Past hormonal contraceptive use and pre-eclampsia among pregnant women in Northwest Ethiopia: a case- control study

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September 11, 2020

Abstract

Objective To determine the association between past hormonal contraceptive use and preeclampsia among pregnant women in public hospitals. Design A case-control study was conducted in the selected public hospitals in Northwest Ethiopia. Setting Public hospitals in Northwest Ethiopia. Sample One hundred ten cases and two hundred twenty controls were selected consecutively in the selected public hospitals. Women who had preeclampsia during diagnosis were considered as cases and women with the absence of preeclampsia were controls. Methods The data was obtained through reviewing women's record, taking measurements and face to face interview using structured interviewer administrator questionnaire. Then the data was entered into EPI info and transferred to STATA version 14 for statistical analysis. Frequency distributions, percentages and multivariate logistic regression were done to assess the association between past hormonal contraceptive use and preeclampsia. Main outcome measures Odds ratios with 95% confidence intervals of pre-eclampsia in pregnancies among women with a history of hormonal contraceptive use, compared with women without a history of hormonal contraceptive use. Results There was no significant association between past hormonal contraceptive use prior to current pregnancy and preeclampsia except implant. Women who used before current pregnancy were less likely to develop preeclampsia (AOR=0.39, 95%CI: (0.13-0.96)). No association was observed between preeclampsia and other hormonal contraceptives (pills, injectables and intrauterine contraceptive devices). Conclusions This stud revealed that there was no significant association between past hormonal contraceptive use and preeclampsia except implant which was negatively associated with preeclampsia. Key words Hormonal contraceptive use, preeclampsia, pregnancy

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Tweetable abstract A case-control study of pregnancy in Ethiopia revealed the absence of association between past hormonal contraceptive use and preeclampsia except implant.

Funding

There was no any funding for this research work.

Introduction

Preeclampsia is one of the pregnancy complications which occur after 20 weeks of gestation, at delivery and post-natal period. Preeclampsia is defined as associated with new-onset hypertension (systolic [?] 140 mmHg and diastolic [?] 90 mmHg) in two or more consecutive occasions at least 4 hours apart in the second half of pregnancy, which occurs most often after 20 weeks of gestation and frequently near term. Although often accompanied by new-onset proteinuria, hypertension and other signs or symptoms of preeclampsia may present in some women in the absence of proteinuria.[1,2]

The impact of the disease is more severe in developing countries, where unlike other more prevalent causes of maternal mortality, medical interventions may be ineffective due to late presentation of cases.[3] The overall prevalence of preeclampsia in Ethiopia accounts about 51.9%.[4]

Several risk factors have been established for the occurrence of preeclampsia including maternal contraception prior to pregnancy, previously existing hypertension, primigravida, previous history of preeclampsia, preexisting diabetes, multiple (twin) pregnancy, nulliparity, family history. [5,6]

Hormonal contraceptives are the most widely used method of birth control in the world.[7] The overall contraceptive prevalence rate among all women in Ethiopia was 29 %. The most commonly used hormonal contraceptive method in Ethiopia was injectable. In Amhara region about 49.1% women used any method, 48% women used any modern method and hormonal contraceptives were 47.8% (1.3% pills, 0.2% intrauterine contraceptive device (IUCD), 38.6% injectable and 7.7% implants).[8]

A study conducted in the previous did not find any association between contraception and preeclampsia.[9] No observed association was existed between past hormonal contraception use and preeclampsia.

