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Regional Variation and Factors Associated with Fetal Macrosomia in Ethiopia

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Abstract

Background: Globally, there is an increase in the prevalence and incidence of fetal macrosomia. In Sub-Sahara African countries including Ethiopia, all infants were not weighed at birth, and there is a limit to knowledge regarding fetal macrosomia in Ethiopia. The main objective of this study is to assess the regional variation and determinants of fetal macrosomia using the multilevel logistic regression model.

Methods: The study was based on the recent Ethiopian Demographic and Health Survey of 2016. A total of 2110 weighted infants at birth were extracted. Multilevel logistic regression analysis is performed to identify the factors associated with fetal macrosomia after various candidate models for their efficiency have been compared based on Akaike’s Information Criteria. Chi-square test of association and the inter-class correlation (ICC) are used to test and compute the variation of fetal macrosomia among the regions, respectively.

Results: The overall prevalence of fetal macrosomia among the weighted infants at birth is 219 (10.4%). Based on the estimated chi-square test, there is a significant difference in fetal macrosomia across the regions of Ethiopia. The ICC reveals that 14% of the variation in fetal macrosomia can be explained by grouping the infants into the regions. Random intercept with fixed slope model fits the study data well as compared to the other competitors. Based on this model, the age of the mother, residence, educational level of mother, body mass index of mother, gestational age, wealth index, multiple pregnancies, and the infant sex are the significant factors associated with fetal macrosomia in all regions of Ethiopia.

Conclusion: Concerned bodies, including the ministry of health and its hierarchical body, need to give special support and attention to women aged between 35 and 49, post-term pregnant women, and overweight or obese women to minimize the prevalence of fetal macrosomia.

Keywords: Birth weight, fetal macrosomia, multilevel, gestational age, regional variation
1. **Introduction**

Birth weight is the first weight of the new born obtained immediately after birth, and this can be classified as low birth weight, normal weight and high birth weight. The high birth weight is also called fetal macrosomia. It is defined as a birth weight greater than 4000 gram, regardless of his or her gestational age, on condition that this mass is about the whole body and not just one of its parts.\(^1\) An alternative definition for fetal macrosomia is a birth weight of more than the 90\(^{th}\) percentile for gestational age.\(^2-3\)

These days, there is an increase of the frequency of macrosomia. Fetal macrosomia was found between 1.6% and 28% of births with a frequency varies according to the results from different countries.\(^4\) Its prevalence is also believed to be higher in industrialized nations and among women of high socioeconomic status within a given population.\(^5\) In developed country in the World the magnitude of macrosomia is ranging from 5 to 20% of all births.\(^6\) In the USA, the macrosomia rate was 8.0% in Europe\(^7\) and other developed countries reported rates range between 5% and 20%.\(^6\) A study conducted on low and middle income countries in Africa, Asia and Latin America reported a prevalence of fetal macrosomia were ranged from 0.6% (India) to 15.2% (Algeria).\(^5\)

In Africa, the frequency of macrosomia varies between 2% (Nigeria) and 15.2% (Algeria).\(^5\) In the other country in Africa, there reported frequencies of fetal macrosomia were 2.7%, 3.1%, 3.9%, 8% and 9.1% in Democratic Republic of Congo, Angola, Kenya, Niger and Uganda respectively.\(^5\) In Sub-Saharan African countries including Ethiopia there is not enough dataset on weight of infants at birth. In Ethiopia, the Ethiopia Demographic Health Survey (EDHS) of 2011 reported that the prevalence of fetal macrosomia among 5% of weighted infants at birth was 10.46%.\(^9\)

Fetal macrosomia affects 3 to 15% of all pregnancies in worldwide. Delivering a macrosomia baby is distressing to the mother, her baby, obstetrician and neonatologist.\(^10\) There are many maternal complications associated with fetal macrosomia, including emergency cesarean section, postpartum hemorrhage, perineal trauma and neonatal complications, including shoulder dystocia, obstetric brachial plexus injury, birth fracture of the humerus or clavicle and birth asphyxia.\(^11\)

