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Prevalence of anemia and its associated factors among pregnant women in Georgia

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Abstract

Introduction

The WHO currently considers maternal anemia global public health concern, and one of the most common complications during pregnancy. Symptoms range from weakness and fatigue, to serious cardiac complications. Maternal anemia also poses a risk to the infant, as it can increase the likelihood of preterm birth and low birth weight babies, among additional concerns. Past research is primarily focused on low and middle-income countries. Georgia is an upper-middle income country located at the intersection of Europe and Asia, and a country that has experienced rapid social and economic growth in the last two decades. Presently, there is no national study regarding the prevalence of maternal anemia in Georgia.

Objective

The objective of this thesis is to establish the prevalence of maternal anemia in Georgia, and to determine the associated factors of its presence.

Materials & methods

This cross-sectional study consisted of women who delivered in Georgia in 2019, using data from the Georgian Birth Registry. This included all women who had serum hemoglobin measured at least once during their pregnancy, with a final population of n=35,677. Anemia was categorized according to WHO guidelines into mild, moderate, and severe, and compared with several associated factors using descriptive statistics. The relationship between the associated factors and the presence of maternal anemia was analyzed using logistic regression.

Results

This study identified a 42% prevalence of maternal anemia in Georgia. Among anemic mothers, 61% were mildly anemic, 36% moderately anemic, and 3% severely anemic. Significant associated factors of anemia presence included 1 previous birth (OR 1.19 [1.14-1.26]), and 2 or more previous births (1.23 [1.16-1.31]), as well as underweight BMI (OR 1.12 [1.03-1.21]). Higher education (OR 0.85 [0.81-0.89]) and maternal age greater than 25 (OR 0.9 [0.85-0.94]) or maternal age greater than 35 (OR 0.89 [0.82-0.96]) were associated with lower presence of anemia.

Conclusion

This study identified that maternal anemia is a serious maternal health concern in Georgia. Several associated factors of maternal anemia presence were identified. The findings of this study may be beneficial for policy workers and healthcare providers interested in preventing and treating maternal anemia within Georgia.

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List of abbreviations

AOR	Adjusted odds ratio
BMI	Body mass index
COR	Crude odds ratio
CI	Confidence interval
GBR	Georgian birth registry
Hb	Hemoglobin
LMICs	Low-to-middle income countries
OR	Odds ratio
SGA	Small for gestational age
REK	Regional Committee for Medical and Health Research Ethics
WHO	World Health Organization

List of definitions

Arrhythmia	The rate or rhythm of the heart is too fast, too slow, or irregular
Hemodilution	Increase in blood plasma in relation to red blood cells
Hemorrhage	Loss of blood from damaged blood vessels
Hypotension	Low blood pressure
Pallor	An unhealthy, pale appearance
Parity	Number of births after 22nd gestational week
Perinatal mortality	Stillbirths and deaths of the neonate in the first week of life
Tachycardia	Rapid heart rhythm

1. Introduction

1.1 Anemia

Anemia is a medical condition represented by decreased levels of red blood cells, or the oxygen-carrying protein, hemoglobin (Hb), which resides within them. A reduced presence of red blood cells will lead to inadequate oxygen levels in the body's tissues, causing an array of symptoms, primarily fatigue and weakness (1). Low oxygen carrying capacity of the blood reduces the metabolic capacity of these tissues (2), and the inability to metabolize properly is inhibited proportionally to the severity of the anemia. Common symptoms of anemia include shortness of breath, weakness, irregular heart rhythms, pallor, hypotension, and even chest pain or heart failure, depending on the type and severity of the diagnosis (3). Causal factors of anemia include iron deficiency, micronutrient (folate and vitamin B-12) deficiency, rare genetic disorders, or severe infections during pregnancy, such as malaria (4). Acute anemia can also occur after a sudden blood loss or hemorrhage, requiring a blood transfusion to replenish blood volume (5).

The development of anemia can occur in individuals from any background, but it disproportionately affects women and children globally (6), as it is most often a micronutrient deficiency disorder. For women of childbearing age, development of anemia during pregnancy is a risk to both the mother and the fetus, and is one of the most common complications of pregnancy worldwide. The World Health Organization (WHO) currently estimates that over 40% of pregnant women worldwide are anemic at some point during their pregnancy (7).

1.2 Anemia during pregnancy

Anemia is diagnosed via a blood test, most often by measuring an individual's serum Hb levels via a blood sample. The WHO categorizes anemia into mild, moderate, and severe categories based on the related serum Hb concentrations (6). For non-pregnant females, a Hb sample below 12.0 g/dL is considered anemic within these recommended guidelines. However, during pregnancy, a woman experiences hemodilution of the blood as blood plasma increases to compensate for the demands of a growing fetus, but red blood cells do not multiply in equal proportion with the increased blood volume (8). This causes the hemodilution and the following relative mild anemia that is expected and normal throughout pregnancy (9), prompting lower hemoglobin levels required for an anemia diagnosis during pregnancy. For a pregnant woman, anemia is therefore diagnosed after Hb readings lower than 11g/dL; specified by mild anemia (Hb 10.0-10.9 g/dL), moderate anemia (Hb 7.0-9.9 g/dL), and severe anemia (Hb $<$ 7.0 g/dL) (6) according to the WHO classification system (6).

In addition to the general mild anemia that is expected while a mother is pregnant, the growing fetus demands increasing amounts of nutrients from the mother's blood supply that will alter hemoglobin levels by trimester (8). These levels differ by trimester due to the increased blood demand from the growing baby, and the corresponding hemoglobin values to diagnose anemia reflect this. In both the first and third trimester, an Hgb of 11.0 g/dL remains the cutoff point for diagnosis with mild anemia. In the second trimester, this criterion is lowered to 10.5 g/dL for mild anemia diagnosis due to the rapid plasma expansion during these months as the fetus grows (6, 10).