A study conducted in England showed that mean diastolic and systolic blood pressure measurements were significantly higher among oral contraceptive users than among non-users [13] which was the opposite of other study.[14] On the other hand, recent use of oral contraceptives was associated with a reduced risk for developing preeclampsia. In contrast, there was a suggestion that recent use was associated with an increased risk of developing preeclampsia, but only among women who had used these agents for [?]8 years.[15]

A study in Indonesia showed that use of hormonal contraception was a risk factor for preeclampsia[16].Similarly, a study conducted in China showed that oral contraceptive use before pregnancy had higher risk for preeclampsia development than IUCD users but the effect of Norplant implants was insignificant. [17] A study done in Great Britain showed that Intrauterine device use is associated with a small reduction risk of preeclampsia, particularity if removed within the year prior to conception but no correlation between IUCD use and preeclampsia among parous women.[11]

A population based study in Korean women showed that the existence of positively association on longer duration of oral contraceptive (OC) use blood pressure.[10] In other hand, a case-control study conducted in Unite States reveled that prior IUCD use was associated with a reduced risk of preeclampsia.[11] In addition to this no association was between duration of hormonal contraception use and high blood pressure. [12]

Since preeclampsia is a multisystem disorder that can progress rapidly, it requires prompt intervention which includes observation in a tertiary care setting and induction of delivery, which is the only known cure for this condition.[18]

Maternal deaths due to preeclampsia showed an increasing trend in Ethiopia. However, majority of deaths due to preeclampsia and eclampsia are avoidable through the provision of timely and effective care to the women presenting with these complications. Scientific evidence based health care to prevent and treat women with these hypertensive disorders is a necessary step towards achieving sustainable development goals.

Studies of contraceptive use were focused in relation to pregnancy induced hypertension (PIH), yet little attention has been given to specific type of PIH.[19] It is not also clear about the effect of commonly used hormonal contraceptives on blood pressure during pregnancy. Based on our knowledge, there is no study is done in Ethiopia on the association of contraceptive use and preeclampsia. Therefore, the aim of this study was to assess the associate of hormonal contraceptive use and preeclampsia among pregnant women.

Materials and Methods

Study Area and Period

The study was conducted in four public Hospitals of Northwest Ethiopia from February to April,2018. These public hospitals have high patient flow and provided service in outpatient department, emergency department, gynecology and obstetrics ward, medical ward and pediatrics ward.

Study Design

Institution based unmatched case control study was done among pregnant women attending antenatal care and who were admitted for delivery in obstetrics and gynecology departments.

Population

The source populations were all pregnant women who attend antenatal care (ANC) or delivery service in Northwest Ethiopia. The study populations were pregnant women who came for ANC or delivery in the selected hospitals during the study period

Definition of cases and controls

Cases are all pregnant women with new onset of hypertension [?] 140/90mmHg at least 4 hours apart and their proteinuria [?]300mg per 24 hours urine collection or dipstick test reading [?] 1+ after 20 weeks of gestation.[1,2]

Controls are pregnant women whose blood pressure is less than 140/90 mmHg and proteinuria $<$ 300mg/24 hours or $<$ 1+ in urine dipstick test after 20 weeks of gestation in the same hospital. Cases were diagnosed and confirmed by obstetrics and gynecology physicians.

Exclusion criteria

Pregnant women who had known Hypertension (HTN), eclampsia, pre-existing renal disease and seriously ill were excluded through women's record review. Pregnant women who had known HTN, eclampsia, pre-existing renal disease and were seriously ill were excluded.

Sample size Determination

The sample size was calculated by using Open Epi version 2.3. statistical software and the formula of two population differences by assuming the case to control ratio 1: 2 with significant level 95%, power 80% and 2.00 minimum detected odds ratio. There is no previous study was done in Ethiopia about the association between past hormonal contraceptive use and preeclampsia. Therefore, the proportion of contraceptive use among controls is taken in the general population from 2014 Ethiopian Demography and Health Survey data in Amhara Region.[8] Based on the above mentioned assumptions and adding 10 percent non-response rate, totally 330 study participants were involved in the study.

Sampling procedures

The four Hospitals were selected purposively due to their high patient flow rate among other hospitals. Cases and controls were identified by physicians' diagnosis during the study period in antenatal care clinic, obstetrics and gynecology wards in these4 hospitals. The diagnosis included history taking, clinical manifestations, physical examination and laboratory tests.