The factors associated with fetal macrosomia have been extensively studied in the developed country in the World with different data structure. There is limited evidence in developing
countries including Ethiopia on factors associated with fetal macrosomia at national level using hierarchical data. Identifying the risk factors associated with fetal macrosomia at the local level have high importance to take appropriate measures during the antenatal period to reduce its prevalence, morbidity, mortality on both maternal and neonatal, eventually reducing the prevalence of the aforementioned complications. In addition, it can be used as a reference for further studies on fetal macrosomia patients. Therefore, the aim of this study was assessing regional variation and factors associated with fetal macrosomia in Ethiopia based on weighted Ethiopian Demographic Health Survey of 2016.

The remainder of this article contains methods of data collection and analysis, results, discussion and main conclusions.

2. Data and Method of Data Analysis

2.1 Source of data

For this study, we have extracted data from the recent Ethiopian Demographic and Health Survey (EDHS) conducted in 2016. It was implemented by the Central Statistical Agency (CSA) from January 18 to June 27, 2016 with nationally representative sample from 9 regions and two administrative cities. The authors accessed these public domain datasets from the MEASURE DHS website by permission. This multistage 2016 weighted EDHS dataset have the hierarchical structure. The hierarchy of this study follows women as ultimate level (level-1) and regions as level-2. This means that women are nested in regions.

2.2 Data extraction

Demographic and Health Survey dataset users should be aware that, in most cases, the data must be weighted. This is because the overall probability of selection of each household is not a constant. So that, first the authors of this study weight EDHS using household weight techniques, and data for this study was extracted from the weights EDHS of 2016.

2.3 Study population

The study population was all live births in the five years delivered by women in reproductive age of 15-49 years who were residents of the nine regions and two administrative cities of Ethiopia during the survey. In total, 2110 weighted infants at birth were included in the study.

2.4 Inclusion and exclusion criteria
This study includes all weighted infants at birth in EDHS of 2016. Infant whose weight were not weighted at birth were excluded during data extraction.

2.5 Variables in the study

The response variable was birth weight of infants at birth which was dichotomous variable as fetal macrosomia or not. Explanatory variables were region, residence, infant’s sex, mother age, mother education level, marital status, father education level, wealth index, body mass index, gestational age, and multiple pregnancy.

2.6 Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Research Ethics Review Committee of the Jimma University College of Natural Sciences. The secondary data were obtained from Central Statistical Agency (CSA) of Ethiopia.

2.7 Multilevel logistic regression model

Multilevel models are statistical models of parameters that vary at more than one level. Multilevel models are models specifically geared toward the statistical analysis of data that have a hierarchical or clustered structure. Multilevel models have become popular for the analysis of a variety of problems, going beyond the classical individuals-within-groups applications. Multilevel models are particularly appropriate for research designs where data for participants are organized at more than one level The units of analysis are usually individuals (at a lower level) who are nested within contextual/aggregate units (at a higher level). Fitting regression models that ignore the hierarchical structure of the data can lead to false inferences being drawn from the data.

Considering the hierarchical structure of the study data, in this paper, a two-level logistic model is applied to assess the regional variation and factors associated with fetal macrosomia in Ethiopia. The units of analysis of this study are lower level (women) who are nested within higher level (region).

Because of the available levels in the EDHS datasets, the two-level logistic regression model is used for this study. Let $Y_{ij}$ be the binary response for women i in region j and $X_{ij}$, an explanatory variable at the women level. The probability of the response equal to one as $P_{ij} = P_r(Y_{ij} = 1)$. Then the two-level model can be written as:

$$\text{logit}(P_{ij}) = \log \left[ \frac{\pi_{ij}}{1-\pi_{ij}} \right] = \beta_0 + \beta_1 X_{ij} + U_{0j},$$

(1)
where $U_{0j} \sim IID(0, \sigma_0^2)$ and $U_{0j}$ is the random effect at level two.

$$\text{logit}(P_{ij}) = \log \left[ \frac{\pi_{ij}}{1-\pi_{ij}} \right] = \beta_0 + \beta_1 X_{ij}$$  \[\text{Level 1 model}\]

and

$$\beta_{0j} = \beta_0 + U_j$$  \[\text{Level 2 model}\]

Three models of two-level logistic regression model are considered, namely, the empty, the random intercept with fixed slope, and the random coefficient models.

