Determinants of preterm birth in public hospitals in central Ethiopia: an unmatched case-control study [version 1; peer review: 1 approved]

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Abstract

Background: Around 15 million babies are born prematurely in the world every year. The most common cause of neonatal death in Ethiopia is premature birth. To reduce the rate of preterm delivery by correcting modifiable or preventable causes, the availability of local data is important. Hence, this study aimed to identify the determinants of preterm birth among women who gave birth in public hospitals in central Ethiopia.

Methods: An Institutional-based unmatched case-control study was conducted at public hospitals in central Ethiopia to select 170 cases and 340 controls. The collected data were entered into EPI INFO and transferred to SPSS for analysis. Tables, graphs, and proportions were used to present the results. Binary and multiple logistic regressions analysis were computed to identify determinants of preterm birth. Adjusted Odds Ratio (AOR), 95% Confidence Interval (CI), and a p-value < 0.05 were computed to determine the presence of an association between preterm birth and independent variables.

Results: A total of 166 cases and 332 controls participated in the study, giving a response rate of 97.6%. Cigarette smoking (AOR=3.77, 95% CI=1.35, 10.56), alcohol consumption (AOR=1.85, 95% CI=1.11, 3.10), wanted but unplanned pregnancy (AOR=3.95, 95% CI=1.68, 8.34), neither wanted nor planned pregnancy (AOR=3.61, 95% CI=1.62, 8.06), lack of antenatal care (ANC) visits (AOR=4.13, 95% CI=1.95, 8.74), adverse birth outcomes (AOR=5.66, 95% CI=2.88, 11.12), presence of a diagnosed illness (AOR=2.81, 95% CI=1.37, 5.76), presence of one or more of obstetrics complications (AOR=6.44, 95% CI=5.49, 3.35, 9), and hemoglobin level < 11g/dl (AOR=2.78, 95% CI=1.48, 5.22) were determinants of preterm birth.

Conclusion: In this study, cigarette smoking status, alcohol drinking status, pregnancy status, adverse birth outcomes, ANC visits, obstetric complications, presence of medical illness, and anemia were identified as determinants of preterm birth. It is important to encourage such women to attend ANC visits, stop smoking, and
abstain from alcohol.

**Keywords**
Central Ethiopia, Determinants, Hospitals, Mothers, Preterm birth
Introduction
The World Health Organization (WHO) defines preterm birth as childbirth that occurs before 37 weeks of gestation starting from the first day of the last menstrual period. Based on gestational age it can be classified as: Extremely preterm (<28 weeks), very preterm (28 to 31 weeks), and late preterm (32 to 37 weeks). Preterm birth can be also classified by its clinical presentations as spontaneous and iatrogenic preterm. From 130 million babies born annually, almost 15 million are preterm birth globally; more than one in ten newborns are born prematurely. Furthermore, more than one million children die due to complications of preterm birth every year. Preterm birth is the top cause of neonatal mortality and the second most common cause of mortality after pneumonia among children under five. Preterm birth also affects developing countries, for instance, USA is among the ten countries with the greatest numbers of preterm births. Worldwide, the incidence of preterm births is; 9.6% globally, 7.5% in developed countries, 12.5% in developing countries, 9.1% in Asia, 6.2% in Europe, 10.6% in North America, and 11.9% in Africa. In developing countries, more than 60% of preterm births occur in Africa and South Asia. The rate of premature birth in southeast Nigeria rose from 9.8% to 17.1%. The rate of preterm birth is 5% in Northern European countries and 18.1% in Malawi. The prevalence of preterm birth varied from place to place for instance it is 18.3% in Kenya, 11.6% in Debremarqos town, Ethiopia, 31.4% in Mettu Karl Hospital, Ethiopia, 34% in Tigray region, Ethiopia, 35% in Dessie Referral Hospital and 25.9% in Jimma, Ethiopia. Preterm birth causes 75% perinatal mortality and greater than 50% of long term morbidity. Prematurity is the second principal reason for death in children under five years and the single most significant direct cause of death in the critical first month of life. In spite of the decline in global child mortality rates, newborn death denotes a growing proportion of all death among children less than five years of age. The risk of dying from preterm birth complications is 10 times greater for babies born prematurely in low-income countries than for those born in high-income countries. Low educational status, advanced maternal age, chronic diseases, parity, lack of antenatal care visits, multiple pregnancies, urinary tract infection, prolonged premature rupture of membrane (PPROM), and pregnancy induced hypertension (PIH) are risk factors of preterm birth. Although preterm birth is common in Ethiopia, the determinants of preterm birth like drinking alcohol, medication intake, and cigarette smoking during pregnancy were not evaluated in previous studies. Although neither planned nor wanted pregnancies are common in Ethiopia, whether they cause preterm birth or not has not been studied. Long term research over the past several decades had failed to solve these problems. To identify the determinants of premature birth among the Ethiopian populations and try to minimize the rate of preterm delivery by correcting modifiable or preventable causes, the availability of local data is important. Thus, this study aimed to identify the determinants of preterm birth among women who gave birth at public hospitals in central Ethiopia.

