Adverse maternal outcomes of pregnancy induced hypertension among pregnant women in Tigray Regional State, Ethiopia: a prospective cohort study

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Abstract
Objective The objective of this study was to assess the effect of pregnancy-induced hypertension on adverse maternal outcomes in Tigray Regional State, Ethiopia. A prospective cohort study was conducted on a total sample of 782 pregnant women attending antenatal care in hospitals of Tigray regional state, Ethiopia. Data were collected using interviewer-administered questionnaire and review of their medical records from February 1, 2018, to February 30, 2019. Data analysis was performed using Stata version 14.0.

Results The overall adverse maternal outcome was 67.7% among women with pregnancy-induced hypertension and 25.1% among normotensive women. Specifically women with pregnancy-induced hypertension were at higher risk of developing Antepartum hemorrhage (Adjusted RR=1.4(1.1,2.5)), postpartum hemorrhage (RR=2.6(1.3,4.9)), induction of labor (RR=5.9(4.0,8.7)) and delivering by cesarean section (RR=2.1(1.6,2.8)) compared to normotensive women.

Introduction
Pregnancy induced hypertension (PIH) defined as new hypertension that appears at 20 weeks or more gestational age of pregnancy with or without proteinuria, which includes gestational hypertension, pre-eclampsia, and eclampsia (1–3). Hypertension is defined as a sustained systolic BP 140 mmHg or diastolic BP 90 mmHg based on the average of at least two measurements, using the same arm(4). World Health Organization (WHO) multi-country survey report showed that maternal near-miss cases were eight times more frequent in women with PIH compared to women without these conditions (5). Nearly 10–15% of maternal deaths are attributed to preeclampsia/eclampsia, out of which 99% occur in developing countries (6). Pregnancy induced hypertension complicates 2–8% of pregnancies in the Western world (7) however the magnitude of pregnancy induced hypertension in developing countries reaches up to 16.7% (8). Additionally, the available literature showed a high burden of PIH in Ethiopia which ranges from 2.23 to 18.25% (9–14). Even though pregnancy induced hypertension is a public health issue in the developed countries however the effect of pregnancy induced hypertension in the developing countries is staggering.

Different studies conducted across the globe on maternal outcomes of pregnancy induced
hypertension showed that pregnancy induced hypertension is associated with higher rates of morbidity and mortality such as preterm delivery, cesarean section, induction of labor and maternal death (6) (15–23). Despite of these studies, there are variations in the incidence and risk of adverse maternal outcomes of pregnancy induced hypertension across countries, populations and ethnic-geographic areas. Besides, a study conducted on hypertension during pregnancy in Ethiopia recommended further study on the adverse outcomes of PIH (24). However, yet little is known about the incidence and risk of adverse maternal outcomes of pregnancy induced hypertension in Ethiopia and specifically in Tigray Regional State. Therefore, the objective of this study was to assess effect of pregnancy induced hypertension on adverse maternal outcomes in Tigray region state, Ethiopia.

Methods

Study setting and design

A prospective cohort study was conducted in multiple hospitals of Tigray regional state. Tigray Regional State is located in the northern part of Ethiopia. The total projected population of the region was 5,396,235 in 2017. Of which 2,741,287 were females. There were 173,892 total expected pregnancies which give a pregnancy rate of 3.5%. The source population of the study was all mothers who attend antenatal care at hospitals located in Tigray from February 1/2018 to February 30, 2019. Eight hospitals namely Lemlem Carl, Mekelle, Adigrat, Adwa, Saint Marry Axum, Suhul Shire, and Kahsay Abera hospitals were included in this study. All the hospitals included in this study provides comprehensive diagnostic and management services for hypertensive disorders of pregnancy starting from the mild form of gestational hypertension to the severe forms of preeclampsia/eclampsia.

Inclusion and exclusion criteria

women with PIH and normotensive women in each antenatal care clinic of hospitals were enrolled consecutively to study by reviewing their blood pressure level and proteinuria. Pregnant mothers diagnosed with PIH during the data collection period in the selected antenatal care clinic of hospitals were included as exposed participant and women without PIH during the same period were also enrolled as a non-exposed participant. Pregnant women with chronic hypertension, critically ill women who could not give consent, women who could not respond to the interview and
those pregnant women likely to become “lost” e.g., planning to move, unwilling to return for the prospective follow up period were excluded from this study at the time of enrollment.

**Sample size determination and sampling procedure**

The sample size was calculated using Epi-info Version 7 STAT CALC (25). By considering confidence interval level of 95%, beta-level (the power level) = 80%, \( r = \) the ratio of exposed to unexposed group \( = 1:2, p_1 = \) proportion of pregnancy induced hypertension women with adverse outcome \( = 5.4\% (26), p_2 = \) proportion of normotensive women with adverse outcome \( = 1.3 \% \) (26). With the consideration of 10% loss to follow up a total of 798 study participants (266 participants with PIH and 532 participants without PIH) were finally included in this study.