2.7.1 Empty model

The empty two level model for a dichotomous outcome variable refers to a population of groups (level-two units, i.e. regions) and specifies the probability distribution for group-dependent probabilities without taking any explanatory variables into account. It can be expressed with logit link function as follows.

$$\text{logit}(P_{ij}) = \beta_0 + U_{0j},$$  \[2\]

where $\beta_0$ the population average of the transformed probabilities and $U_{0j}$ is the random variance from this average for group j, and $U_{0j} \sim IID(0, \sigma_0^2)$.

2.7.2 Random intercept with fixed slope model

In the random intercept with fixed slope model, the intercept is the only random effect. Its function is as follow.

$$\text{logit}(P_{ij}) = \log \left[ \frac{\pi_{ij}}{1-\pi_{ij}} \right] = \beta_0 + \sum_{h=1}^{p} \beta_h X_{hij} + U_{0j},$$  \[3\]

where $P_{ij}$ is the log-odds that $y : 1$ when $x = 0$ and $u = 0$, is the effect on log-odds of dependent variable in same group (same value of $u$), $\exp(\beta_h)$ is an odds ratio, comparing odds for individuals in the same group. $U_{0j}$ is the effect of being in group j on the log-odds that $y : 1$ also known as a level 2 residual, $\sigma_0^2$ is the level 2 (residual) variance, or the between-group variance in the log-odds that $y : 1$ after accounting for $x$ and $U_{0j} \sim IID(0, \sigma_0^2)$.

2.7.3 Random coefficient model

This model assume that the effects of the explanatory variables are the same for each regions. So that, a random coefficient model represents heterogeneity in relationship between the response and explanatory variables. The model, with $p$ level-1 predictors and $q$ level-2 predictors, can be expressed as:

$$\text{logit}(P_{ij}) = \log \left[ \frac{\pi_{ij}}{1-\pi_{ij}} \right] = \beta_{0j} + \sum_{h=1}^{p} \beta_h X_{hij} + U_{0j} + \sum_{k=1}^{q} U_{kij} X_{kij}.$$  \[4\]

$Y_{ij}$ is the value of the response variable for the $i^{th}$ woman in the $j^{th}$ region. $X_{hij}$ is the value of individual-level explanatory variable $X_p$ for the $i^{th}$ woman in the $j^{th}$ region. $X_{kij}$ is the value of region-level explanatory variable $X_q$ for the $j^{th}$ region. $U_{0j} \sim Normal(0, \sigma_0^2)$ is the region-level
residual of the \( j \)th region. It is a random effect that represents the discrepancy between \( \beta_0 \) and the true intercept of the \( j \)th region and \( n_j \) is the number of women respondents in the \( j \)th region. The first part of equation (3.24), \( \beta_{0j} + \sum_{h=1}^{p} \beta_{h} X_{hij} \), is called the fixed part of the model. The second part \( U_{0j} + \sum_{i=1}^{q} U_{0ij} X_{hij} \) is called the random part.

3 Results

Table 1 summarizes the descriptive analysis of the categorical predictors associated with fetal macrosomia. Of all 2110 infants 219 (10.4%) of them had fetal macrosomia. Prevalence of fetal macrosomia was high in males (6.1%) than in females (4.3%). Infants who were born in urban area (5.3%) had fetal macrosomia as compared to the rural infants (5.1%). The prevalence of fetal macrosomia is high in Oromia region (2%), whereas it is low in Afar region (0.2%). The prevalence of fetal macrosomia in mothers who are rich based on wealth index, post-term during pregnancy, overweight and single pregnancy were is high (7.4%, 8.8%, 6.4% and 10.3%), respectively, as compared to the other categories.