Methods
Study design, period, and setting
An institutional-based unmatched case-control study was conducted from 1st February to 30th June 2020 in public hospitals in North Shewa, central Ethiopia. The North Shewa zone has a total population of 1.6 million. From the total population, 49,667 were pregnant women according to the North Shewa Zone health office report. Fiche is the capital city of the zone and 114 kilometers away from Addis Ababa. It has five hospitals and 64 health centers. It also has 2,420 health professionals out of whom 213 are midwives. We have conducted this study in two general and three primary hospitals. All of the hospitals in this Zone provide maternal health services like family planning, ANC, delivery, and postnatal care to the surrounding communities. We selected all of the five hospitals present in the zone purposely given the extensive maternal health services provided.

Source and study populations
All women 15-49 years old that gave birth at all public hospitals in the North Shewa zone during the study period were the source population of the study. All women 15-49 years of age that delivered their babies at public hospitals in the North Shewa zone during the data collection period and who were included in the study were the study population. Women who gave live newborns before 37 completed weeks of gestational age were cases (preterm) whereas women who gave live newborns at or after 37 completed weeks of gestational age were controls (non-preterm).

Inclusion and exclusion criteria
All women who gave birth during the data collection period at selected hospitals and whose gestational age were known or estimated from the last menstrual period or by ultrasound were included in the study whereas, women with induced termination of pregnancy for medical reasons, women who gave birth before 28 weeks of gestation, and those who had

Abbreviations
ANC; antenatal care, HIV/AIDS; human immunodeficiency virus/acquired immune deficiency syndrome, IFA; iron folic acid, LBW; low birth weight, PIH; pregnancy induced hypertension, PTB; preterm birth, PROM; premature rupture of membrane, WHO; World Health Organization.
stillbirths were excluded from the study. Cases were selected by taking all cases until the required number of cases were obtained and controls were selected using systematic random sampling, which was conducted in hospital before the discharge of the mother from the hospital after consent was obtained.

Sample size determination
We have calculated the sample size by using two population proportion formula and through EPI INFO version 7 statistical software package with the assumptions of confidence interval 95% (Z?/2=1.96), power 80% (Z?= 0.84), case to control ratio 1:2, where P1 is the proportion of cases exposed and P2 is the proportion of controls exposed. The variables used for sample size calculations were reactive to STI, lack of formal education, lack of ANC care visit, maternal anemia as taken from previous similar articles. Sample size was calculated for all of the variables mentioned above and of all variables, the sample size calculated from anemia during pregnancy was the largest of all, where the proportion of cases exposed was 79%, proportion of controls exposed was 11.2%, and AOR=2.2, which gave a final sample size of 170 cases and 340 controls with a total of 510 after adding a 10% non-response rate.

Sampling procedure
The number of study participants was allocated proportionally to each hospital based on estimations obtained from the average of previous quarter delivery services by referring to delivery registration books at each hospital. Therefore, the sample of each hospital was calculated by multiplying the average number of pregnant women who delivered in each hospital per five months with the total sample size, dividing by a total number of pregnant women attending antenatal care units for five months for all hospitals which was obtained from delivery registration of the previous months. Cases were selected by taking all cases until the required sample size obtained and controls were selected using systematic random sampling [Table 1].

Data collection tool, procedure, and management
The data collection instrument was developed by reviewing the existing literature. The questionnaire was developed and arranged according to study objectives. The questionnaire was prepared in English and then translated to Afan Oromo and Amharic languages that are local languages of the area to improve understanding of both the data collectors and respondents, and translated back to the English version by a language expert. The reliability of the used questions was checked with Cronbach’s alpha, which was found to be 0.860. Two days of training was provided for data collectors and supervisors on the objective of the study, contents of the questionnaire, confidentiality, the right of respondents, and how to collect data. The questionnaire was pre-tested on 5% (17 cases and 34 controls) of the sample at Chencho Hospital which is outside the study area. To assess the reliability of data collection instruments and findings, data collectors and supervisors discussed the questionnaire so that; the tool was modified for any inconsistencies and ambiguity before actual data collection. Ten diploma midwives and five BSc Public Health professionals were selected for data collection and supervision respectively. Information such as socio-demographic, substance-use related, and obstetrics related factors was collected by face to face interviews by using pretested questionnaire during a post-delivery hospital stay of women in the first 24 hours or during discharge from hospitals in the post-natal care room of the hospital. Gestational age was obtained from ANC records which in turn was estimated from the last menstrual period or early ultrasound conducted during the first-trimester pregnancy of women. Information related to obstetric, fetal characteristics and diagnosed illness of mothers (renal diseases, diabetes mellitus (DM), and urinary tract infection (UTI)), and newborns were also obtained from ANC records.