From the total of fifteen public hospitals providing comprehensive maternity care in Tigray regional state, eight hospitals were selected using simple random sampling technique. The calculated sample size was proportionally allocated to selected hospitals based on the number of pregnant mothers attending antenatal care in each hospital. Cases were recruited consecutively until we get the required sample and two non-exposed participants (controls) next to diagnosed cases were selected by simple random sampling method using antenatal care registration as a frame list.

**Data collection methods and instruments**

A structured questionnaire containing information on socio-demographic data, living condition, obstetrics, and reproductive health issues, pregnancy induced hypertension, adverse maternal outcomes were used. The questionnaire was prepared by reviewing literature related topics like published works, research articles and EDHS tool and adapting to the local context to maintain validity (18, 26–36).

Overall the questionnaire of this study was initially prepared in English version and translated to the local language called Tigrigna by language expert and back converted again to English by another person to check the consistency.

Eight midwives and four MSc Nurses were involved in the data collection and supervision of the study. Three days training was provided for all data collectors and supervisors before the commencement of the actual data collection.
Women who fulfill the inclusion criteria were enrolled to study during antenatal care. All selected women were followed by data collectors from time of enrollment until the end of the postnatal period to assess adverse maternal outcomes of PIH. Data regarding adverse maternal outcomes were collected prospectively during pregnancy, within 6 hours after delivery and six weeks after childbirth. During follow up we used complete tracking information (address, phone number of participants, close friends, relatives and health extension workers working in the participant’s residence area) and maintaining periodic contact (reminders, updates) to minimize “lost to follow-up”:
The overall data collection process was coordinated and supervised by supervisors and principal investigator.

Adverse maternal outcome defined as a women having any of the following outcomes Antepartum hemorrhage, initiating labour by induction, Caesarean Section and Postpartum hemorrhage.

Data analyses methods

Data were entered and cleaned using Statistical Package for Social Sciences (SPSS) version 21.0. Descriptive statistics, frequencies and summary statistics (mean, standard deviation, and percentage) were used to describe the study population. Bivariate and multivariable analyses were also performed using STATA version 14 for analysis of adverse maternal outcomes among women with PIH. Adjusted risk ratio with 95% confidence intervals was used to evaluate the effect of pregnancy induced hypertension on maternal outcomes. P-values < 0.05 were considered as statistically significant.

Results

Socio-demographic characteristics of study participants

Overall 260(97.7%) among women with PIH and 522(98.1%) among normotensive women have completed the follow-up study. The reasons for the loss-to-follow-up were traveling to other places for assistance during pregnancy and delivery and loss of mobile address by participants and network problem makes difficult to trace the participants. Majority of the women with and without PIH were residing in urban 178(68.5%) and 435(83.3%) respectively and 58(22.3%) of women with PIH and 36(6.9%) normotensive women had no formal education. With regard to the occupation, 201(77.3%) of women with PIH and 250(47.9%) of normotensive women were unemployed. Concerning wealth
status, 138(53.3%) of women with PIH and 120(23.3%) of normotensive participants were in the lowest wealth status. (Table1)

Incidence of adverse maternal outcomes of study participants

The overall adverse maternal outcome was 67.7% among women with pregnancy induced hypertension and 25.1% among normotensive women. Specifically, 31 (11.9%) of women with PIH and 30 (5.7%) of normotensive pregnant women had Antepartum hemorrhage. Similarly, 27(10.4%) and 18 (3.4%)of women with PIH and normotensive women developed postpartum hemorrhage respectively.

Four cases (1.54%) of maternal mortality occurred among women with PIH. Hundred ten (42.3%) women with PIH and 36 (6.9%) of normotensive women initiated their labor by induction. More than one third (35.8%) of women with PIH and 16.3% normotensive pregnant women were delivered by cesarean section (C/S) (Table 2).

Risk of adverse maternal outcomes associated with pregnancy induced hypertension

The risk of Antepartum hemorrhage, induction of labor, premature initiation of labor, cesarean section delivery and postpartum hemorrhage were significantly higher among women with pregnancy induced hypertension compared to normotensive women after adjusted for maternal age, wealth status, educational status, residence and number of gravida (Table 3).

Discussion

The aim of this study was to assess the adverse maternal outcomes of pregnancy induced hypertension in Tigray regional state. Findings of this study will be used as a baseline data for program coordinators to design and implement effective strategies for the prevention and early management of adverse maternal outcomes of pregnancy induced hypertension.