Due to the rare nature of the cases, they were selected consecutively after they are diagnosed and confirmed to have preeclampsia. Then the next immediate two corresponding controls were selected in the same way of cases in similar antenatal and labour rooms.

Data Collection Procedures

A questionnaire was prepared by reviewing similar articles with this objective and Demography and Heath Survey document. The questionnaire was designed in English language. Then it was converted into Amharic language and translated back to English language to check its consistency.

Then the data was collected by face to face interview by using interviewer administrative structured questionnaire, through women's record review and some measurements. The measurements included blood pressure, weight, height and urine of the women. They were interviewed about their sociodemographic characteristics, medical history, obstetric factors and behavioral factors by trained and experienced health professionals immediately before and/or after ANC and delivery services.

Blood pressure was measured while the women seated in the upright position using a mercury sphygmomanometer apparatus. Before taking the measurement, the participants were allowed to take rest for 5 minutes. The measurement was taken from participant's right hand which covers two-thirds of the upper arm. Standard mercury sphygmomanometer was used throughout the study to minimize measurement error.

Data regarding proteinuria and other clinical data was taken from the women's medical records or midstream urine sample was taken for each case and control if no previous records.

Data Quality Assurance

Eight midwiferies who have experience on data collection in similar studies were recruited as data collectors. Training was given for data collectors and supervisors about two days before data collection. A clear explanation about the purpose of the study was provided for the respondents at the beginning of the interview. A pretest was conducted in Lumame Primary Hospital before one week of actual data collection. Then based on the result of the pretest, some modification was done on the questionnaire. Close supervision was done by the principal investigator and supervisors. The data from each respondent was checked for its completeness, clarity, consistency and accuracy by the data collectors and principal investigator.

Statistical Analysis

After data collection the data was checked, coded and entered into EPI-info version7 software. Then the data was transformed to STATA version 14 for statistical analysis. Descriptive analysis like frequency distribution, percentages, mean and standard deviation (SD) were performed. Bivariate and multivariate logistic regression were done to identify the association between preeclampsia and each variable. Those variables with p-value less than 0.05 in multivariable logistic regression analysis were considered as statically significant factors for preeclampsia. The crude and adjusted OR with 95% CI were presented using texts and tables.

Ethical Approval and Consent

Ethical approval was obtained from Addis Ababa University, College of Health Science, School of Public Health, Institutional Review Board. A written letter was given for each hospital from the School of Public Health. An informed consent was obtained from each respondent. Confidentiality and privacy of the respondents' responses were maintained.

Results

A total of three hundred thirty women were involved in this study. One hundred ten (33.3%) were cases and 220 (66.7%) were controls. The mean age of cases and controls was 28 years (28 ± 6 SD), 27 years (27±5 SD) respectively. Concerning educational status, about 65(59.1%) of cases and 105(47.7%) of controls had no formal education (Table 1).

Among women who attended ANC or delivered in Northwest Ethiopia hospitals, nearly half 48(43.6%) of cases and 71(32.3%) of controls were gravida one (Table 2).

Contraceptive use related results

About 95(86.4%) of cases and 176(80.0%) of controls were using contraceptives before their current pregnancy. In this study ma who used IUCD were very rare so that it was not analyzed i.e. 1(0.91%) cases and 1(0.45%) controls were used IUCD prior to their pregnancy.

Associated Factors of preeclampsia

From bivariate analysis, women who were using implant contraceptive before current pregnancy were 0.48 (95% CI: (1.20, 6.28)) times less likely to develop preeclampsia as compared with those who were using other hormonal contraceptive methods. The following table showed the eligible variables for multivariable analysis (Table 3).

Multivariable logistic regression analysis was done to identify the association between contraceptive use and preeclampsia after controlling the effect of confounding factors. Multiplicity of current pregnancy, using of contraceptive method before current pregnancy, prior use of oral pills, duration of OC use, injectable and implant contraceptive were entered into the final multivariable analysis model. However, using of contra-

ceptive method before current pregnancy and duration of OC use were omitted in the final model due to collinearity.