| S/N | Name of Hospitals               | Average number of deliveries for 5 months | Number of Cases | Number of Controls | Total number of sample size per Hospital |
|-----|---------------------------------|------------------------------------------|-----------------|-------------------|----------------------------------------|
| 1   | Fitche General Hospital         | 520                                      | 41              | 82                | 123                                    |
| 2   | Kundo meskel Hospital           | 415                                      | 32              | 64                | 96                                     |
| 3   | Muka Turi primary Hospital      | 410                                      | 32              | 64                | 96                                     |
| 4   | Kuyu general Hospital           | 425                                      | 33              | 66                | 99                                     |
| 5   | Shano Hospital                  | 415                                      | 32              | 64                | 96                                     |
| 6   | Total                           | 2185                                     | 170             | 340               | 510                                    |
Data processing and analysis
We checked the data for completeness after data collection. The data was then coded, cleaned, and entered using EPI INFO version 7 and transferred to SPSS version 23 for cleaning and analysis. Tables, graphs, and proportions were used to present the results of this study. Bivariate and multi variables logistic regressions analysis were carried out to determine the presence of an association between preterm birth and independent variables. Bivariate analysis was carried out to determine a significant association between each predictor variable and preterm birth at a p-value < 0.25. Multivariate logistic regression was carried out to identify the determinants of preterm birth. The enter model selection method was used to identify variables that remained for the final model. The goodness of fit model (Hosmer and Lemshow) was used to select the best multivariate model and the p-value of the model fitness test was 0.850. Multicollinearity and confounding effects were checked by using standard error and Hosmer and Lemshow goodness of fit test. Finally, AOR with 95% CI and p-value < 0.05 were considered to indicate significant association.

Ethical considerations
The study protocol and methodology were approved by Salale University Ethical Review Committee on February 02, 2020 with the reference number SLU ERC/010/2020. A formal letter of cooperation was written to each hospital. Before starting the interview the respondents were informed the purpose of the study and how their data could be used. The respondents were told as their participation in the study is voluntary and they have right to withdraw from the study at any time. Written consent was obtained from every study participant for those aged ≥ 18 years and written assent was obtained from the guardians for those aged below 18 years for access to ANC records for review as well as participation in the face-to-face interview. The privacy and confidentiality of the study participants were also strictly protected. Data collectors were told to code the questionnaire and not to write the name of the study participants.

Results
Socio-demographic characteristics of study participants
A total of 498 women (166 cases and 332 controls) participated in this study making the response rate 97.6%. The age of study participants ranged 17-43 years for cases and 17-42 years for controls with the mean age of 27.77 ± 5.5 for cases and 26.94 ± 5.007 for controls. About one-third (56, 33.7%) of cases and around a quarter (78, 23.5%) of controls had no formal education [Table 2].

Previous obstetrics and gynecologic related characteristics of study participants
Near to one-third (35, 31.8%) of cases and 39 (17.6%) of controls had a birth interval < 2 years. More than a quarter (32, 29.1%) of cases and 10 (4.5%) controls had a previous history of preterm birth. Near to half (51, 46.4%) of cases and 36 (10.8%) controls had a previous history of adverse birth outcomes [Table 3].

Obstetric characteristics of current pregnancy and medical problems
From women who came to the hospitals for delivery services, 50 (30.1%) cases and 23 (6.9%) controls neither wanted nor planned their current pregnancies. Around a quarter (44, 26.5%) of cases and 21 (6.3%) controls had no ANC visit during their pregnancy. In total, 34 (20.5%) of cases and 26 (7.8%) controls had medical illness (renal diseases, DM, and UTI) during their current pregnancies. In total, 104 (62.7%) cases and 95 (28.6%) controls had obstetrics complications (Premature rupture of membrane, pregnancy-induced hypertension, antepartum hemorrhage) during their pregnancy [Table 4].

Substance use-related characteristics of the study participants
Cigarette smoking during their pregnancy was reported by 16 (9.6%) cases and 8 (2.4%) controls. Furthermore, 29 (17.5%) cases and 21 (6.3%) controls, had husbands who smoked cigarettes over the course of the pregnancy. In total, 69 (41.6%) cases and 86 (25.9%) controls reported a history of alcohol consumption during their current pregnancies [Table 5].

Fetal characteristics
In total, 12 (7.2%) neonates born from cases and 12 (3.3%) neonates born from controls were twins. Regarding preterm birth, 37.3% were induced and 62.7% were spontaneous preterm births [Figure 1]. More than three quarters (78.9 %) of neonates born from cases and 21.1% of neonates born from controls had low birth weight [Figure 2].

