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Maastricht University

Faculty of Sciences

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Master of Statistics and Data Science

Master's thesis

Spatiotemporal trends in hemoglobin concentrations among pregnant women in Ethiopia: Using Geostatistical model-based analysis.

Gebrekidan Ewnetu Tarekegn
Thesis presented in fulfillment of the requirements for the degree of Master of Statistics and Data Science, specialization Quantitative Epidemiology

SUPERVISOR :
Prof. dr. Thomas NEYENS

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Abstract

Introduction: Anemia is defined as a low hemoglobin level in human blood cells, and among pregnant women. In low- and middle-income countries, including Ethiopia, it remains a major public health problem. It has a high impact on pregnant women's health, such as increased morbidity and mortality rates, and poor health-related quality of life. The prevalence of anemia in Ethiopia has varied across regions. This study aimed to conduct a model-based spacial analysis of hemoglobin concentration among pregnant women aged 15–49 years in Ethiopia and to select the new locations that could be added to the existing sample for the follow-up studies.

Methodology: Data from 645 locations across the 11 regions of Ethiopia in the Ethiopian demography and health survey database were extracted. A linear geostatistical model was used to assess the association of predictors such as body mass index, age, residence, and wealth index with the redaction of hemoglobin concentration levels among pregnant women. Spatial risk maps were constructed using the exceedance probability of a hemoglobin concentration level less than 110g/l. We utilized a spatially adaptive sampling technique for unsampled household locations in the study area.

Results: The average hemoglobin concentration among pregnant women in Ethiopia was 131g/l. Based on the geostatistical model that included important covariates, significant hot spot areas with risk of anemia were found in east, north, and central Afar, Somalia, Dire Dawa, Harari, and west Tigray regions of Ethiopia. Pregnant adolescents, pregnant women who lived in rural areas, pregnant women who were heads of households, those with low body mass index, and those coming from poorer families were significantly associated with the reduction of hemoglobin concentration levels among pregnant women in Ethiopia.

Conclusion: The risk of anemia among pregnant women aged 15–49 years varied across the country. Environmental, clinical, and socio-economic related variables were key determinants of hemoglobin level reduction among pregnant women in Ethiopia. To improve the certainty of model-based prediction of anemia among pregnant women in Ethiopia, additional sample locations from Afar, Dire Diwa, Harari, and Somalia region could be considered for the follow-up studies. This helps to develop and provide effective anemia intervention programs for pregnant women in Ethiopia.

Keywords: Adaptive sampling; Aneamia; Geostatistics; Linear geostatistical model

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List of Abbreviation

BMI	Body Mass Index
CI	Confidence Interval
CSA	Central Statistical Agency
DHS	Demography and Health survey
EAs	Enumeration Areas
EDHS	Ethiopia Demography and Health Survey
g/l	gram per letter
GPs	Geographic locations
Hgb	Hemoglobin concentrations
LMICs	Low and Middle Income Countries
LRT	Likelihood Ratio Test
MBG	Model-Based Geostatistics
McMC	Markov Chain Monte Carlo
MSE	Mean Square Error
PHS	Population and Housing Census
SA	Sensitivity Analysis
SSA	Sub-Saharan Africa
WHO	World Health Organization

1 Introduction

Anemia, characterized by low hemoglobin concentration (Hgb) insufficient to meet an individual's physiological requirements, is a common blood disorder affecting about one-third of the global population [32, 48]. The World Health Organization (WHO) Hgb cutoffs to define anemia are different for pregnant and non-pregnant women; for pregnant women, it is described as Hgb less than 110g/L and less than 120g/L for non-pregnant women [47].

Anemia during pregnancy causes decreased physical functioning and birth weight, preterm births, and maternal and perinatal deaths [39]. It is a severe public health burden in developed and developing countries, causing high morbidity and mortality rates in pregnant women. Pregnant women and children are more susceptible to this hematological abnormality than other human populations [13].

Anemia during pregnancy can decrease the Hgb concentration levels, affecting placental blood vessel formation, which may limit oxygen supply to the fetus and potentially lead to restricted fetal growth [5]. It is assessed by measuring Hgb concentration levels in the body rather than clinical symptoms, which are less observable than those associated with vitamin A deficiency and iodine deficiency disorders [23].

Menstrual bleeding, nutritional deficiencies of iron, acute or chronic blood loss, chronic disease, vitamin B12 deficiency, parasitic disease, and frequent pregnancy are the main causes of anemia during pregnancy. The types of anemia are more than 400; iron deficiency anemia, folate deficiency anemia, vitamin B12 deficiency anemia, and hemolytic anemia are the most common types of anemia during pregnancy [36, 22].