A chi-square test was performed to assess the heterogeneity among the regions of Ethiopia with respect to the prevalence of fetal macrosomia (Table 2). The test shows that there is regional variation for fetal macrosomia (p-value<0.001).

A smallest AIC value (AIC=1381.7) is obtained using the random intercept with fixed slope model as compared to the empty and random coefficient models (Table 3). This implies that the random intercept with fixed slope model suits the most to describe the factors associated with fetal macrosomia for the EDHS 2016 data.

The results in Table 4 shows that, empty model with random intercept used to test whether the overall prevalence of fetal macrosomia vary across the regions without including any covariates to the model. The variance of the random effect of the region (\( \sigma^2 = 0.512 \), p-value=0.034) reveals that there is a significant difference of fetal macrosomia across regions in Ethiopia. Interclass Correlation (ICC) is the correlation between two individuals in the same region. The computed ICC (0.512/(3.14+0.512))= 0.14 showed that 14% of the variation in fetal macrosomia can be explained by grouping the infants into the regions. The remaining 86% of the variation of in fetal macrosomia is explained within region/ variation between individual infants (Table 4).
Based on the fixed part of random intercept with fixed slope model the age of mothers, residence, mothers educational level, body mass index, gestational age, wealth index, multiple pregnancy and infant sex are found to be the significant factors associated with fetal macrosomia across the regions of Ethiopia (Table 5). The random part of random intercept with fixed slope model shows that the variance of intercept is 0.342 whereas the variance of intercept for the empty model is 0.512. The variance of the intercept is decreased when all covariates which are included in the model are fixed. That is, taking into account the fixed covariates, variables can provide extra predictive value on fetal macrosomia in each region. The significance of the random effect intercept variance (p-value=0.021) indicates that the regional variation with respect to the fetal macrosomia is significant (Table 5).

In this study, the odds of fetal macrosomia for urban infant is 33.2% (OR: 1.332, 95%CI: 1.018, 1.742) times more than infants born in rural area (Table 5). The odds of fetal macrosomia for an infant with his/her mother age between 25 and 34 years is 7.1% (OR: 0.929, 95%CI: 0.783, 1.103) times less than between 15-24 year. However, the odds of fetal macrosomia with mother age between 35 and 49 years is 36.3% (OR: 1.363, 95%CI: 1.242, 1.496) times more than between 15 and 24 years. Body mass index of mothers is also another key factor associated with fetal macrosomia. The odds of fetal macrosomia with normal mother body mass index and overweight/obesity were 17.1% (OR: 1.171, 95%CI: 0.628, 2.265) and 68.1% (OR: 1.681, 95%CI: 0.784, 3.627) times more than underweight mother, respectively. The odds of fetal macrosomia for post-term gestational age of infant is 21.0% (OR: 1.210, 95%CI: 0.925, 1.816) times than term infant. The odds of fetal macrosomia for mother with middle and rich wealth indices are 21.7% (OR: 1.217, 95%CI: 1.002, 1.477) and 32.5% (OR: 1.325, 95%CI: 1.086, 1.616) times more than that of the poor, respectively. Finally, the odds of fetal macrosomia for male infants is 38.3% (OR: 1.383, 95%CI: 1.029, 1.858) times more than the female infants (Table 5).

**Discussion**

This study intended to identify the regional variation and factors associated with fetal macrosomia in Ethiopia. Descriptive analysis, chi-square test and multilevel logistic regression analyses were used in this study. Multilevel ordinal logistic regression model allows to shows the regional variation and identify the factors associated with fetal macrosomia in Ethiopia. Before the analysis of data using multilevel approach, the researcher test variation of the levels of fetal macrosomia using chi-square test, and it was significantly showed that there is regional variation regarding fetal macrosomia in the regions. Results obtained based on the empty model
the overall variance of the constant term suggest that fetal macrosomia were differed across regions.