Determinants of preterm birth
We conducted bivariate logistic regression for each independent variable. Multivariate analysis was done for all variables with p-value <0.25 in the bivariate logistic regression analysis after adjusting for covariates. The fitness of the model was also assessed. The result of multiple logistic regressions indicated that women who had a of history of cigarette smoking during their current pregnancies had four-folds higher odds of preterm birth compared to women who did have a history of cigarette smoking (AOR=3.77, 95% CI: 1.35,10.56, p-value:0.007). Women who had history of drinking alcohol during
their pregnancies had two folds higher odds of preterm birth compared to their counterparts (AOR=1.85, 95% CI: 1.11, 3.10, p-value: 0.019). Women who wanted but did not plan their pregnancies had four times higher odds of preterm birth compared to those who wanted and planned their pregnancies (AOR=3.95, 95% CI: 1.68, 5.34, p-value: 0.002). Women who neither wanted nor planned their current pregnancies had 3.61 folds higher odds of preterm birth compared to their counterparts (AOR=3.61, 95% CI: 1.62, 8.06, p-value: 0.001). Women who had no ANC visit for their current pregnancies had four-fold higher odds of preterm birth compared to those who had ANC care follow-up (AOR=4.13, 95% CI: 1.95, 8.74, p-value: 0.001). Women who had a previous history of adverse birth outcomes like stillbirth, low birth weight, and

Table 2. Socio-demographic characteristics of women who gave birth at public Hospitals in central Ethiopia, from February to June 2020.

| Variables               | Cases: n (%) | Controls: n (%) |
|-------------------------|--------------|-----------------|
| **Residence**           |              |                 |
| Urban                   | 68 (41%)     | 161 (48.5%)     |
| Rural                   | 98 (59%)     | 171 (51.5%)     |
| **Age groups**          |              |                 |
| 15-24                   | 56 (33.7%)   | 116 (35%)       |
| 25-34                   | 90 (54.2%)   | 186 (56%)       |
| >=35                    | 20 (12.1%)   | 30 (9%)         |
| **Ethnicity**           |              |                 |
| Oromo                   | 112 (67.5%)  | 238 (71.7%)     |
| Amahara                 | 50 (30.1%)   | 74 (22.3%)      |
| Others a                | 4 (2.4%)     | 20 (6%)         |
| **Religion**            |              |                 |
| Orthodox                | 78 (47%)     | 155 (46.7%)     |
| Protestant              | 62 (37.4%)   | 128 (38.6%)     |
| Muslim                  | 18 (10.8%)   | 34 (10.2%)      |
| Others b                | 8 (4.8%)     | 15 (4.5%)       |
| **Family size**         |              |                 |
| ≤5                      | 93 (56%)     | 218 (65.7%)     |
| >5                      | 73 (44%)     | 114 (34.3%)     |
| **Educational status of mother** |          |                 |
| No formal education     | 56 (33.7%)   | 78 (23.5%)      |
| Have formal education   | 110 (66.3%)  | 254 (76.5%)     |
| **Marital status of mother** |        |                 |
| Married                 | 163 (98.2%)  | 320 (96.4%)     |
| Others c                | 3 (1.8%)     | 12 (3.6%)       |
| **Educational status of husband** |          |                 |
| No formal education     | 52 (31.3%)   | 45 (13.6%)      |
| Have formal education   | 114 (68.7%)  | 287 (86.3%)     |
| **Occupation of mother** |           |                 |
| Employed                | 34 (20.5%)   | 108 (32.5%)     |
| Unemployed              | 132 (79.5%)  | 224 (67.5%)     |
| **Occupation of Husband** |           |                 |
| Employed                | 37 (22.3%)   | 124 (37.3%)     |
| Unemployed              | 129 (77.7%)  | 208 (62.7%)     |

a = Tigre and Gurage; b = Catholic and Wakefata; c = single, widowed and divorced
preterm birth had 5.66 times higher odds of preterm birth compared to those who had no previous history of adverse birth outcomes (AOR=5.66, 95% CI:2.88,11.12, p-value: 0.001). Women who had a diagnosed illness during their current pregnancies had three folds higher odds of preterm birth compared to their counterparts (AOR=2.81, 95% CI: 1.37, 5.76, p-value: 0.005). Women who had one or more obstetrics complications (Premature rupture of membrane, pregnancy-induced hypertension, Antepartum hemorrhage) during their current pregnancies had 6.44 folds higher odds of preterm birth compared to their counterparts (AOR=6.44, 95% CI: 5.49, 3.35, 9, p-value: 0.001). Women who had anemia had three folds higher odds of preterm birth compared to those who were not anemic (AOR=2.78, 95% CI: 1.48, 5.22, p-value: 0.001) [Table 6].

Discussion
Preterm birth is the primary cause of neonatal deaths in Ethiopia, where information on the determinants of preterm birth is commonly recorded. This study aimed to identify the determinants of preterm birth at public hospitals in central Ethiopia. The chance of preterm birth was higher among mothers that drank alcohol, smoked cigarettes, had unplanned pregnancies, neither wanted and nor planned pregnancy, had previous history of adverse birth outcomes, had no ANC visit, were anemic, had co-morbidities, and had obstetrics complications during their current pregnancies.

Anemia was significantly associated with the occurrence of preterm birth in this study. The finding is consistent with studies conducted in Debramarkos town, Ethiopia, and Teran, Iran. This is because anemia decreases the immunity of the mother and leads to genital tract infection which in turn causes PROM and then causes preterm birth.