Pregnant women who had multiple pregnancies were 2.75 (95% CI: (1.20, 6.28)) times more likely to develop preeclampsia as compared with women without preeclampsia. In contrast, pregnant women who used implant contraceptive method were 0.39 (95% CI: (0.13, 0.96)) times less likely to develop preeclampsia compared with controls. There is no significant association between other contraceptives and using of duration before current pregnancy (Table 4).

Discussion

Those women who used implant contraceptive prior to current pregnancy were 0.39 times less likely to develop preeclampsia as compared with those who were using other hormonal contraceptive methods. This finding was in line with a study done in Thailand.[20]

The reason behind this effect may be due to fewer doses of the hormone, containing only progesterone hormone and adapting within the body. Since implants contain only progestin, a newer progestin, drospirenone, has antimineralocorticoid diuretic effects.[21]

However, no significant association was observed in a study conducted in China.[9, 16] This result variation may be due to the data was secondary data which may be full of errors. But the current data source was primary data sources obtained by direct measurement and face to face interview of the study participants. In addition to this there may be due to the cross sectional nature of the design, the non-specificity of the outcome variable (i.e. it was pregnancy induced hypertension) and differences in socioeconomic and lifestyles between these countries.

On the other hand, no observed association between oral and injectable contraceptives and preeclampsia. This finding was consistent with a study conducted in New York where the study included only educated women.[16]

In contrast, oral contraceptive was a risk factor for preeclampsia as a study done in Indonesia (AOR=2.5).[15] Emerging evidence from recent clinical trials indicates a small increase in systolic blood pressure with oral estrogen administration in postmenopausal women, without any detectable effect on diastolic blood pressure. Mechanisms underlying this selective rise in systolic blood pressure remain unknown, but it may be due to supraphysiologic concentration of estrogen in the liver. Intradermal insertion of estrogen, which avoids the first-pass hepatic metabolism of estradiol, seems to have a small blood pressure-lowering effect in postmenopausal women and may be a safer alternative in hypertensive women.[22]

Similarly, the effect of hormonal contraceptive was that using of high-dose estrogen results a mean elevation in blood pressure.[23] It also a function of the dose of estrogen (ethinyl estradiol), dose of the progestin and the duration of contraceptive us. [24,25] When a newer progestin is given in combination with estrogen as oral contraceptive, it increases BP due to increasing effect of estrogen.[21] This may also be due to small sample size and the result may be cofounded by passive smoking in the area.

Regarding duration of contraceptive used, no association was occurred between duration of contraceptive used and preeclampsia. But when we looked the non-significant results of COR, those women who had preeclampsia and were using oral contraceptive for 24 months or more before current pregnancy seemed 2.88 times higher the odds of those women without preeclampsia. Similarly, women who were using injectable contraceptives for [?] 24 months were 1.15 times higher the odds of those who were using less than this period. The result was consistent with a study conducted in Australia[12] but both of the findings were insignificant.

Conclusions

This study revealed the absence of significant association between past hormonal contraceptive use and preeclampsia except implants. Implant was negatively associated with preeclampsia. Women who used

contraceptives for more prolonged time before pregnancy were suggested to develop preeclampsia as compared to women who used for shorter duration.

Disclosure of interests

The authors declare that they have no competing interest.

Contribution to authorship

AWA, AWT, AA: Participated on conception, design, data collection, data analysis, interpretation of the result and drafting of the paper. AWT, GA: Participated on result, discussion, manuscript drafting and writing. AWA, ST, AA: Participated in manuscript writing, critically reviewing and approving of the manuscript. All Authors read and approved the final version of this manuscript.

Details of ethics approval

Ethics approval was obtained from Addis Ababa University, College of Health Science, School of Public Health, Institutional Review Board with a date of approval 01/02/17 and protocol number of SPH 2009/17-18.

Funding

There is no financial support for this work that could have influenced its outcomes.

Acknowledgements

We would like to acknowledge the administrative offices of the selected hospitals, study participants, data collectors and supervisors.

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