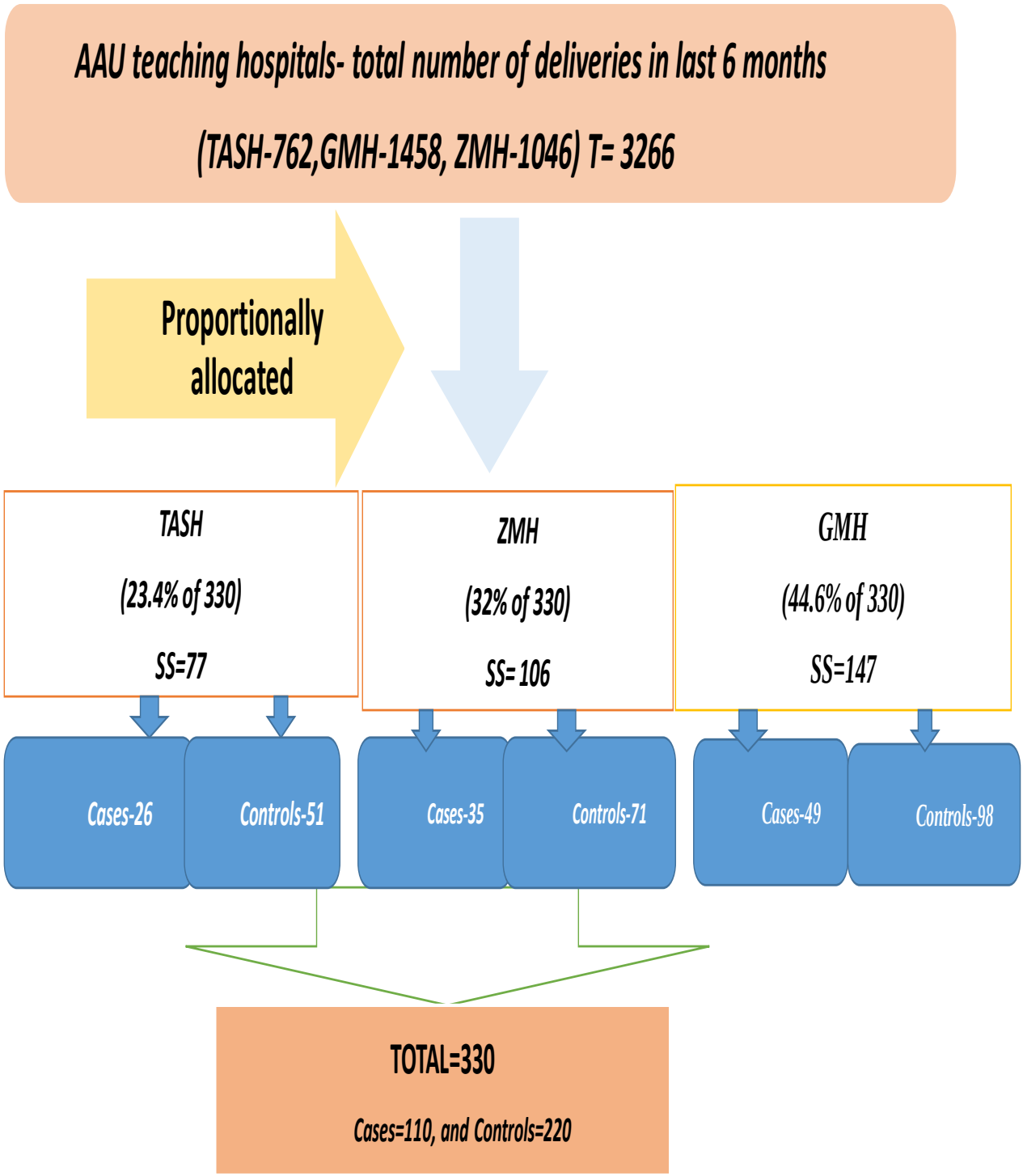


Figure 2: sample is proportionally allocated to the hospitals on the basis of the number of deliveries

4.12 Data Management

Data was managed with privacy and protection. The structured questionnaire was stored in a locked box and a locked room. The SPSS was stored in a password protected computer. The file was backed up in two hard disks with password protection. Patient privacy was protected with maximal effort.