In this study, cigarette smoking during the pregnancy was an independent predictor for preterm birth. The finding is similar to other studies where cigarette smoking was positively associated with preterm birth. This might be due to the fact that from the 3000 chemicals present in cigarettes, nicotine, and carbon dioxide cause decrease blood flow to the utero-placenta and damage the placenta because of their dominant vasoconstriction nature. Cigarette smoking can also
cause a systemic inflammatory response which in turn causes spontaneous preterm birth. Tobacco causes preterm birth by causing low birth weight and placental abruption.

Women who drank alcohol during their pregnancy were at higher risk of delivering preterm birth compared to their counterparts. The finding is in agreement with a study from South Africa, and another study in which women who took more than three drinks per day were at high risk of delivering preterm birth. The possible reason might be due to unidentified factors that precipitate preterm birth.

Unwanted and unplanned pregnancy was another independent predictor for preterm birth in this study. Moreover, wanted but unplanned pregnancies were also positively associated with preterm birth. One possible reason for this is the stress

| Variables                                      | Cases: n = 166 (%) | Controls: n = 322 (%) |
|------------------------------------------------|--------------------|-----------------------|
| **Status of current pregnancy**                |                    |                       |
| Wanted and planned                            | 74 (44.6%)         | 241 (72.6%)           |
| Wanted but not planned                        | 51 (30.7%)         | 68 (20.5%)            |
| Neither wanted nor planned                    | 41 (24.7%)         | 23 (6.9%)             |
| **Had ANC visit for current pregnancy**        |                    |                       |
| Yes                                           | 122 (73.5%)        | 311 (93.7%)           |
| No                                            | 44 (26.5%)         | 21 (6.3%)             |
| **Number of ANC visits**                      |                    |                       |
| < 4 times                                      | 88 (72%)           | 158 (50.8%)           |
| ≥ 4 times                                      | 34 (28%)           | 153 (49.2%)           |
| **HIV/AIDS status of the mother**              |                    |                       |
| Negative                                       | 154 (92.8%)        | 327 (98.5%)           |
| Positive                                       | 12 (7.2%)          | 5 (1.5%)              |
| **Medical illness during current pregnancy**   |                    |                       |
| Yes                                           | 34 (20.5%)         | 26 (7.8%)             |
| No                                            | 132 (79.5%)        | 306 (92.2%)           |
| **Obstetrics complications during current pregnancy** |        |                       |
| Yes                                           | 104 (62.7%)        | 95 (28.6%)            |
| No                                            | 62 (37.3%)         | 237 (71.4%)           |
| **Hemoglobin level**                          |                    |                       |
| < 11g/dl                                       | 68 (41%)           | 46 (13.9%)            |
| ≥ 11 g/dl                                      | 98 (59%)           | 286 (86.1%)           |
| **Gestational hypertension**                   |                    |                       |
| Yes                                           | 39 (23.5%)         | 30 (9%)               |
| No                                            | 127 (76.5%)        | 302 (91%)             |
| **Premature rupture of membrane**             |                    |                       |
| Yes                                           | 62 (37.3%)         | 44 (13.3%)            |
| No                                            | 104 (62.7%)        | 288 (86.7%)           |
| **Antepartum hemorrhage**                     |                    |                       |
| Yes                                           | 14 (8.4%)          | 21 (6.3%)             |
| No                                            | 152 (91.6%)        | 311 (93.7%)           |
| **Multiple pregnancy**                        |                    |                       |
| Yes                                           | 12 (7.2%)          | 8 (2.4%)              |
| No                                            | 154 (92.8%)        | 324 (97.6%)           |
Table 5. Substance use-related characteristics of women who gave birth at public Hospitals in central Ethiopia from February to June 2020.

| Variables                              | Cases: n = 166 (%) | Controls: n = 332 (%) |
|----------------------------------------|--------------------|-----------------------|
| History of mother cigarette smoking   |                    |                       |
| Yes                                    | 16 (9.6%)          | 8 (2.4%)              |
| No                                     | 150 (90.4%)        | 324 (97.6%)           |
| History of mother alcohol drinking     |                    |                       |
| Yes                                    | 69 (41.6%)         | 86 (25.9%)            |
| No                                     | 97 (58.4%)         | 246 (74.1%)           |
| History of mother chat chewing         |                    |                       |
| Yes                                    | 13 (7.8%)          | 10 (3%)               |
| No                                     | 153 (92.2%)        | 322 (97%)             |
| Took medication on current pregnancy   |                    |                       |
| Yes                                    | 96 (57.8%)         | 120 (36.1%)           |
| No                                     | 70 (42.2%)         | 212 (63.9%)           |
| History of husband cigarette smoking   |                    |                       |
| Yes                                    | 29 (17.5%)         | 21 (6.3%)             |
| No                                     | 137 (82.5%)        | 311 (93.7%)           |
| History of husband alcohol drinking    |                    |                       |
| Yes                                    | 86 (51.8%)         | 145 (43.7%)           |
| No                                     | 80 (48.2%)         | 187 (56.3%)           |
| History of husband chat chewing        |                    |                       |
| Yes                                    | 20 (12%)           | 32 (9.6%)             |
| No                                     | 146 (88%)          | 300 (90.3%)           |

Figure 1. Percentage of a type of preterm among neonates born at public Hospitals in the central Ethiopia from February to June 2020.