While a diagnosis of mild anemia can present symptoms of increased weakness and fatigue, development of moderate or severe anemia during pregnancy can cause hypotension, tachycardia, and risk for maternal infections after birth due to hemorrhage or excessive bleeding (11). The amount of postpartum hemorrhage is directly linked to hemoglobin levels prior to labor, and severe postpartum hemorrhage can lead to death if not promptly treated (12). Maternal anemia also impacts the newborn, as there is higher risk for preterm births, small for gestational age (SGA) babies, or low birth weight births (13). The risk for these complications and additional adverse events increases in proportion to the severity of the mother's anemia (14).

During pregnancy, the most common form of anemia is iron deficiency anemia due to lack of proper nutrition, causing over 75% of maternal anemia (15). There is an increased demand for iron during pregnancy; due to this, anemia may develop from dietary deficiencies of iron, gastrointestinal complications that affect iron absorption, or short intervals between multiple pregnancies (16). A developing fetus requires iron from the mother, reducing the mother's natural iron stores and potentially leading to development of anemia. Additional associated factors of anemia development during pregnancy have been found to be maternal age, multiple pregnancies within a short time, and socio-demographic and lifestyle factors of the mother (17, 18).

Iron deficiency anemia contributes to 22% of maternal deaths and 24% of perinatal deaths globally (19). In a large WHO multi-country survey, women with severe anemia were found to have twice the risk of death during or after childbirth (20). The risks from maternal anemia are classified as a global public health concern for both the mother and newborn, leading the WHO to encourage decreased rates of anemia in women of reproductive age by 50% in 2025, via the Global Nutrition Targets (21). Notably, most cases of maternal anemia can be addressed with proper nutrition or micronutrient supplementation (22), reducing adverse outcomes for the newborn during both pregnancy and birth.

Currently, much global research on maternal anemia has been focused on low and middle-income countries (LMICs) (23), as there is a large disparity between prevalence and severity of anemia depending on a country's demographic level and the subsequent nutritional deficits that often coincide. A systematic review of global anemia in pregnant women found prevalence of anemia to be 14% in high-income countries of Europe, compared with 53% of pregnant women in south Asia (24), and such trends are mirrored worldwide based on a country's socioeconomic development status (25, 26).

1.3 Anemia in Georgia

The country of Georgia is located between Eastern Europe and Central Asia, with a population of approximately 3.7 million in 2021 (27). Approximately half of the country's population lives in an urban setting, and over 30% lives within the country's capital district, Tbilisi (28). Georgia was formerly within the Soviet Union, and the country declared independence in 1991 amidst a turbulent political transition. After a difficult beginning, stabilization and economic reform in the late 1990s lead to rapid social and economic development that continues today (29). Georgia has made notable movement in continuing this growth, and as of 2020, Georgia is classified by the World Bank as an upper-middle income country (27).

Healthcare is provided under a universal healthcare system and almost all expectant mothers, over 99%, give birth in a hospital setting regardless of geographic location (30). Since 2018, the government covers eight prenatal care visits for all pregnant women if they initiate prenatal care before week 12 of the pregnancy. Delivery costs are also covered, regardless of the time prenatal care was initiated. [Personal communication, T. Manjavidze, May 25th, 2021]. Despite the availability of healthcare coverage and high proportion of hospital births, Georgia has a high perinatal mortality rate compared to most high-income countries. Most recently, 12.1 deaths per 1,000 births were recorded in 2019 (30); almost four times the average in the EU during the same period (31). There is also a high maternal mortality rate, with 28.9 deaths per 100,000 live births in 2019 (30), also much higher than the EU average of 6 per 100,000 live births in the same year (32).

Previous research on anemia in Georgia has been limited to small geographic studies on various micronutrient disorders (33, 34, 35), and none of these studies regarded pregnant women as the primary population source. Currently, there is no national study concerning the prevalence of maternal anemia in Georgian women, or the associated factors that may lead to the development of anemia during pregnancy within this population.

1.4 Aim and objectives

The aim of this study is to explore these questions:

> *What is the prevalence of maternal anemia among pregnant women in Georgia, and what are the associated factors for its presence?*

The specific objectives include:

- To establish the prevalence of anemia among pregnant women in Georgia.
- To analyze the relevant associated factors related to the presence of maternal anemia in Georgia.

2. Materials & Methods

2.1 Study design

A cross-sectional study design was used. The study was conducted using pre-existing electronic health medical record data from the national Georgian Birth Registry (GBR). Data were used from all women who delivered in the country of Georgia during the year 2019, and who had Hb measured at least once during their pregnancy. Data include demographic, socioeconomic, and health data from the participants measured at prenatal visits throughout the pregnancy. Maternal anemia prevalence and the significance of chosen associated factors were analyzed using descriptive statistics, univariate regression, and multivariable logistic regression analysis.

2.2 Data collection: The Georgian Birth Registry

The Georgian Birth Registry is a national electronic database introduced in Georgia in 2016, in collaboration with UNICEF (36). It was modeled after the national-based Nordic birth registries, and developed to record maternal and newborn health throughout the pregnancy and delivery (37). The GBR includes multiple variables regarding the woman's demographics and health from conception up to the infant's birth, and until discharge from the hospital (38). Filling the GBR is mandatory for healthcare workers, and with over 99% of women in Georgia giving birth in a hospital setting, the birth registry should therefore be representative of the true population of pregnant women (30). The GBR also includes records of hemoglobin levels of expecting mothers during pregnancy, offering the opportunity to research the impact and presence of maternal anemia within Georgia.