4.13 Data Processing and Analysis

Collected data was crosschecked for completeness and was entered to SPSS (Statistical Package for Social Science) version 25 for data management and further analysis. Frequency counts were performed to assess completeness of all variables. Correlates of preeclampsia with MAP were assessed by linear logistic regression. From these models, a crude and adjusted odds ratio along with 95% confidence intervals, separately for each case and control was done.

4.14 Operational Definitions

Preeclampsia: it is based on the current guidelines of the National High Blood Pressure Education Program (NHBPEP) Working Group on High Blood Pressure in Pregnancy, which define preeclampsia as: sustained blood pressure of ≥140/90 mm Hg, with readings performed ≥6h apart; and urine protein concentration of ≥300 mg/dL or ≥+2 urine dipstick or 1+ on a urine dipstick on ≥2 urine specimens collected≥4 h apart. Urine dipsticks were routinely used to measure proteinuria in this setting (33).

Additionally, (3) BP as defined above and 24 hour urine protein greater or equal to 300mg; (4) if there is at least one record of blood pressure measurement of greater or equal to 160/110 mm HG, (5) if patient is managed as PE case.

4.16 Ethical Considerations

The proposal was evaluated by my advisors for feedback and approval before conducting the study then ethical approval was requested from obstetrics and gynecology research and community service ethical review committee. Formal letter of permission was obtained from

Addis Ababa University and Addis Ababa city Health Bureau and Official letter of cooperation from the above organization was given to TASH, GMH and ZMH. The importance of the study was explained to the participants of the study. For this a one-page informed consent letter was attached to the cover page of each questionnaire.

The details of the study was explained to study participants. Participation was voluntary. The right of the respondent to withdraw from the interview or not to participate was respected. The information collected from the study subjects were kept confidential and used only for the study and management of the patient.

4.17 Dissemination plan and use of findings

The result of the study will be submitted to TASH, department of obstetrics and gynecology, AAU. The final report will submitted to TASH, GMH & ZMH. Further efforts will be done to publish the findings of the study through journals and scientific publications.

5. Result

5.1 Sociodemographic characteristics of the study participants

Majority of the study participants were in the age group of 25-29 years (27.3% cases and 44.1% control) with mean and SD of 27.48±5.22 respectively. All of the participants were from urban area and 98.5% (98.3% case & 99.1% control) of the participants were married. Thirty six

percent (27.3% case & 40.9% control) were an education level of secondary and 63.9% (60.9% cases & 65.5% control) had a house hold monthly income of 5000-10000ETB. Age of the study participants were a statistically significant factor for preeclampsia by chi-square test.

Table 1. The sociodemographic characteristics of the study participants who delivered at three teaching hospitals in AA, Ethiopia

Variable	Cases (%)	Control (%)	Total (%)	p-value
Age of the participants				
18-24	31(28.2)	69(31.4)	100(30.3)	
25-29	30(27.3)	97(44.1)	127(38.5)	0.001
30-34	31(28.2)	38(17.3)	69(20.9)	
≥35	18(16.4)	16(7.3)	34(10.3)	
Residency				
Urban	110(100)	220(100)	330(100)	
Marital status				
Married	107(97.3)	218(99.1)	325(98.5)	0.202
Unmarried	3(2.7)	2(0.9)	5(1.5)	
Education level				
Illiterate	7(6.4)	7(3.2)	14(4.2)	
Primary	41(37.3)	66(30)	107(32.4)	0.073
Secondary	30(27.3)	90(40.9)	120(36.4)	
collage and above	32(29.1)	57(25.9)	89(27)	
Household monthly income				
<5000	32(29.1)	53(24.1)	85(25.8)	
5000-10000	67(60.9)	144(65.5)	211(63.9)	0.618
>10000	11(10)	23(10.5)	34(10.3)	

5.2 Obstetric related characteristics of the study participants

Forty-four percent of the study participants (44.5% case and 44.1% control) were nulliparous with 27% (26.4% case & 27.3% control) had a history of abortion. Almost twenty-eight percent (62.3% case and 10.7% control) of the participants had history of preeclampsia. Ninety-eight percent of the participants had singleton gestation and all of the participants had spontaneous conception. The finding also showed that history of preeclampsia and duration of interpregnancy interval were statistically significant factors for preeclampsia.