Figure 2. Percentage of birth weight of newborns at central Ethiopia public Hospitals from February to June 2020.
induced by the pregnancy, which can lead to depressions that in turn causes preterm birth. Moreover, the more women want and plan their pregnancies, the more they take care for their pregnancies by consuming a variety of foods, visiting health institutions for ANC follow-up, and limiting heavy work. It is currently suggested that mothers of unplanned pregnancies will neglect their child, which leads to preterm birth. In addition, women with unplanned pregnancies are more likely to drink alcohol and smoke cigarettes that in turn lead to preterm birth.

Having a previous history of adverse birth outcomes (low birth weight, preterm birth, and stillbirth) was positively associated with preterm birth. The finding is in line with a study conducted in Amahara region, Ethiopia, Sidama zone, South Ethiopia, Jimma zone South-west, Ethiopia, a study conducted at Gonder Hospital, and a case-control study conducted in West Iran where a previous history of adverse birth outcomes was positively associated with preterm birth. This might be due to women with a previous history of negative birth outcomes (adverse birth outcomes) experiencing stressful conditions that lead to recurrences (re-occurrence of preterm birth).

### Table 6. Determinants of preterm birth among women who gave birth at public Hospitals in the central Ethiopia from February to April 2020 (Multivariable analysis).

| Variables                        | Cases: n (%) | Controls: n (%) | COR (95%CI) | AOR (95%CI) |
|----------------------------------|--------------|-----------------|-------------|-------------|
| **Family size**                  |              |                 |             |             |
| < 5                              | 93 (56%)     | 218 (65.7%)     | 1           | 1           |
| ≥ 5                              | 73 (44%)     | 114 (34.3%)     | 1.5 (1.03, 2.2) | 0.50 (0.50, 1.57) |
| **Educational level**            |              |                 |             |             |
| No formal education              | 56 (33.7%)   | 78 (23.5%)      | 5.11 (3.23,8.1) | 0.47 (0.25, 0.90) |
| Formal education                 | 110 (66.3%)  | 254 (76.5%)     | 1           | 1           |
| **History of cigarette smoking**|              |                 |             |             |
| Yes                              | 16 (9.6%)    | 8 (2.4%)        | 4.32 (1.81,10.3) | 3.77 (1.35,10.56) ** |
| No                               | 150 (90.4%)  | 324 (97.6%)     | 1           | 1           |
| **History of alcohol drinking**  |              |                 |             |             |
| Yes                              | 69 (41.6%)   | 86 (25.9%)      | 2.04 (1.37,3.0) | 1.85 (1.11,3.10)** |
| No                               | 97 (58.4%)   | 246 (74.1%)     | 1           | 1           |
| **Previous history of adverse birth outcomes** |           |                 |             |             |
| Yes                              | 51 (46.4%)   | 36 (10.8%)      | 4.27 (2.55,7.17) | 5.66 (2.88,11.12) ** |
| No                               | 59 (53.6%)   | 185 (59.2%)     | 1           | 1           |
| **Hemoglobin level**             |              |                 |             |             |
| < 11g/dl (have anemia)           | 68 (41%)     | 46 (13.9%)      | 4.31 (2.78,6.69) | 3.51 (2.03, 6.08) ** |
| ≥11g/dl (have no anemia)         | 98 (59%)     | 286 (86.1%)     | 1           | 1           |
| **Current medical illness**      |              |                 |             |             |
| Yes                              | 34 (20.5%)   | 26 (7.8%)       | 3.03 (1.75,5.25) | 2.81 (1.37, 5.76)** |
| No                               | 132 (79.5%)  | 306 (92.2%)     | 1           | 1           |
| **Obstetrics complications**     |              |                 |             |             |
| Yes                              | 104 (62.7%)  | 95 (28.6%)      | 4.19 (2.82,6.21) | 5.49 (3.35, 9) ** |
| No                               | 62 (37.3%)   | 237 (71.4%)     | 1           | 1           |
| **ANC visit**                    |              |                 |             |             |
| Yes                              | 122 (73.5%)  | 311 (93.7%)     | 1           | 1           |
| No                               | 44 (26.5%)   | 21 (6.3%)       | 5.34 (3.10,9.34) | 4.13 (1.95, 8.74)** |
| **Pregnancy status**             |              |                 |             |             |
| Wanted and planned               | 74 (44.6%)   | 241 (72.6%)     | 1           | 1           |
| Wanted but not planned           | 51 (30.7%)   | 68 (20.5%)      | 2.44 (1.56,3.82) | 3 (1.68,5.34)** |
| Neither wanted nor planned       | 41 (24.7%)   | 23 (6.9%)       | 5.81 (3.27,10.3) | 3.61 (1.62, 8.06)** |

** = statistically significant at p-value < 0.05, 1= reference
This study signified that women who had no ANC visit for their index pregnancies were at higher risk of delivering preterm birth compared to their counterparts. It is consistent with a study conducted in the Amhara region, Dabramarkos town, North-west Ethiopia, and Hossana town, Southwest Ethiopia. Women who do not have ANC follow-up cannot get nutritional counseling, ferrous sulfate supplementation, and are unaware of the danger signs of obstetrics complications that lead to adverse birth outcomes like preterm birth.