2.3 Study population

The population for this study includes women in Georgia who delivered during the year 2019, and who have their information recorded in the GBR (n=47,472). For the purpose of this study, all women who had one or more biologically plausible Hb value recorded during their pregnancy were included in the final study population.

Exclusion criteria consisted of women with chronic anemia due to a previous attributable disorder. Though underreporting of such chronic conditions is a concern with the GBR, few mothers found with the inherited thalassemia trait (n=6) were removed, and one mother found with bone marrow suppression was removed (n=1), as both are causes of chronic anemia that would influence Hb concentration prior to pregnancy (37). Women who had delivered abroad were excluded (n=21). Women were also excluded due to entirely missing Hb data. This included those who had *no* recorded visits during pregnancy (n=2224) and those who did have recorded visits, but lacked any recorded Hb entries (n=5356), giving a total of 7580 women excluded for missing Hb data. A number of women had Hb recordings, but their levels were biologically implausible Hb values, and were thereby also excluded from the final population (n=4188). If a woman had one biologically implausible value during her pregnancy, but the remainder of the values was biologically plausible, the implausible value was removed and the woman was still included in the final analysis. A woman was removed from the final analysis if she had *only* biologically implausible Hb recordings. In total, 35,677 women were included in the final data analysis (Figure 1).

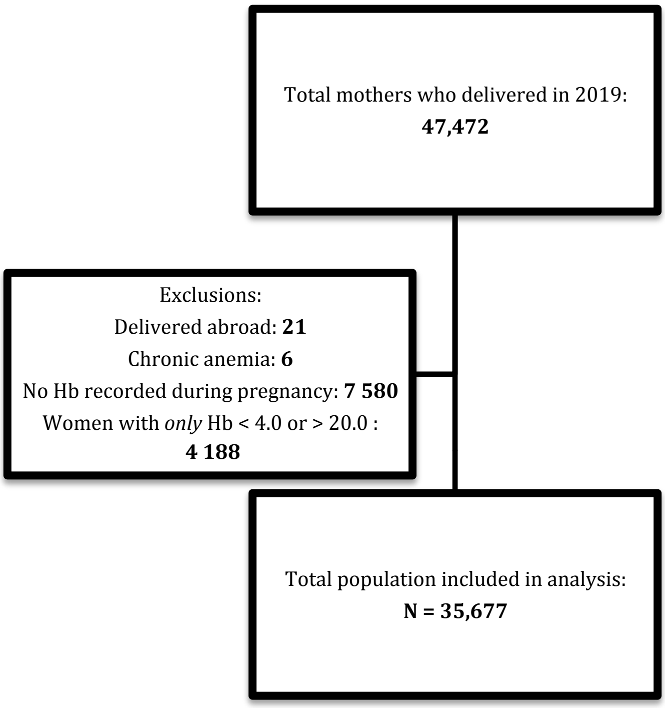

Figure 1. Flowchart of inclusion and exclusion criteria

2.4 Variables

All variables were recorded in the GBR and were selected based on review of current literature due to their relationship with maternal anemia. The study includes one primary outcome variable, with several predictor variables.

2.4.1 Outcome variable

The outcome variable in this study is the presence of anemia, measured by serum Hb concentration (g/dL). For descriptive statistics, Hb level was further stratified into mild (Hb 10.0-10.9 g/dL), moderate (Hb 7.0-9.9 g/dL), severe (Hb $<$ 7.0 g/dL), and no anemia (Hb $\geq$ 11.0 g/dL) based on the WHO recommendations for anemia classification (6). As women in the second trimester have a differing classification for the presence of mild anemia, (10.5 g/dL instead of 11.0 g/dL), this is accounted for in the data analysis. Any Hb concentration obtained during the second trimester was categorized based on the classification of 10.5 g/dL as the cutoff for diagnosing mild anemia. For women with multiple Hb readings taken during the pregnancy, the lowest recorded value was used to represent the presence of anemia.

In regression analysis (section 3.3), anemia level was treated as a binary variable coded as 1 = any anemia (Hb < 11.0 g/dL, or Hb < 10.5 g/dL if recorded in the second trimester) and 0= no anemia (Hb ≥ 11.0 g/dL).

2.4.2 Predictor variables

Predictor variables included in this study are maternal age, body-mass index (BMI), parity, and maternal education.

Maternal age is defined as the mother's age at the time of delivery. Age is treated as a categorical variable in both descriptive statistics and regression analysis, with age categorized into the following: < 18, 18-24, 25-34, and ≥35 years old. No cutoffs to age were applied, as all ages in the study population were biologically plausible and fit to be included in the analysis. There was no missing information in this variable.

Body mass index (BMI) was categorized into weight groups according to the WHO's classification system: underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), and obese (30.0+ kg/m^2) (39). BMI was calculated using the woman's measured height and weight at the first prenatal appointment, which overwhelmingly occurred during the first trimester (95.5%) before significant weight gain may influence the results. Extreme and biologically implausible BMI values (< 15.0 or > 60.0 kg/m^2), were excluded; a total of 66 women, and these were coded as missing data.

Parity is the total number of times a mother has given birth at gestational week 22 or later. Parity is categorized into 0 (nulliparous), 1, and 2 or more previous births. There was no missing data for this variable.

Maternal education was categorized into primary, secondary, higher, and unknown levels of education. There were no missing data for this variable.

2.5 Statistical Analysis

All data analysis were conducted using R-studio software, version 1.3.1073.