Table 2. Obstetric related characteristics of the study participants

Variable	Cases (%)	Control (%)	Total (%)	p-value
Parity				

Nulliparous	49(44.5)	97(44.1)	146(44.2)	
Primiparous	13(11.8)	36(16.4)	49(14.8)	0.115
Multiparous	44(40)	86(39.1)	130(39.4)	
Grand multiparous	4(3.6)	1(0.5)	5(1.5)	
History of abortion				
Yes	29(26.4)	60(27.3)	89(27)	0.861
No	81(73.6)	160(72.7)	241(73)	
History of preeclampsia(n=183)				
Yes	38(62.3)	13(5.9)	51(27.9)	0.000
No	23(37.7)	109(49.5)	132(72.1)	
Interpregnancy interval in years				
<1	0(0)	11(5)	11(3.3)	
1-5	46(41.8)	101(45.9)	147(44.5)	0.005
6-10	15(13.6)	11(5)	26(7.9)	
Type of current gestation				
Single	108(98.2)	216(98.2)	324(98.2)	
Twin	2(1.8)	4(1.8)	6(1.8)	1.000
Method of conception				
Spontaneously	110(100)	220(100)	330(100)	

5.3 Health related characteristics of the study participants

Forty-nine percent (55.5% case & 46.4% control) had been done physical activity frequently and 7% of the participants (10% case and 5.5% control) had a family history of preeclampsia. Almost forty-percent (42.7% case & 38.2% control) of the participants had O blood group and 7.3% (3.6% case and 9.1% control) had negative blood group antigen. Sixty-two percent of the participants (60% case & 63.6% control) had normal body mass index and 80.3% of the participants (78.2% of case and 81.4% of control) had drunken coffee.

Table 3. Health related characteristics of the study participants

Variable	Cases (%)	Control (%)	Total (%)	p-value
Physical activity in pregnancy				
very frequently	61(55.5)	102(46.4)	163(49.4)	
Frequently	23(20.9)	85(38.6)	108(32.7)	0.000
Occasionally	17(15.5)	33(15)	50(15.2)	

Non	9(8.2)	0	9(2.7)	
Family history of hypertension				
Yes	10(9.1)	26(11.8)	36(10.9)	0.454
No	100(90.9)	194(88.2)	294(89.1)	
Types of family				
AUNT	0	1(3.8)	1(2.8)	
Father	0	9(34.6)	9(25)	0.129
Mother	9(90)	16(61.5)	25(69.4)	
Sister	1(10)	0	1(2.8)	
Family history of preeclampsia				
Yes	11(10)	12(5.5)	23(7)	0.126
No	99(90)	208(94.5)	307(93)	
Types of family having preeclampsia				
Aunt	0	2(16.7)	2(8.7)	
Mother	3(27.3)	2(16.7)	5(21.7)	0.282
Sister	4(36.4	5(41.6)	9(39.1)	
sister and mother	4(36.3	3(25	7(30.4)	
Took any medication during pregnancy				
Yes	77(70)	132(60)	209(63.3)	0.076
No	33(30)	88(40)	1219(36.7)	
Blood group				
A	42(38.2)	77(35)	119(36.1)	
B	16(14.5)	45(20.5)	61(18.5)	0.495
AB	5(4.5)	14(6.4)	19(5.8)	
O	47(42.7)	84(38.2)	131(39.7)	
RH iso immunization				
Negative	4(3.6)	20(9.1)	24(7.3)	0.072
Positive	106(96.4)	200(90.9)	306(92.7)	
DM				
Yes	4(3.6)	7(3.2)	11(3.3)	0.828
No	106(96.4)	213(96.8)	319(96.7)	
Body mass index				
Underweight	7(6.4)	16(7.3)	23(7)	
normal weight	66(60)	140(63.6)	206(62.4)	0.853
Overweight	29(26.4)	49(22.3)	78(23.6)	
Obese	8(7.3)	15(6.8)	23(7)	
Drink coffee				
Yes	86(78.2)	179(81.4)	265(80.3)	0.493
No	24(21.8)	41(18.6)	65(19.7)	
Drink alcohol				
Yes	22(20)	46(20.9)	68(20.6)	0.847
No	88(80)	174(79.1)	262(79.4)	

5.4 The related characteristics of the cases

Majority (44.5%) of the cases were diagnosed at term pregnancy and 62.7% of the cases were delivered at term. Almost fifty three percent and forty seven percent of the participants had ≥160 and ≥100 systolic and diastolic blood pressure respectively. Thirty-nine percent of the study participants had +2 urine protein.