The results showed a significant difference in adverse maternal outcomes among women with pregnancy induced hypertension and normotensive women. Pregnant women with PIH were at an increased risk of Antepartum hemorrhage (Adjusted RR = 1.41(1.13, 2.46)), postpartum hemorrhage (RR = 2.55(1.33, 4.87)), induction of labor (RR = 5.91(4.03, 8.66)), and cesarean section delivery (RR = 2.12(1.61, 2.78)).
About 11.9% of women with pregnancy induced hypertension suffered from Antepartum hemorrhage. This finding was similar with the study conducted in India (11%), Tanzania (15.8%), Iran (9%) and Pakistan (8%) (5, 29, 37–40) but higher than the reports from Ghana (4.3%), Benin City, Nigeria (5.8%), Turkey (7.5%), Taiwan (5.0%) (19, 21, 31, 41–43). The increased risk of Antepartum hemorrhage among women with PIH compared to normotensive pregnant women might be related with the effect of PIH on uteroplacental under perfusion or ischemia can lead to poor placentation and poor placentation can cause placental separation from the uterus causing bleeding in the mother (44, 45).

Labor was initiated by induction in 42.3% of women with PIH. This finding was in line with the study conducted in Mettu Karl Referral Hospital, Ethiopia(44.6%), Haryana India (48%) (33) (40) but lower than the study conducted in Thailand(74.2%), Kerala, India (58.5%) (23, 46). The higher risk of induction of labor might be related to the health care providers' management of initiating labor by induction to terminate the pregnancy due to the fear of the fetomaternal adverse outcome of pregnancy induced hypertension.

More than one third (35.8%) of women with PIH were delivered by cesarean section (C/S). This finding was in line with the study conducted in Iran(39.4%) and Kerala, India(29.5%) (29) (46) but lower than the study conducted in Ghana(45.7%), Tanzania (66.2%) and Taiwan (77.4%) (5) (42) (19). However, the result was higher than the previous study conducted in Ethiopia (18.0%) and India (20%) (33, 47). The risk of delivering by cesarean section was 2.12 times higher among women with PIH compared to normotensive pregnant women. The higher proportion of delivering by cesarean section might be due to the emergency delivery approach usually required to avert further maternal and perinatal complications from pregnancy induced hypertension with uncontrolled blood pressure especially when the cervix is unfavorable. However, the literature suggests that very high proportion of cesarean section rate are associated with increased morbidity such as infection, hemorrhage, and surgical complications, exceeding the risks of vaginal deliveries(48–50). Similarly, 10.4% of women with PIH developed postpartum hemorrhage (PPH). This result was consistent with the study conducted in Nanded, India (8.51%), Mettu Karl Referral Hospital, Ethiopia (7.0%) (33, 51) but higher than the
studies conducted in Pakistan (4.2%), India (1.3%) and Namibia (1%) (18, 31, 52). The increased risk of postpartum hemorrhage was worrying since both PIH and PPH are among the leading causes of maternal death in Ethiopia (53, 54).

Overall we conclude that there was higher incidences of adverse maternal outcomes among women with pregnancy induced hypertension in Tigray regional state, Ethiopia. Therefore Tigray Regional Health Bureau and district health offices should use this evidence to improve maternal health outcomes. In addition, health care providers should strengthen the prevention, early diagnosis and prompt management of pregnancy induced hypertension to reduce the incidence of adverse maternal outcomes.

Limitations
Even though it is insignificant there was loss to fellow up of study participants. In addition there might be problem in the consistent use of standard diagnosis for adverse maternal outcomes among the health care providers in the study areas.

Declarations

Ethics approval and consent to participate
Ethical approval and clearance for the study was obtain from University of Ibadan, University College Hospital /UCH/ institutional ethical review committee (Ref.NHREC/05/01/2008a). An official letter of cooperation was getting from Tigray Regional State Health Bureau to selected hospitals. Permission from each Chief Executive Officer of the hospitals was received too. Data collectors were approached individually to study participants and given information regarding the purpose of the study, confidentiality of study, their right to participate or withdraw from the study and then finally written consent was obtained for the study.

Consent for publication
Not applicable for this section

Availability of data and materials
The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.
Competing interests