2.5.1 Descriptive Statistics

Descriptive statistics were applied to understand the prevalence of maternal anemia in the study population, as well as the characteristics and demographics of the study participants.

All mentions of prevalence of maternal anemia calculated in this thesis refer to *period prevalence*, or the proportion of a population that has a certain condition over a given period of time. In this case, period prevalence of maternal anemia is calculated for all women who delivered in 2019. To first determine the prevalence, Hb was categorized into no anemia, mild anemia, moderate anemia, and severe anemia based on Hb levels per WHO's guidelines (6), and displayed as percentages of the total study population. The prevalence was further assessed by geographic region, to assess anemia distribution throughout the country. The additional descriptive statistics (age, BMI, parity, and education) were categorized accordingly and included to display the proportion of anemic mothers within each independent variable.

2.5.2 Univariate analysis

Predictor variables age, BMI, parity, and education were analyzed individually with serum Hb level in univariate analysis to determine the relationship between the specific predictor variable and presence of maternal anemia. Results are presented with crude odds ratios (ORs) and 95% confidence intervals (CIs).

2.5.3 Multivariable analysis

Multivariable logistic regression was applied to the dichotomous outcome variable, presence of anemia, in association with the predictor variables (age, BMI, education, parity) included in the univariate model. Predictor variables that were significant in the univariate analysis at the 0.25 level were included in the multivariable model. Multicollinearity was checked for, using the variance inflation factor (VIF) < 5 as problematic (40). The model was checked for goodness-of-fit using the Hosmer-Lemeshow test. The results were presented with adjusted ORs with 95% CIs.

2.6 Missing Data

There were 7580 women in the GBR who had a total absence of Hb recordings during their pregnancy. These women were therefore not included in the final population.

Of the women with at least one Hb value, 4188 women had Hb values that were biologically implausible, either Hb < 4.0 g/dL or Hb > 20.0 g/dL. If a woman had multiple readings, those with one or more biologically plausible readings within Hb 4.0 to Hb 20.0 were still included in the study. It is unknown why there were so many of these implausible readings within this variable. When the 4188 cases were examined using a sensitivity analysis, there were no significant differences between the women that were removed and the women that were included in the study (Appendix 1). Mean age and parity, median BMI, and education status were almost identical in both groups of women. Therefore, it is plausible that removing these women created little bias in the final results.

There were very little missing data within the geographical region variable, with only 5 women having missing information, less than 0.01% of the total study population. The BMI variable also had 0.01% biologically implausible values, that upon further examination did not significant differ from the rest of the population. Therefore, these values were coded as missing.

2.7 Ethical considerations

This study used pre-existing data from the GBR, where registered data is mandatory for pregnant women in Georgia and health personnel handle all entry of the data. There are no personal identifiers in the data, as any characteristics are removed and individuals are represented by codes. All data are stored on a password-protected computer and held on a password-protected USB port, and will be removed after completion of the thesis. There is no risk or harm on any individuals as a result of this thesis. The Regional Committee for Medical and Health Research Ethics (REK) of Northern Norway concluded no permission is necessary for use of the data (2017/404/REK Nord).

3. Results

3.1 Prevalence of anemia

The study population consisted of 35,677 women, all of whom had at least one Hb value recorded during their pregnancy. The outcome variable, anemia, was divided into three groups according to diagnostic criteria: mild, moderate, and severe anemia (Figure 2). Accordingly, 42% of women who delivered in 2019 were classified as anemic for at least one Hb recording during their pregnancy; 26% of the total population with mild anemia, 15% with moderate, and 1% with severe (Table 1).