From the world population, around 1.62 billion people are anemic, and 46.3% of them live in low and middle-income countries (LMICs), specifically African and Asian countries. Pregnant women also contribute 38% of the global magnitude of anemia [33]. Due to differences in lifestyle, health-seeking behaviors, cultures, and socioeconomic status, anemia prevalence significantly differs among pregnant women. The evidence also showed that about 20% of maternal mortality was because of anemia during pregnancy [18].

In low and middle-income countries, lack of balanced nutrients contributes to the majority cause of anemia among pregnant women, as the global data shows [49]. It is a main and widespread health burden in developing countries, including Ethiopia, leading to various maternal complications and low birth weight, particularly during the 1^{st} trimester of pregnancy [8].

According to an Ethiopian Demography and Health Survey (EDHS) report, the magnitude of anemia among pregnant women in Ethiopia decreased by 10% from 2005 to 2011, however, it increased by 7% from 2011 to 2016, which indicates that the prevalence of anemia in Ethiopia is still growing more than expected [7].

It is important to assess this evolving landscape by defining patterns and associated factors of the spatiotemporal distribution of anemia during pregnancy at the zonal, regional, and national levels for optimal targeting of public health interventional policies. To the best of our knowledge, no previous studies have examined the changes in the anemia burden across Ethiopia over time by including important socio-demographic, environmental, and clinical-related variables.

The most important spatially-related variables that examine the effect of geographical locations on anemia like maternal, biometric measurements, and socioeconomic variables were included in the statistical analysis.

The EDHS data were collected using two stage sampling procedure by dividing the region of the country into 21 strata. However, the collected data was unbalanced across different regions, with insufficient data from the eastern part of the country. This imbalance of data affects the certainty of geostatistical model-based prediction of anemia.

Considering additional sample locations will improve the uncertainty of the geostatistical model-based prediction of anemia in this eastern part of Ethiopia. The most widely used sampling design in the application of risk disease mapping in a limited resource context for such inaccurate registry data is the adaptive sampling technique. Collecting data using adaptive sampling design helps identify target areas with high prevalence and identify which community and household level covariates influence these properties. Understanding these characteristics can guide the development of area-wide public health policymaking [16]. Based on the prediction geostatistical model framework, we select new locations in areas where representative data is not available using adaptive sampling design.

The main objectives of this study are: 1) geostatistical mapping of the distribution of hemoglobin concentration among pregnant women in Ethiopia; 2) identifying variables that are important for estimation in location for which the EDHS program does not collate enough data; and 3) identify potential new locations that could be added adaptively to existing sample for the follow-up studies.

2 Methods and Materials

2.1 Study area

Our research was conducted in Ethiopia, situated between 33° and 48° longitude 3° and 14.8° latitude in sub-Saharan Africa. It has the second-largest population in Africa next to Nigeria and, is categorized as a low and middle-income country. It is currently facing social, economic, political, and natural disasters. Recently, the Ethiopian House of Parliament approved the creation of three new regional states. Presently, Ethiopia is administered by 12 regional states and two city administrations, Addis Ababa, the capital city, and Dire Dawa. Furthermore, each regional state is organized into many zonal administrations.

2.2 Source of data

This study used the most recent 2016 EDHS data. We note that data from EDHS 2005 and 2011 were also available but not included in this study because data were not collected in all areas of the country. Several individual and community-level data were collected in the EDHS survey. The data were collected using two-stage sampling techniques and the 2007 and 1994 Population and Housing Census were used as a sampling frame for EDHS 2016 2011, and 2005 respectively. 21 strata were created by dividing each region into rural and urban areas. In the first stage from 21 strata, 645 Enumeration Areas (EAs) for EDHS 2016, 624 EAs for EDHS 2011, and 540 EAs for EDHS 2005 were selected. The selected EAs are proportional to each stratum and independent of each other. From the selected EAs households were selected using a systematic sampling technique in the second sampling stage.

2.3 Variables of the study

2.3.1 Dependent variable

Hemoglobin level of the pregnant women aged 15–49 years was used as the response variable in this study. It was measured using the "Hemocue blood hemoglobin testing system" after blood was collected using a finger prick [27].

2.3.2 Independent variables

Based on the available literature, numbers of covariates that have potential relationships with Hgb concentration of pregnant women were identified to be included in our study [60, 43, 44, 2, 34, 40, 23, 31, 62, 32]. Based on those studies, variables that affect the Hgb concentration of pregnant women were household wealth index (poor, middle, and rich), type of residence (Urban or rural), toilet type (pit, flush, and unsanitary), drinking water source (bottled water, tanker water, piped water, rainwater, and other), number of children aged $1-5$ years in the household, kitchen fuel type (gas/electric, wood, and animal/plant waste), length of current pregnancy in months, iron supplementation, number of ANC visits, educational level, parity, sex of household head, body mass index, malaria prevalence, drought episodes, temperature, and current working status of pregnant women. Some of the above variables, like malaria prevalence, drought episodes, and temperature, were collected at community levels, so we did not include those variables in this study.