The authors declare that they have no competing interests

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Authors’ contributions

AKB was the principal author participated in the conceptualization, design, acquisition, analysis, and interpretation of the data and drafted the manuscript and acted as the corresponding author. AOI was the primary academic advisor, contributed for design, acquisition, analysis, and interpretation of the data and critically revised the manuscript. COA & AMB were co-advisors, contributed for design, acquisition, analysis, and interpretation of the data and critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Tables
Table 1: Socio-demographic characteristics of study participants attending antenatal care in public hospitals of Tigray regional state, Ethiopia, 2019.
| Variable                        | Normotensive N (%) | Women with PIH N (%) |
|--------------------------------|--------------------|----------------------|
| Maternal Age                   |                    |                      |
| ≤ 19 years                     | 22 (4.2)           | 24 (9.2)             |
| >19 years                      | 500 (95.8)         | 236 (90.8)           |
| Residence                      |                    |                      |
| Urban                          | 435 (83.3)         | 178 (68.5)           |
| Rural                          | 87 (16.7)          | 82 (31.5)            |
| Mothers educational status     |                    |                      |
| No formal education            | 36 (6.9)           | 58 (22.3)            |
| Primary                        | 114 (21.8)         | 103 (39.6)           |
| Secondary                      | 188 (36.0)         | 62 (23.8)            |
| Diploma and above              | 184 (35.2)         | 37 (14.2)            |
| Religious                      |                    |                      |
| Orthodox                       | 459 (87.9)         | 214 (82.3)           |
| Catholic                       | 17 (3.3)           | 15 (5.8)             |
| Muslim                         | 38 (7.3)           | 26 (10.0)            |
| Protestant                      | 8 (1.5)            | 5 (1.9)              |
| Mothers occupation             |                    |                      |
| Unemployed                      | 250 (47.9)         | 201 (77.3)           |
| Employed                       | 272 (52.1)         | 59 (22.7)            |
| Wealth index                   |                    |                      |
| Lowest                         | 120 (23.3)         | 138 (53.3)           |
| Middle                         | 189 (36.7)         | 69 (26.6)            |
| Highest                        | 206 (40)           | 52 (20.1)            |
| Hospitals                      |                    |                      |
| Lemlem Carl                    | 59 (11.3)          | 29 (11.2)            |
| Mekelle                        | 78 (14.9)          | 39 (15)              |
| Wukro                          | 50 (9.6)           | 24 (9.2)             |
| Adigrat                        | 78 (14.9)          | 39 (15)              |
| Adwa                           | 53 (10.2)          | 28 (10.8)            |
| Saint Marry Axum               | 79 (15.1)          | 39 (15)              |
| Suhul Shire                    | 70 (13.4)          | 35 (13.5)            |
| Kahsay Abera                   | 55 (10.5)          | 27 (10.4)            |

Table 2: Maternal outcomes of pregnancy-induced hypertension and normotensive pregnant women in Tigray regional state, Ethiopia, 2019
| Outcome Variables          | Women with PIH | Normotensive women |
|----------------------------|----------------|--------------------|
|                            | Frequency (%)  | Frequency (%)      |
| Antepartum hemorrhage      |                |                    |
| Yes                        | 31 (11.9)      | 30 (5.7)           |
| No                         | 229 (88.1)     | 492 (94.3)         |
| Type of labour             |                |                    |
| Spontaneous labor          | 127 (48.8)     | 454 (87.0)         |
| Induced of labor           | 110 (42.3)     | 36 (6.9)           |
| Direct C/S                 | 23 (8.8)       | 32 (6.1)           |
| Mode of delivery           |                |                    |
| Spontaneous vaginal delivery | 150 (57.7)     | 407 (78.0)         |
| Assisted Vaginal delivery  | 17 (6.5)       | 30 (5.7)           |
| Caesarean Section          | 93 (35.8)      | 85 (16.3)          |
| Postpartum hemorrhage      |                |                    |
| Yes                        | 27 (10.4)      | 18 (3.4)           |
| No                         | 233 (89.6)     | 504 (96.6)         |

Table 3: Univariate and multivariable logistic regression analyses of adverse maternal outcomes associated with pregnancy-induced hypertension in Tigray regional state, Ethiopia, 2019
| Maternal Outcome Variables                  | Pregnancy-induced hypertension (n=260) | Normotensive women (n=522) | Unadjusted RR (95% CI) |
|--------------------------------------------|----------------------------------------|----------------------------|------------------------|
| Induced labor                              |                                        |                            |                        |
| Yes                                        | 110 (42.3)                             | 36 (6.9)                   | 6.13 (4.34, 8.67)      |
| No                                         | 150 (57.7)                             | 486 (93.1)                 | 1                      |
| Caesarean section delivery                 |                                        |                            |                        |
| Yes                                        | 93 (35.8)                              | 85 (16.3)                  | 2.19 (1.70, 2.83)      |
| No                                         | 167 (64.2)                             | 437 (83.7)                 | 1                      |
| Antepartum hemorrhage                      |                                        |                            |                        |
| Yes                                        | 31 (11.9)                              | 30 (5.7%)                  | 2.22 (1.31, 3.76)      |
| No                                         | 229 (88.1)                             | 492 (94.3)                 | 1                      |
| Postpartum hemorrhage                      |                                        |                            |                        |
| Yes                                        | 27 (10.4)                              | 18 (3.4%)                  | 3.01 (1.68, 5.36)      |
| No                                         | 233 (89.6)                             | 504 (96.6)                 | 1                      |

RR- Risk Ratio; * Adverse maternal outcome indicators were adjusted for maternal age, wealth status, educational status, residence, gravida and type of pregnancy 1= reference