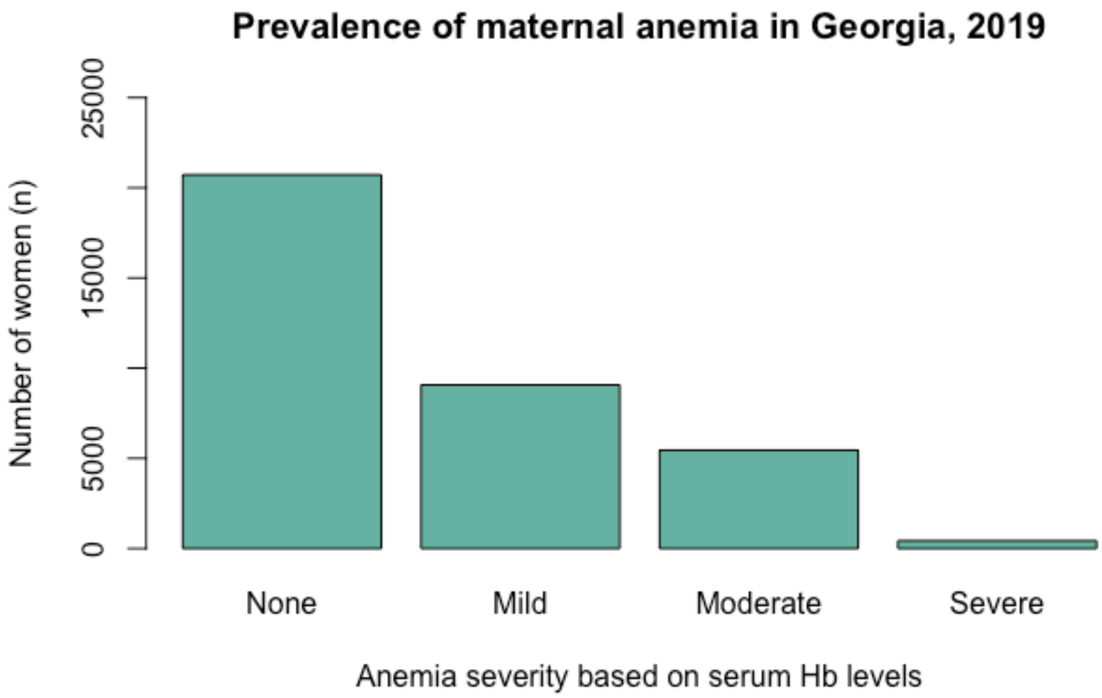

Figure 2. Prevalence of maternal anemia in 2019

Table 1. Prevalence of maternal anemia in 2019

Anemia Classification	Frequency (%)
No anemia (Hb > 11.0 g/dL, or > 10.5 in 2nd trimester)	20,721 (58)
Mild anemia (Hb 10.0 - 10.9 g/dL, or to 10.5 in the 2nd trimester)	9071 (26)
Moderate anemia (Hb 7.0 – 9.9 g/dL)	5453 (15)
Severe anemia (< 7.0 g/dL)	432 (1)
Total (n)	35,677

3.2 Demographic characteristics

The mean age of mothers at the time of delivery was 28.6 (±5.7), with the mean age slightly lower in anemic mothers, at 27.9 years. In comparison to all age groups, women aged 18-24 had the highest prevalence of anemia, at 43%. 54% of expecting mothers were in the 25-34 age category.

Nearly 40% of mothers in the study had completed higher education, and in comparison to those with primary, secondary, or unknown education, they also had the lowest percentage of anemia as a group, with 39% considered anemic. The highest percentage of anemia was in the unknown education group, with 46% anemic, and this group represents 13% of the total study population.

40% of mothers in this study were nulliparous, meaning the pregnancy considered during the study was the mother's first delivery after 22 weeks gestation. Mothers who had 2 or more prior deliveries after 22 weeks had the highest percentage of anemia, at 43%. First-time deliveries had the lowest, with 40% of women anemic.

Women with underweight BMI had the highest prevalence of anemia, with 46% of underweight women having anemia. Over half of women in the study were of normal weight, with the median BMI at 22.9. Only 11% of women were categorized as obese, and this category also had the lowest percentage of anemic mothers, with 37% considered anemic.

Georgia consists of 12 administrative regions. In this study, 36% of women resided in Tbilisi, the country's capital city. The highest percentage of anemic mothers resided in Samegrelo and Zemo Svaneti, a total of 55% of women in the region. However, only 5% of women represented in the study resided in this region. For regions where 10% or more of study participants resided, the highest percentage of anemic women lived in Imereti, at 51%. The lowest distribution of anemic mothers, 27% anemic, occurred in the Samtskhe-Javakheti region. Again, this is a small portion of the total study population, with 4% of women residing in this region. For regions where 10% or more of study participants reside, the lowest percentage of anemic mothers reside in Tbilisi, with 39% of women considered anemic (Table 3).

Table 2. Demographic characteristics of women who delivered in 2019

Age	**Anemia level (%/n)**			**Any Anemia** Hb < 11.0 g/dL, or < 10.5 in the 2nd trimester	**Total**
Mean(SD)				27.9(5.7)	28.6(5.7)
	Mild	Moderate	Severe		n (%)
< 18	26	15	1	42	631(2)
18-24	26	16	1	43	11,040(31)
25-34	25	15	1	41	19,411(54)
35+	24	15	1	40	4,595(13)
					35,677
Education					
	Mild	Moderate	Severe		
Primary	25	16	1	41	2,381(7)
Secondary	26	16	2	44	14,675(41)
Higher	25	13	1	39	13,797(39)
Unknown	25	19	2	46	4,824(13)
					35,677
Parity					
Mean (SD)				1.92(0.94)	1.89(0.94)
	Mild	Moderate	Severe		(%/n)
0	25	14	1	40	14,507(40)
1	26	16	1	43	13,051(37)
2+	26	16	1	43	8,119 (23)
					35,677
BMI					
Median(25th – 75th %ile)				22.9 (20.6-25.9)	23.1 (20.7-26.2)
	Mild	Moderate	Severe		(%)
Underweight	28	17	1	46	2,535 (7)
Normal	26	16	1	43	21,505 (60)
Overweight	25	14	1	40	7,636 (21)
Obese	23	13	1	37	3,935 (11)
					35,611*

*Does not add to total N due to missing values

Table 3. Prevalence of maternal anemia by region of residence

	Anemia (%) (Hb < 11.0 g/dL, or 10.5 g/dL in 2nd trimester)	Total N (%)
Region		
Abkhazia	45	199 (0.5)
Adjara	47	3,744 (11)
Guria	45	794 (2)
Imereti	51	4,874 (14)
Kakheti	35	2,350 (7)
Qvemo Qartli	43	4,088 (11)
Mtskheta-Mtianeti	35	644 (2)
Racha-Lechkhumi & Kvemo Svaneti	40	198 (0.5)
Samegrelo and Zemo Svaneti	55	1,904 (5)
Samtskhe-Javakheti	27	1,593 (4)
Shida Qartli	36	2,326 (7)
Tbilisi	39	12,958 (36)
		35,672*

*Does not add to total N due to missing values

3.3 Logistic regression

Age, education, parity, and BMI were all found to be significantly associated with presence of anemia in the univariate analysis, and therefore included in the multivariable model.