Table 4. The preeclampsia related characteristics of the study participants having preeclampsia

Variable	frequency	Percent
Gestational age of preeclampsia diagnosis		
<34	31	28.2
34-36^{+6}	30	27.3
≥37	49	44.5
Gestational age at delivery		
<34	13	11.8
34-36^{+6}	28	25.5
≥37	69	62.7
Systolic blood pressure		
<160	52	47.3
≥160	58	52.7
Diastolic blood pressure		
<100	58	52.7
≥100	52	47.3
Urine protein		
Negative	23	20.9
+1	16	14.5
+2	43	39.1
+3	28	25.5
Other preeclampsia diagnostic criterias		
Cerebral symptoms	24	21.8
Eclampsia	2	1.8
HEELP syndrome	6	5.4

5.5 The determinant factors for the prediction of preeclampsia

In this study age, history of previous preeclampsia, early pregnancy MAP has an association with the preeclampsia. The multivariate logistic regression revealed that study participant whose age of >=35 years had 14.6 times increased chance of having preeclampsia compared to those of age

18-24 years (AOR=14.6, 95%CI=2.30, 93.26) and study participants having a history of preeclampsia had 23.2 folds increase risk of recurrent preeclampsia compared to those not having previous history (AOR=23.2, 95%CI=7.53, 71.22). Study participant whose mean arterial pressure of ≥90 were 3.1 times increase its preeclampsia compared to those of having MAP<90 (AOR=3.1, 95%CI=1.26, 7.39).

Table 5. The bivariate and multivariate logistic regression of association between preeclampsia and independent variable among women who gave birth in the three teaching hospitals of AAU.

Variable	Preeclampsia-cases	Normotensive-controls	p-value		p-value	
Age in years						
18-24	31(28.2)	69(31.4)	1		1	
25-29	30(27.3)	97(44.1)	0.214	0.69(0.38, 1.24)	0.110	11.1(0.78, 19.29)
30-34	31(28.2)	38(17.3)	0.066	1.8(0.96, 3.43)	0.421	4.2(1.64, 28.28
≥35	18(16.4)	16(7.3)	0.024	2.5(1.13, 5.55)	0.004	**14.6(2.30, 93.26)**
Parity						
Nulliparous	49(44.5)	97(44.1)	1		1	
Primiparous	13(11.8)	36(16.4)	0.362	0.72(0.35, 1.47)	0.211	0.49(0.17, 1.49)
Multiparous	44(40)	86(39.1)	0.960	1.0(0.61, 1.67)	0.142	6.6(0.53, 80.58)
Grand multiparous	4(3.6)	1(0.5)	0.067	7.9(0.86, 72.77)	0.061	2.4(0.14, 12.36)
History of preeclampsia						
Yes	38(62.3)	13(10.7)	0.000	13.8(6.39, 30.03)	0.000	**23.2(7.53, 71.22)**
No	23(37.7)	109(89.3)	1		1	
Family history of preeclampsia						
Yes	11(10)	12(5.5)	0.132	1.9(0.82,4.72)	0.539	1.8(2.88, 10.83)
No	99(90)	208(94.5)	1		1	
Early pregnancy MAP						
≥90	57(51.8)	47 (21.4)	0.000	3.9(2.42, 6.gryi49)	0.014	**3.1(1.26, 7.39)**
<90	53(48.2%)	173(78.6)	1		1	

5.6 The prediction of preeclampsia by early pregnancy means arterial pressure

The mean MAP of the case was 88.36, while the mean MAP of the control was 83.81. The maximum MAP of the cases was 105, while the maximum MAP of the control group was 100. The minimum MAP of the cases was 70, while the minimum MAP of the controls was 60.