In addition to this, random intercept with fixed slope model is the best model to assess the regional variation and factors associated with fetal macrosomia in Ethiopia. The descriptive results of this study shows that the overall prevalence of fetal macrosomia was 10.4% which is relatively consistent with the studies in Ghana (9.69%)\textsuperscript{12} and in Hawassa (11.86%)\textsuperscript{13}, but it is higher than some studies in Africa; example a study in Tanzania (2.3%).\textsuperscript{14}

The result of multilevel logistic regression analysis reveals that the age of mother, place of residence, education level, wealth index, BMI, gestational age, multiple pregnancy and infant’s sex are found to be significantly factors associated with fetal macrosomia in Ethiopia. According to our analysis, the age of mother is the most risk factors associated with fetal macrosomia. It is indicated that the risk of fetal macrosomia was higher among elder women. This might be due to older women have strong and mature body that enables to withstand the stress and complication during pregnancy. This finding is consistent with the previous studies in Ethiopia.\textsuperscript{15,17}

The findings of this study also shows that the residence of mother is the most important factor of fetal macrosomia. Infants whose family lived in urban area are more likely to get fetal macrosomia than the rural area. This is the fact that women in urban area getting good life condition and had balanced diet that lead them to get overweight/obesity. However, one of the limitation of this study is that the EDHS dataset is not included influential factors such as nutritional factors and behavioral factors. So that, this study doesn’t incorporate the nutritional factors.

The result of this study is compatible with the finding of previous studies in Ethiopia.\textsuperscript{2,4,11,15} In this paper, it is found that the wealth index is significantly affects the fetal macrosomia. Infants with family from low economic class are more probable to get LBW and the higher economic class have high probability of getting fetal macrosomia. Higher economic class also associated with fetal macrosomia.\textsuperscript{16,21} Our finding reveals that BMI of mother is an important factor associated with fetal macrosomia. The results of this study shows that overweight (obesity) mother had more chance to get fetal macrosomia which is in line with studies.\textsuperscript{18,20,22}

Moreover, gestational age plays an important role in determining the infant weight at birth. Infants who are delivered in post maturely (>40 weeks), called post-term, have high chance to be fetal macrosomia. This is the fact that during the period of post-maturity, they gain excessive
fetal weight. The result of this study, as compared with pre-term gestational age prevalence of fetal macrosomia in post-term gestational age are high which is consistent with the previous studies in Northern Ghana, in Tanzania, and in Tigray region, Ethiopia. Moreover, this study shows that sex of infant is the most factor associated with fetal macrosomia. The study reveals that, male infants are more probable to get fetal macrosomia. There is biological reasons which could expose male infants to excessive weight gain during pregnancy. This findings is line with the previous studies conducted in Ghana and in different area of Ethiopia.

Conclusion
Random intercept with fixed model is the best model to assess regional variation and factors associated with fetal macrosomia. Based on best model (random intercept with fixed slope), the age of mother, residence, educational level of mother, body mass index of mother, gestational age, wealth index, multiple pregnancy and the infant sex are the significant factors associated with fetal macrosomia in all regions of Ethiopia. The study reveals that infants from urban area, older women (35-49 years), overweight/obesity women, infants born at post-term gestational age, from high economic class and who are male had high probability to be fetal macrosomia.

Declarations

Abbreviations
AIC: akaike information criteria; BMI: body mass index; CI: confidence interval; CSA: central statistical agency; ICC: interclass correlation; EDHS: Ethiopian demographic and health survey; LBW: low birth weight; OR: odds ratio; WHO: World health organization.

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Conflicts of interest
The authors declare that there is no conflict of interest.

Author’s Contributions
GN conceived the idea. GN, AB and JA contributed to the design and extraction of the data; analysis. GN drafted the manuscript. All authors read and approved the manuscript.

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There was no direct fund for this study.
Ethics approval and consent to participate

The study involves secondary use of data which is collected by the Central Statistical Agency (CSA) of Ethiopia. The data we obtained is anonymized data with no personal identifiers. To obtain this data from CSA, we get written ethical approval from the Institutional Research Ethics Review Committee of the College of Natural Sciences, Jimma University.

Availability of data and materials

All data analyzed during this study are included in this paper with its supplementary information and on MEASURE DHS website.

Consent for publication

Not applicable.

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