Women who had conditions like diabetes and hypertension during their current pregnancies had a higher incidence of preterm birth compared to their counterparts. It is similar to studies conducted in Debramarkos, and Aksum towns, Ethiopia. This might be due to the fact that diabetes and hypertension cause a reduction in nutrient and oxygen delivery to the fetus via the placenta which leads to pre-eclampsia which in turn causes preterm birth.

Similarly, this study also found that women who had one or more obstetrics complications (PIH, PROM, multiple pregnancy, and polyhydramnios) were more likely to give birth prematurely than those who had no obstetrics complications. It is consistent with a study conducted at Debramarkos town, Ethiopia. This might be due to the fact that complications like pregnancy-induced hypertension and PROM can cause damage to the vasculature of the placenta which in turn causes preterm birth. Multiple pregnancies and polyhydramnios (high amount of amniotic fluid) can stretch the myometrium (muscle of uterus); and it induces the oxytocin receptors which results in labor, and delivery. As far as we know, this study is the first to find a significant association of preterm births with smoking cigarettes, drinking alcohol, wanted but, unplanned pregnancy, and neither wanted nor planned pregnancy in Ethiopia.

**Limitation of the study**
This study maybe susceptible to recall bias due to its retrospective nature and social desirability bias with regard to face to face interview

**Conclusion**
In this study, cigarette smoking; alcohol consumption during current pregnancies; wanted but, unplanned pregnancies; neither wanted, nor planned pregnancies; lack of ANC visit for their current pregnancies; previous history of adverse outcomes; obstetric complications; presence of comorbidities; and being anemic were identified as determinants of preterm birth in this study.

Oromia regional health bureau is recommended to disseminate health information via the media on the impact of identified determinants of preterm birth and how to mitigate the problems surrounding premature birth. North Shewa health facilities or health professionals are recommended to counsel pregnant women to visit ANC, provide counseling at ANC clinics, encourage pregnant women to stop cigarette smoking and alcohol drinking, provide modern family planning to females in reproductive age groups, early identification, and treatment of medical illness among pregnant women.

**Data availability**

**Underlying data**
Figshare: Determinants of preterm birth in public hospitals in central Ethiopia: An unmatched case-control study. https://doi.org/10.6084/m9.figshare.13713172.v1.26

This project contains the following underlying data:
- SPSS 4 preterm birth.4 analysis.sav

**Extended data**
Figshare: Determinants of preterm birth in Public hospitals in central Ethiopia: An unmatched case-control study. https://doi.org/10.6084/m9.figshare.13713172.v1.26

This project contains the following extended data:
- English version questionnaire.docx
- Afan Oromo version questionnaire.docx
- Amharic version questionnaire.docx
Data are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication).

Acknowledgments

The authors acknowledge Salale University, all of the five hospitals, and the study participants for their unreserved contribution to the success of this study.

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Reviewer Report 13 August 2021

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1. Under the Methods section, the authors repeatedly wrote logistic regression. There are several types of logistic regression, such as binary logistic regression, multinomial logistic regression, ordinal logistic regression, etc. So it is better to write the specific logistic regression used for this study.

2. The authors mentioned that they have used the combined data collection technique (interview and record review) and the study population is those women who gave birth during the data collection period. However, under the ethical consideration section, they mentioned written assent was taken from the guardians for women who gave birth and age <18 years. 2.1. How was assent considered for women who gave birth and maybe married? 2.2. Assent could not be taken from the guardian but from those not eligible to give informed consent.

3. Under Data processing and analysis, the method and result are mixed. For example “the goodness of fit model (Hosmer and Lemeshow) was used to select the best multivariate model and the p-value of the model fitness test was 0.850.” Please separate them by taking p-value indicates about the goodness of fit and give your conclusion under the result section.

4. The authors plan to check multicollinearity using standard error. However, they did not say anything about whether collinearity is present or absent under the Results section. Why do you plan to use standard error in presence of other options like VIF and Tolerance?

5. Under Sample size determination, the authors mentioned assumption 95% as a confidence interval. It should be corrected as a 95% confidence level.

6. Sampling technique: write kth to sample controls using systematic random sampling.
7. Why do the authors use the term "counterparts" in comparison to two groups using the Odds ratio? Better to write the exact name of the comparison group.

8. No need to write what you have done under the Results section. Better to write what you have found under the Results section. So please move the following statement under the Methods section: "We conducted bivariate logistic regression for each independent variable. Multivariate analysis was done for all variables with p-value <0.25 in the bivariate logistic regression analysis after adjusting for covariates. The fitness of the model was also assessed."

9. In some bivariate tables under the Results section, sparse data was observed for ethnicity, marital status, ANC visit, history of cigarette smoking, and history of previous abortion. How did the authors manage those variables with sparse data in multivariable binary logistic regression?