In multivariable analysis, all age groups had an inverse relationship with development of anemia in comparison to ages 18-24. There was a significant inverse relationship with the development of anemia in women above age 25 and 35 (OR 0.9 [0.85-0.94] and OR 0.89 [0.82-0.96], respectively) compared to women ages 18-24, meaning that women above age 25 were 10% less likely to develop anemia during their pregnancy. Having an age under 18 did not significantly alter the odds of anemia compared to ages 18-24. Women with higher education had a significant inverse relationship with anemia development, with a 15% decreased chance of anemia development compared to those with secondary education (OR

0.85 [0.81-0.89]). Multiparous women were significantly associated with an increased development of anemia compared to nulliparous women, with 1 prior birth having a 19% increased presence of anemia (OR 1.19 [1.14-1.26]), and 2 or more prior births with a 23% increased presence of anemia (1.23 [1.16-1.31]). Lastly, underweight women were significantly associated with a 12% increased risk of anemia compared to normal weight women (OR 1.12 [1.03-1.21]). Overweight and obese women (OR 0.89 [0.84-0.94] and OR 0.76 [0.71-0.81], respectively) had a decreased chance of presence of anemia than normal weight women.

The results from both univariate and multivariable analysis are displayed below in Table 4.

Table 4. Regression analysis: Odds ratios with 95% confidence intervals.

		Univariate analysis COR (95% CI)	Multivariable analysis AOR (95%CI)
Maternal age			
	< 18	0.92 (0.78-1.09)	0.96 (0.81-1.14)
	18-24	Reference	Reference
	25-34	0.91 (0.87-0.95)	0.9 (0.85-0.94)
	≥35	0.88 (0.82-0.94)	0.89(0.82-0.96)
Education			
	Primary	0.93 (0.85-1.01)	0.9 (0.82-0.99)
	Secondary	Reference	Reference
	Higher	0.83 (0.79-0.87)	0.85(0.81-0.89)
	Unknown	1.13 (1.06-1.2)	1.14(1.07-1.22)
Parity			
	0	Reference	Reference
	1	1.15 (1.1-1.21)	1.19(1.14-1.26)
	≥2	1.15 (1.09-1.22)	1.23(1.16-1.31)
BMI			
	Underweight	1.11 (1.02-1.21)	1.12(1.03-1.21)
	Normal	Reference	Reference
	Overweight	0.9 (0.85-0.95)	0.89(0.84-0.94)
	Obese	0.78 (0.73-0.84)	0.76(0.71-0.81)

4. Discussion

4.1 Main findings

This study identified that 42% of pregnant women in Georgia who delivered in 2019 had Hb measurements classified as anemic at least once during their pregnancy. Among the women who were anemic, 61% were mildly anemic, 36% were moderately anemic, and 3% were severely anemic. Georgia's most populated region, Tbilisi, had a 39% prevalence of maternal anemia, lower than the national average found during this study. Significant associated factors of presence of maternal anemia include multiparity and underweight BMI. Higher education and maternal age 25 and above were associated with lower presence of anemia.

4.2 Prevalence of anemia in Georgia

The WHO currently estimates that 40% of pregnant women globally are affected by maternal anemia (41), placing Georgia near the current global averages. However, there is a sharp discrepancy between high and low-income countries when further analyzing global anemia prevalence (42). Among LMICs, there is a higher prevalence of anemia in comparison to high- income countries according to the WHO: in 2019, high-income countries averaged 17% maternal anemia, and low-income countries approximately 42% (42). The World Bank also reported the average maternal anemia prevalence in upper-middle income countries to be 24.5% in 2019 (43). Overall, the 42% prevalence of anemia in Georgia is higher than estimated averages from countries of similar income status, and instead reflects numbers seen in low-income or lower-middle income countries (44).

Other upper-middle income countries geographically close to Georgia include Armenia and Azerbaijan, both of which directly border Georgia (45). The prevalence of maternal anemia in Armenia was approximately 18% in 2019 according to the World Bank, and in Azerbaijan it was estimated at 35% in the same year (46). Georgia appears to have somewhat elevated prevalence of maternal anemia in comparison to its neighboring countries of similar income status; however, it is worth noting that Georgia is the only country of these mentioned that has a comprehensive birth registry detailing medical statistics for nearly every pregnant woman in the population. Therefore, the data underlying this study's statistics regarding maternal anemia are likely more comprehensive than other countries of similar income or development. Additionally, in this study the prevalence of maternal anemia was calculated for all women who gave birth in the year 2019, rather than at a single point in time. The prevalence of anemia within Georgia itself was significantly higher in this study than current data estimates indicate from both the WHO and the World Bank suggest. Both databases currently estimate the prevalence of maternal anemia in Georgia in 2019 is approximately 28%. This suggests that rates of anemia may also be underestimated for other countries, due to differences in methodology or data collection methods.

The prevalence of anemia within Georgia differed regionally in this study, ranging from 27% to 55%. As maternal anemia is vastly due to nutritional deficiencies (47), the mother's diet before and during pregnancy is possibly associated with the presence of anemia. Geographically, 80% of Georgia is mountainous, with historically self-contained regions and customs (48), and a variety of food preparation and diet practices within different regions. Regional diet practices and variety of local food availability possibly accounts for some of the difference in anemia prevalence from region to region. However, Georgia may also follow the global pattern, where a cheaper, nutrient-poor diet is increasing in rural or impoverished communities where imported and unhealthy foods are easily available (49). This change to less nutrient-dense food may be another possible explanation for the higher rates of maternal anemia within the country. Malnutrition is still a concern in Georgia (50), and in regions of increased poverty or inequality, food availability and food quality possibly contributes to higher prevalence of anemia. However, information on a mother's diet was not available in this study, so these are only possible explanations for the regional differences seen.