Report of mean arterial pressure						
Predicting variable	Mean	Std. Deviation	Median	Minimum	Maximum	N
Preeclampsia	88.3648	6.63289	90.0000	70.00	105.00	110
Control	83.8195	6.68280	83.3000	60.00	100.00	220
Total	85.3346	6.99349	85.0000	41.00	105.00	330

5.7 The prediction of preeclampsia by early pregnancy means arterial pressure, SBP, DBP and MAP

The area under curve (AUC) for MAP=0.698, 95% CI=0.637, 0.759), for early pregnancy SBP=0.691, 95% CI=0.629, 0.753) and for early pregnancy DBP=0.647, 95%CI=0.585, 0.709). A MAP cut off of ≥90 mm Hg was taken as cutting point (from a study done by Dr Upadhyay Anupama, Lecturer Obstetrics and Gynecology, India (Upadhyay-2019)) and the estimated sensitivity (true positive) of 51.8%, specificity (true negative) of 78.6%, positive predictive value of 54.8% and negative predictive value of 76.5%.

Table 6. The test result of area of prediction on SBP, DBP and MAP for preeclampsia.

Area Under the Curve					
Test Result Variable(s)	AUC	Std. Error [a]	Asymptotic Sig. [b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Early pregnancy SBP	.691	.032	.000	.629	.753
Early pregnancy DBP	.647	.031	.000	.585	.709
MAP	.698	.031	.000	.637	.759
The test result variable(s): Early pregnancy SBP, Early pregnancy DBP, MAP has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.					
a. Under the nonparametric assumption					
b. Null hypothesis: true area = 0.5					

Table 7: MAP

Area Under the Curve				
Test Result Variable(s): MAP				
Area	Std. Error	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound

.694	.031	.000	.633	.755

Table 8.The sensitivity and specificity of the mean arterial pressure for predicting of preeclampsia.

Diagnosis test		Truth		Total
		Preeclampsia	Normotensive	
MAP	≥90	57(51.8%) (a)	47 (21.4%) (b)	104
	<90	53 (48.2%) (c)	173(78.6%) (d)	226
Total		110(100%)	220 (100%)	330

- Sensitivity (true positive)=a/a+c x100=51.8%
- Specificity (true negative) =d/b+d x100=78.6%
- False negative (type 1error) =48.2%
- False positive (type 2 error) =21.4%

Table 9. The PPV and NPV of mean arterial pressure to predict preeclampsia.

Diagnosis test		Truth		Total
		Preeclampsia	Normotensive	
MAP	≥90	57(54.8%) (a)	47 (45.2%) (b)	104 (100%)
	<90	53(23.5%) (c)	173(76.5%) (d)	226(100%)
Total		110(33.3%)	220 (66.7%)	330(100%)

- PPV=a/a+b x100=54.8%
- NPV=d/c+d x100=76.5%

6. Discussion

This study found that study participant whose age of >=35 years had 14.6 times increased risk of preeclampsia compared to those of age 18-24 years (AOR=14.6, 95%CI=2.30, 93.26). This finding was in line with the study done Rocha et al (30). This may be due to genetic and epigenetic changes associated with aging that affect the body's response to pregnancy and increase the risk of pre-eclampsia. Aging is associated with increased oxidative stress and

inflammation, which can contribute to endothelial dysfunction (damage to the lining of blood vessels) and increase the risk of pre-eclampsia.

The study participants having a history of preeclampsia had 23.2 folds increased risk of recurrent preeclampsia compared to its compartment (AOR=23.2%, 95%CI=7.53, 71.22). The finding was supported by the study done in Asin Women (27). This could be due to Pre-eclampsia involves endothelial dysfunction (damage to the lining of blood vessels). Women who have had pre-eclampsia may have lingering endothelial dysfunction or a predisposition to such dysfunction, making them more susceptible to developing the condition again. On the other hand, pre-eclampsia has a genetic component. Women who have had pre-eclampsia before may carry genetic markers that increase their risk of developing the condition again. Additionally, a family history of pre-eclampsia (e.g., mothers or sisters who had the condition) can further increase this risk.

Study participant whose mean arterial pressure of ≥90 were 3.1 times has increased risk of having preeclampsia later compared to those of having MAP<90 (AOR=3.1, 95%CI=1.26, 7.39). The finding is in line with the study done by Dahiana Gallo et al (25). This may be due to elevated MAP can suggest that the placenta is not receiving adequate blood flow early in pregnancy. Poor perfusion can lead to placental ischemia (insufficient blood supply), which triggers the release of factors that cause widespread endothelial damage, inflammation, and, characteristic of pre-eclampsia.