10. In Table 6, the COR and AOR direction change or reverse for variable family size and educational level.

11. Under the Discussion section, there are several inconsistent uses of terms like the risk of preterm and the incidence of preterm. As the study design of this study is a case-control study design, better to use odds of preterm in the interpretation of AOR rather than using incidence or risk.

Is the work clearly and accurately presented and does it cite the current literature?  
Partly

Is the study design appropriate and is the work technically sound?  
Yes

Are sufficient details of methods and analysis provided to allow replication by others?  
Partly

If applicable, is the statistical analysis and its interpretation appropriate?  
Yes

Are all the source data underlying the results available to ensure full reproducibility?  
Yes

Are the conclusions drawn adequately supported by the results?  
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: I am an Epidemiologist and I have much research published on maternal-child health.
I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 17 Aug 2021

Berhanu Senbeta Deriba, Salale University College of health sciences Department of Public Health, Fitche, Ethiopia, Fitche, Ethiopia

Dear reviewer and editors

We thank you for reviewing and providing us with important and valid comments that helped us to enrich our manuscript. Really I would like to appreciate and thank you for your valuable, constructive comments too. Based on your suggestions, I have incorporated the comments into the manuscript, and I have also provided a response to each comment as follows.

1. Under the Methods section, the authors repeatedly wrote logistic regression. There are several types of logistic regression, such as binary logistic regression, multinomial logistic regression, ordinal logistic regression, etc. So it is better to write the specific logistic regression used for this study.

Authors' response: We used binary logistic regression and if editor allow us we have incorporated the comment into the manuscript.

2. The authors mentioned that they have used the combined data collection technique (interview and record review) and the study population is those women who gave birth during the data collection period. However, under the ethical consideration section, they mentioned written assent was taken from the guardians for women who gave birth and age < 18 years. 2.1. How was assent considered for women who gave birth and may be married? 2.2. Assent was could not be taken from the guardian but from those not eligible to give informed consent.

Authors' response: Thank you it is a nice observation we have accepted the comment and corrected accordingly. Actually what we did was for mothers < 18 years old we took assent from attendants available with her during data collection (guardians, husband or any other relatives).

3. Under Data processing and analysis, the method and result are mixed. For example "the goodness of fit model (Hosmer and Lemeshow) was used to select the best multivariate model and the p-value of the model fitness test was 0.850." Please separate them by taking p-value indicates about the goodness of fit and give your conclusion under the result section.

Authors' response: Thank you for your constructive comments we have accepted the comment and corrected accordingly.

4. The authors plan to check Multicollinearity using standard error. However, they did not say anything about whether collinearity is present or absent under the Results section. Why do you plan to use standard error in presence of other options like VIF and Tolerance?

Authors' response: We have used standard error, VIF, and Tolerance to check Multicollinearity for this study. The reason why we used (focused) standard error is that standard error is used to check Multicollinearity in logistic much better than others. If standard error is inflated, which means greater than two it indicates presence of Multicollinearity and if it is less than two, it indicates absence of
Multicollinearity in logistic regression. No collinearity was found in our study.

5. Under Sample size determination, the authors mentioned assumption 95% as a confidence interval. It should be corrected as a 95% confidence level.

Authors’ response: Thank you for your constructive comments we have accepted the comment and corrected accordingly.

6. Sampling technique: write kth to sample controls using systematic random sampling.

Authors’ response: We have used Kth every 4th to select controls.

7. Why do the authors use the term “counterparts” in comparison to two groups using the Odds ratio? Better to write the exact name of the comparison group.

Authors’ response: We thought counterpart can indicate the opposite of what was mentioned. Now we have corrected it accordingly.

8. No need to write what you have done under the Results section. Better to write what you have found under the Results section. So please move the following statement under the Methods section: "We conducted bivariate logistic regression for each independent variable. Multivariate analysis was done for all variables with p-value.

Authors’ response: We would like to appreciate your nice observation and corrected it accordingly.

9. In some bivariate tables under the Results section, sparse data was observed for ethnicity, marital status, ANC visit, history of cigarette smoking, and history of previous abortion. How did the authors manage those variables with sparse data in multivariable binary logistic regression?

Authors’ response: In the face of sparse data, the performance of logistic regression is problematic. A typical issue in such a circumstance is the occurrence of large odds ratios (ORs) with very broad 95 percent confidence intervals (CI). We solved this issue in this study by employing the penalized logistic regression (PLR) approach.

10. In Table 6, the COR and AOR direction change or reverse for variable family size and educational level.

Authors’ response: Thank you we have corrected it accordingly.

11. Under the Discussion section, there are several inconsistent uses of terms like the risk of preterm and the incidence of preterm. As the study design of this study is a case-control study design, better to use odds of preterm in the interpretation of AOR rather than using incidence or risk.

Authors’ response: We thank you and we have corrected it accordingly.

Competing Interests: There is no competing interest that might be construed to influence our judgment of article's or peer review report's validity or importance.
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