Tbilisi, one of Georgia's 12 regions and also home of the country's capital city of the same name, is the most populated region in Georgia, both by numbers and population density (51). Women here had a low prevalence of maternal anemia in comparison to most other regions of the country – 39% of women in this region had anemic Hb values measured at least once during the pregnancy. Additional regional differences included the next-highest populated regions, Imereti and Adjara, with prevalence of 51% and 47%, respectively. Socioeconomic disparities may contribute to maternal health, so differences within regions may be linked to lifestyle and cultural differences from region to region. However, both regions Imereti and Adjara have a high human development index score (52), so reasons for the high prevalence found in both areas are undetermined.

The current nutritional guidelines from Georgia's National Center for Disease Control were dated from 2005 (53). These guidelines acknowledge that anemia is a concern in Georgia, citing this may be due to poor nutrition, and suggest eating the recommended 30mg/day of iron for pregnant women (15). There is no mention of prenatal vitamin supplementation within the guidelines themselves, though iron and folic acid medicine is covered by Georgia's maternal and child state program [Personal communication, T. Manjavidze, May 25th, 2021]. The WHO recently released updated maternal health recommendations in 2020, stating that multivitamin supplementation in pregnancy is recommended, particularly iron and folic acid vitamins in areas where maternal anemia is a concern. The WHO also considers a prevalence of anemia greater than 40% in a given region to be a severe public health concern (54). In areas at severe risk for anemia, as Georgia is under these conditions, the updated recommendation for iron intake during pregnancy is 60 mg/day, which is an amount that is typically achieved through supplementation (55). Therefore, Georgia's current nutrition recommendations appear to be outdated and do not reflect the severity of maternal anemia within the country. Consideration of the WHO's updated guidelines for supplementation before and during pregnancy may be of importance in Georgia. Adequate nutrition and supplemental vitamin use prior to conception may be an area of improvement within Georgia's maternal health field.

In addition, a common successful pathway to combating anemia within at-risk populations is fortification of flour and bread products (56, 57, 58). Currently, wheat flour fortification is not mandated in Georgia. The WHO considers wheat flour fortification a global intervention for targeting malnutrition and anemia in women and children (59). Georgia presently has the potential to benefit from improved access to fortified flour products (60), as the country has high consumption of wheat and bread products (61). Wheat is the second largest agricultural import to Georgia, with large amounts of wheat flour imported from Russia (62). However, wheat flour fortification is not mandated in Russia (63). Thus, availability and consumption of fortified wheat flour may vary, particularly in areas where imported flour is regularly consumed. Since wheat flour fortification has been repeatedly shown to be a successful intervention in targeting anemia, and due to Georgia's high wheat consumption and lack of successful national wheat fortification, this is an area for potential improvement for addressing maternal anemia.

This study suggests that taking further action to address anemia during pregnancy may be of benefit to maternal health Georgia. While over half of anemic women in this study were found to be mildly anemic, having Hb levels below 11.0 g/dL are still a deviation from the generalized mild anemia expected during pregnancy, and this has an influence on the health of both the mother and infant (64).

4.3 Associated factors of anemia development

The associated factors of anemia development analyzed in this study followed patterns seen in previous research results.

Regarding the factor of maternal age, women above age 25 in this study were less likely to exhibit maternal anemia during their pregnancy in comparison to ages 18-24. This is consistent with previous studies (65, 66, 67), which suggest that younger mothers are more at risk for development of anemia during pregnancy than older mothers. Younger women are also more at risk for poor nutrition compared to older women, particularly in adolescence as rapid growth demands increased intake of nutrients, such as iron and folic acid (69). However, other studies have found that increasing maternal age also has increased risk for maternal anemia (68), although this was not a finding in this study for ages 25 and greater. Older age of mothers is associated with factors such as higher education and improved socioeconomic factors that decrease chance of developing maternal anemia, so this may contribute to lower chance of developing anemia as maternal age increases.

The BMI results from this study showed that over half of women in Georgia are considered of normal weight. This is a higher percentage of normal weight women than many high-income countries, which typically have a greater percentage of pregnant women categorized as overweight and obese than Georgia did in this study (70). Importantly, underweight women were found to be 12% more likely to present as anemic during their pregnancy. Past studies have indicated that underweight women are more likely to develop anemia (71). As malnutrition is still a concern in parts of Georgia (50), this is of interest as women may be underweight or malnourished before conception, and therefore at higher risk for development of maternal anemia later during their pregnancy. Further research on nutritional attributes of women of childbearing age prior to pregnancy, and regional diet differences within Georgia, would be of interest.

The association between parity and maternal anemia has been well studied. The findings in this study are comparable to previous studies suggesting that multiparty is associated with an increased risk for anemia (72, 73, 74). This study found 23% increased odds of having anemia for mothers who had 2 or more previous births over 22 weeks gestation, in comparison to mothers with no previous births over 22 weeks. Even 1 previous birth had a 19% increased risk for presence of anemia during the subsequent pregnancy. This is again an expected finding comparing to past research. According to these results, then, women with previous births are at higher risk for anemia development and may be candidates for more frequent, regulated Hb monitoring or nutritional supplementation if necessary.

Women who had completed higher education were 15% less likely to have a presence of anemia during their pregnancy. Higher education of mothers is correlated with reduced risk of complications during pregnancy (75), and also correlated with increased healthcare literacy in comparison to less educated mothers (76). Mothers with higher education are more likely to seek and understand healthcare information, including preventative measures for developing maternal anemia, which may explain results from this study. Education may also be linked to various socioeconomic factors such as income, adequate nutrition, and lifestyle factors that may contribute to a lower prevalence of anemia within this education category.

4.4 Strengths & limitations

The comprehensive nature of the GBR and the use of registry-based data, with nearly complete representation of pregnant women in Georgia, is a major strength of this study. The results of this study, therefore, can be generalized to Georgia's population of expecting mothers residing in the country, because over 99% of mothers in the country were represented in the registry. Hence, the representativeness of this study is strong when generalizing to the population of pregnant women in Georgia.