The research also showed that the prediction of area under the curve (AUC) for MAP=0.698, 95% CI=0.637, 0.759). This finding is in line with the study done by Dahiana Gallo et al, Leona C.Y. et al and Verma MK, Kapoor P et al (25, 28, 29). For early pregnancy SBP=0.691, 95% CI=0.629, 0.753) and for early pregnancy DBP=0.647, 95%CI=0.585, 0.709). The finding is in line with the study done by Dahiana Gallo et al (25). This similarity may be due to the similarity of biomarkers and risk factors for predicting pre-eclampsia, such as blood pressure, proteinuria, placental growth factor. These standardized markers lead to similar predictive performance across different populations and studies. The other reason may be due to the diagnostic criteria for pre-eclampsia are generally consistent across studies, as they follow guidelines from organizations like the American College of Obstetricians and Gynecologists (ACOG) and the World Health Organization (WHO). This consistency ensures that studies are predicting the same condition, leading to similar predictive accuracy.

A MAP cutoff of ≥90 mm Hg taken as the reference of cutting point from a study done by Dr Upadhyay Anupama, Lecturer Obstetrics and Gynecology, India (Upadhyay-2019) and the estimated sensitivity (true positive) of 51.8%. This finding was lower than the study done by Dahiana Gallo et al (78%) (25). the specificity (true negative) of 78.6%. This finding was higher than the study done by Dahiana Gallo et al (63%) (25). the positive predictive value of 54.8%. This finding was higher than the study done by Dahiana Gallo et al (6%) (25). The negative predictive value of 76.5%. This finding was lower than the study done by Dahiana Gallo et al (99%) (25). This different level of predication was due variations in the age, ethnicity, and socioeconomic status of study populations which can affect the prevalence and risk factors of pre-eclampsia, difference in the risk factor of preeclampsia like diabetes, obesity, and other health conditions can impact the sensitivity and specificity of MAP as a predictor. Differences in the equipment used and the protocols followed for measuring MAP can affect the accuracy and consistency of the measurements. different definitions or criteria for diagnosing pre-eclampsia, affecting the sensitivity, specificity, PPV, and NPV. Different studies may use different MAP cut-off values to define high risk, which can impact sensitivity and specificity.

Limitation of the Study

The study is not prospective study and simply the early pregnancy mean arterial pressure is calculated from the chart and that might be question of its measurement accuracy.

7. Conclusion and Recommendations

7.1 Conclusion

In this study age, history of previous preeclampsia, early pregnancy MAP has an association with the preeclampsia by bivariate logistic regression.

Majorities (44.5%) of the cases were diagnosed at term pregnancy and 62.7% of the cases were delivered at term.

The mean MAP of the case was 88.36, while the mean MAP of the control was 83.81. The maximum MAP of the cases was 105, while the maximum MAP of the control group was 100. The minimum MAP of the cases was 70, while the minimum MAP of the controls was 60.

In this study the prediction of preeclampsia using MAP by AUC and ROC MAP=0.698, 95% CI=0.637, 0.759), for early pregnancy SBP=0.691, 95%CI=0.629, 0.753) and for early pregnancy DBP=0.647, 95%CI=0.585, 0.709). The sensitivity (true positive) of MAP was 51.8%, specificity (true negative) of MAP was 78.6%, positive predictive value of MAP was 54.8% and negative predictive value of MAP was 76.5%.

Other determinates of preeclampsia were study participant whose age of ≥35 years compared to those of age 18-24 years, having a history of preeclampsia and mean arterial pressure of ≥90 .

7.2 Recommendations

Given the moderate predictive performance of MAP, SBP, and DBP in early pregnancy, these measures should be routinely monitored and used as part of a comprehensive preeclampsia screening strategy. Can use as a components of the early screening and can also be used alone in resources limited areas that doesn't get the access to biomarkers.

Healthcare providers should carefully assess other known risk factors for preeclampsia, such as maternal age, history of previous preeclampsia, and elevated mean arterial pressure.

The study findings suggest that a combination of clinical factors, including blood pressure measurements and other risk factors, should be used to assess a woman's overall risk of developing preeclampsia.

Further comprehensive followup (cohort) study that includes MAP, maternal characteristics, laboratory and imaging parameters is recommended.

By implementing these recommendations, healthcare providers can enhance their ability to identify women at risk of preeclampsia, facilitate timely interventions, and ultimately improve maternal and fetal outcomes.