As data entry was often regarding objective data and entered by a healthcare professional, this prevents some degree of response bias or recall bias from the study participants. For example, height and weight used to document BMI were recorded in the healthcare setting rather than relying on the individual's recollection or self-reported data. All women delivering in the hospital setting were represented, preventing volunteer or selection bias within the population when data were recorded.

The primary outcome variable, the presence of anemia, is an objective measurement of serum Hb level in the blood. This objective measurement prevents information bias or leading questions influencing this variable, as it is obtained biologically and not via questioning from either the participant or the health professional recording the data.

A limitation of this study is the cross-sectional design and methodology. This prevented cause/effect relationships to be established between the presence of maternal anemia and the associated factors in this study; rather, it displayed the association between the chosen covariates and the presence of anemia or no anemia. Therefore, causal factors of maternal anemia within Georgia cannot be deduced from the present results and were considered beyond the scope of the study.

The findings of this study were in line with previous research studies. However, due to the methodology of the study design, there is likely overlap between associated factors in the multivariable regression analysis. For example, factors age and parity have a correlation, as the women who are older are likelier to have more children. It is worth considering the relationship between covariates when interpreting the study results. Furthermore, the strength of the odds ratios for the associated factors of this study were not extraordinary, meaning none of the associated factors examined were greatly protective against the presence of maternal anemia.

Some variables not available in the GBR would have been of interest in this study due to their relationship to both anemia and the chosen covariates. These include smoking status, which is underreported in the GBR [Personal communication, T. Manjavidze, February 1st 2021], and both income status and diet, which are not represented in the GBR. However, education is typically related to income status and was thus used in place of income. Having complete access to this currently unavailable information could confound results and would be of interest in future studies if availability or reliability of the variables later increases.

An additional limitation was the number of biologically implausible values of Hb that were removed in this study. It is unknown why there were so many implausible values, and the current estimation is that this is entry error by individuals imputing information to the GBR. When the women with biologically implausible Hb readings were removed and examined closer with a sensitivity analysis and descriptive statistics, there was no significant difference in demographic and descriptive characteristics between the women that were removed and those who were included in the study. However, improving accuracy in the recording of Hb data and data entry in general would be ideal, and the women removed from the study may still have had an influence on the final results of anemia prevalence, since their Hb readings and subsequent anemia status are currently unreliable and not included in this study.

However, based on the sensitivity analysis, it can be assumed this did not significantly bias the results. The GBR is a relatively new registry, and hence it will likely take time for data entry accuracy to improve. Action has been taken regarding this concern, and improvement of the Hb variable in the GBR is currently being addressed due to the findings from this study.

Because the GBR data are manually entered by healthcare workers, this introduces room for bias with data entry mistakes. This was seen in this study with the Hb variable discussed above. Due to methodology and the registry-based data use, there was no control in the data collection process, and therefore there may be inconsistencies between patient appointments and entry methods from healthcare personnel. These are expected limitations with registry-based data (77), but still have the potential to create bias in the final results.

5. Conclusion

This study identified a 42% prevalence of maternal anemia in the Georgian population, with regional differences within the country. As any prevalence above 40% is above the WHO's criteria for anemia as a severe public health concern, this is a finding worth addressing in Georgia. The associated factor findings were similar to past research, with underweight and multiparous mothers having a higher presence of anemia, and higher educated mothers, and those above age 25, having a decreased presence of anemia.

Based on current knowledge, this is the first prevalence study of maternal anemia in Georgia that represents the country's population of pregnant women. Therefore, the results from this study may have implications for policy makers or public health advisors when considering the prevalence of anemia within the country, and the treatment of pregnant women. Based on findings of nutritional and health guidelines for pregnant women currently available in Georgia, it would be beneficial to update nutrition and maternal anemia treatment protocol, with consideration to woman's nutrition prior to conception.

Further studies may look closer at associated factors of anemia development, particularly regional differences within Georgia. There is also opportunity to study the causal relationship between covariates and the development of anemia. Diet and nutritional differences on a regional basis would be of interest, as this would dictate the best avenue for policy makers and healthcare providers to focus on education and prevention. The hope of this study is that the results can be of use within Georgia, to assist in targeting and improving maternal health within the country.

Appendix

1. Descriptive statistics comparing women with implausible Hb values.

Descriptives comparing Hb without value limits and Hb with limits on < 4g/dL and > 20g/dL:

Hb w/o limits	**Anemia**	**No Anemia**	**Total**	**Hb with limits (<4 & >20)**	**Anemia**	**No Anemia**	**Total**
Total %	42	58			42	58	
Age: Mean (sd)	27.8 (5.7)	28.1 (5.8)	27.9 (5.7)		27.9 (5.7)	28.2 (5.8)	28.0 (5.7)
BMI Median (25^{th}-75^{th})	22.9 (20.6-25.9)	23.2 (20.8-26.45)	23.1 (20.7-26.2)		22.9 (20.6-25.9)	23.2 (20.8-26.4)	23.1 (20.7-26.2)
Parity Mean (sd)	1.91 (0.94)	1.89 (0.95)	1.90 (0.95)		1.92 (0.94)	1.87 (0.94)	1.89 (0.94)
Education %							
Primary (%)	42	58	2922 (7)		41	59	2,381 (7)
Secondary (%)	42	58	17192 (43)		43	57	14,675 (41)
Higher (%)	38	62	14612 (37)		39	61	13,797 (39)
Unknown (%)	47	53	5139 (13)		46	54	4,824 (13)
(n)			39,865				35,677

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