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Annexes

Study instruments and tools

Informed Consent:

Dear Sear/madam;

Hello, my name is _____. I am working as a data collector for the study being conducted in this hospital by Dr. Masreshaw Bogale who is studying for specialty in Obstetrics and Gynecology at Addis Ababa University, College of Health Sciences. I kindly request you to give me your attention to explain about the study and about you being selected as the study participant.

The Study Title: Early pregnancy mean arterial pressure and maternal risk factors for prediction of preeclampsia among women who delivered at three teaching hospitals in AA, Ethiopia.

Purpose of the Study: The findings of this study will have a very importance for pregnant women to have better screening methods such as early pregnancy mean arterial pressure and other maternal characteristics so that we can prevent preeclampsia and its complications using this study as a base line study for further researches. Moreover, the aim of this study is to write a research paper as a partial requirement for the fulfillment of a specialty program of obstetrics and gynecology for the principal investigator.

Procedure and Duration: you will be interview using standard questionnaire. I will not take more than 40 minutes of your time.

Risks and Benefits: The risk of being participated in this study has minimal risk, but only taking about 40 minutes from your time. There would not be any direct payment for participating in this study and your input (the data you will give as based on questions on this questionnaire and your early pregnancy BP measurement documented in your clinical record) significant contribution for the success of the study.

Confidentiality: The information that you will provide will be kept secret. No information from you gave us will identify you. The results of the study will be general for the study population and will not reflect anything particular of individual person. The questionnaire will exclude

showing names. There will not be made in oral or written reports that could link participants to the research. You have full right to refuse to take part or to interrupt at any time.

Are you willing to participate in the study? 1- Yes …….(if yes, continue the interview)

2-No……Thank you (skip to the other participants)

Name of Enumerator _____ Signature _____

Questionnaire Code_____

Name of the supervisor _____Signature _____

Questionnaire

Part I. Sociodemographic characteristics of the study participants

1. Age of the study participants in year_____
2. Residence

I. Urban

II. Rural

3. Marital status

I. Married

II. Not in marriage (divorced, widowed, single)

4. Education

I. Illiterate

II. Primary

III. Secondary

IV. Collage and above

5. Monthly household income in birr_____

Part II. Obstetric characteristics of the study participants

6. Parity

I. Nulliparous

II. Primiparous

III. Multiparous

IV. Grand multiparous

7. History of abortion

I. Yes

II. No

8. History of preeclampsia

I. Yes…(if yes GA at delivery/expulsion…you can mention month of amenorrhea)

II. No

9. Interpregnancy interval in years between the birth of the last Child

I. <1

II. 1-5

III. 6-10

IV. >10

10. Type of gestation

I. Singleton

II. Twin

III. Other high order gestation

11. Method of conception:

I. spontaneous,

II. ovulation induction,

III. invitro fertilization

Part III. Health related characteristics of the study participants

1. Physical activity in pregnancy

I. Very frequently

II. Frequently

III. Occasionally

IV. No

2. Family history of hypertension

I. Yes (mother, father, other----------specify)

II. No

3. Family history of PE

I. Yes (sister, mother, other----------specify)

II. No

4. Took any medication during pregnancy

I. Yes

II. No

5. If yes specify the types of medication _____

6. Blood Group_____

7. DM

I. Yes…(if yes how is the control….good or poor)

II. No

8. Pre-pregnancy weight in Kg_____
9. Current weight in kg_____
10. BMI----------

Part IV. Substance utilization characteristics

11. Drink coffee

I. Yes
II. No

12. Smoking

I. No
II. Yes (cigarette, cocaine…….specify, during pregnancy, before pregnancy……..specify)

13. Alcohol drinker

I. Yes
II. No

Part V. Characteristics of the blood pressure

14. Early pregnancy blood pressure_____
15. Specify the gestational age at which the early blood pressure measured_____
16. MAP_____ (NB; MAP=$\frac{2DBP+SBP}{}$)

For cases only

1. Currently diagnosis preeclampsia
   I. Yes
   II. No
2. Gestational age when preeclampsia diagnosed_____
3. Gestational age at delivery_____
4. The blood pressure level of the case_____
5. Urine protein concentration dipstick_____
6. Other diagnostic criteria (HELLP, cerebral symptoms,……..specify)

17. For control

1. Current blood pressure
2. The nearest urine protein result (if determined)
3. Gestational age during data collection (after delivery/expulsion before discharge)