2.4 Data collection procedure

The data for our study were accessed from the DHS website (www.measuredhs.com). We got permission to access the data after explaining the objective of the study and writing the mini proposal of our study. Data related to mothers' socio-economic status, health, nutrition, household income, household structure, biomarkers, demographic information, weather-related information, latitude and longitude, environmental factors, and other behavioral-related information of the pregnant women were collected across the area of Ethiopia.

2.5 Ethical issues, societal relevance, and stakeholder awareness

The data do not contain any personal identifying information that could be linked to the study participants and confidentiality was maintained anonymously, as outlined in the DHS report. Furthermore, the exact location of the study participants was displaced to maintain their confidentiality, sometimes known as 'geo-masked' or 'geo-scrambled'. During the data collection, the clusters were displaced by 2 kilometers for urban areas and 10 kilometers for rural areas from their actual locations [14]. Utilizing the estimated Hgb distribution to pinpoint local regions at risk of anemia allows the government to focus on addressing this issue. It facilitates the identification of anemia-related factors necessitating preventive measures. Mothers residing in high-risk anemia areas can gain awareness and be alerted to potential causes of anemia. Our study findings have significant implications for responsible bodies. The Ethiopian Ministry of Health, Ethiopian Public Health Institute, and regional health offices are key stakeholders in uncovering locations with high anemia risk. Additionally, as the study addresses anemia distribution across different zonal levels, stakeholders at lower levels, such as district health officers, can also be engaged.

2.6 Spatial exploratory analysis

Visualizing the spatial data analysis based on the raw outcome data can give the first insight. Assessing spatial correlation visually from a plot can be challenging. To obtain a better assessment, the empirical variogram is a valuable exploratory tool [53]. We used a variogram to test for residual correlation after we fit the linear regression model. It describes how the data are correlated with distance [24]. The concept of the variogram is based on the assumption that when there is no spatial correlation, the squared differences between pairs of predicted residuals, $(\hat{Z}_i, \hat{Z}_j)^2$, should vary around a constant value. This constant value is equal to twice the variance of the $\hat{z}_i$ because $\hat{z}_i$ and $\hat{z}_j$ are independent regardless of the distance h between their respective locations. We would expect the squared differences to be smaller on average at shorter distances h in the presence of residual spatial correlation in our data, as a result of the stronger correlation between $\hat{z_h}$ and $\hat{z_k}$ [55]. Therefore, the empirical variogram can be calculated as:

$$\hat{\rho}_{(h)} = \frac{1}{2|N(h)|} \sum_{N(h)} (Z_i - Z_j)^2 \tag{1}$$

where $N(h) = (i, j) : ||x_i - x_j|| = h$, i.e., it is the set of all pairs of data points whose locations are a distance h apart, and $|N(h)|$ is the set of all pairwise distances. We first fitted the theoretical variogram model with covariates to the empirical variogram and used estimates from the fitted model as the initial value for the spatial component of the linear geostatistics model.

2.7 Statistical models

2.7.1 Linear geostatistical model

"Geostatistics" is commonly used to refer to statistical models and methods used to analyze the finite realization of a continuous spatial phenomenon [26]. This methodology has been applied in several scientific areas and currently, it is a widely used method for spatial data analysis [20]. The descriptive The term "model-based geostatistics" was introduced by Diggle, Tawn, and Moyeed in 1998 [26] to refer to the introduction of geostatistics to the general framework of statistical modeling and likelihood-based inferences for analyzing continuous spatial data. Most geostatistical models focus on spatial predictions rather than parameter estimation. In terms of model-based geostatistics terminology, it can be expressed as: { (y_i, x_i): i = 1...n} are random variables, Y_i related with locations $x_i \in R^2$. Y_i are assumed dependent random variables, S(x): x $\in R^2$, can be described in statistical model [S, Y] = [S][Y][Y], where [.]= the distribution of Y and S. It is a conditional distribution and has a direct application of Bayes' theorem, which can be written as;

$$[S|Y] = \frac{[S][Y|S]}{[\int [S][Y|S]dS]} \tag{2}$$

The linear Gaussian modal is the most tractable model so far, for which $Y_i|S \sim N(S(x_i), \tau^2)$ and S follows a Gaussian process. A linear geostatistical model can be defined as:

$$Y = t'\beta + S(x) + Z \tag{3}$$

where Y: hemoglobin concentration measured at location x_i, t: a set of independent variables, β: regression coefficients associated with the independent variables, S(x): isotropic and stationary spatial process, and it has Matèern covariance function with scale parameters ϕ, shape parameters κ, and variance σ^2 [42]. The shape parameter κ is treated as fixed in the estimation. The variance of the nugget effect is also included in our parameter estimation by fixing its effect on relative variance, $\nu^2 = \frac{\tau^2}{\sigma^2}$. In our study, multiple households were selected at single sample locations. The model described above was modified in the following way; let Y_{ij} represent the random variable related to j^{th} individual hemoglobin concentration level at location x_i. Therefore, the linear geostatistical model can be modified as;

$$Y_{ij} = t'_{ij}\beta + S(x_i) + z_i + U_{ij} \tag{4}$$

where U_i are independent and identically normally distributed with mean zero and variance ω^2, $S(x_i$ and Z_i are as described in the previous geostatistical model. We fitted this model by specifying an ID vector for unique set locations in prevmap R package.

2.7.2 Initial selection of covariates

We selected a set of uncorrelated independent variables using a forward stepwise selection procedure for use in a linear geostatistics model. This approach expands the method developed by Austin and Tu [9] by fitting bi-variable linear geostatistical models of the initial predictor covariates. The likelihood ratio test (LRT), a likelihood-based test, was used to assess the effectiveness of each predictor variable in the prediction of the hemoglobin level of pregnant women at specific validation locations.

2.7.3 Sensitivity analysis

Sensitivity analysis (SA) in the geostatistical analysis is focused on examining how uncertainty in the estimated model parameters can be attributed to various uncertainties in the model inputs [4]. We examined how variations in the covariance sill and covariance nugget affect the spatial correlation within our model. This assessment involved fitting the model using different values of the range parameter (ϕ) and the nugget variance. We found that the model results remained consistent by systematically varying ϕ while keeping the nugget variance fixed, and vice versa. This indicates that choosing different values for these parameters does not impact the spatial correlation result in our model.

2.7.4 Spatial prediction

We used simple kriging to predict the spatially continuous elevation surface, which is the simplest geostatistical prediction method. It is based on a stationary Gaussian model for minimum mean square error (MSE) prediction without accounting for parameter uncertainty. All geostatistical model parameter estimates were plugged into the prediction model. Let $\hat{S}(x)$ be the minimum MSE predictor of S(x) at an arbitrary location x. It is the function of the data $y = y_1, y_2, ..., y_n$, which minimizes the expected value of the MSE predictor. Since we are assuming a spatial

Gaussian process, we can write this predicted value as a linear function of data as follows:

$$\hat{S}(x) = \mu + \sum_{i=1}^{N} wi(x)(x_i - \mu) \tag{5}$$

where wi are covariance parameters, namely, σ^2, τ^2, and ϕ.

2.7.5 Exceedance probability

Exceedance probabilities are vital to assess the localized spatial behavior of the model and to identify the unusual elevation of disease risk [9]. The set of $p(w) = p(x) : x \in Z$ represents the surface of hemoglobin concentration covering the area of interest Z. We first simulate 1000 samples from the predictive distribution of W to predict p. Exceedance probabilities surfaces give a map of uncertainty in the hemoglobin concentration level estimates. In this study, we created a map of exceedance probability at a certain threshold, which we have set at Hgb level of 110 g/l in pregnant women in Ethiopia, as shown in equation 6. This threshold was based on the evidence that pregnant women with Hgb concentration levels below 110 g/l are considered to be anemic.

$$\theta(x) = p(x) < 110|y : x \in Z \tag{6}$$

Areas with exceedance probability θ close to 1 indicate that the Hgb concentration of the pregnant women is highly likely to be below 110 g/l, and the other way around. In this study, we used exceedance probability surface as a good predictive summary, since we aimed to pinpoint areas at risk of anemia that need immediate intervention, as they are expected to exceed the threshold (110 g/l). The set of areas with $p(x) < 110g/l$ are therefore considered "hotspot" areas of anemia among pregnant women in Ethiopia.

2.7.6 Spatially adaptive sampling

Adaptive sampling designs utilize existing data to guide the selection of additional sample locations during each stage of the sampling procedure [50]. Sampled locations are grouped into batches over a series of time intervals, and the locations within each batch leverage data from previous batches to enhance data collection in line with the study objective. The criterion for adaptive sampling design ensures that data is only collected from locations that will provide valuable additional information [17]. Depending on the objective of the geostatistical analysis, the first step in adaptive sampling design is deciding and implementing the initial sampling design. After the data has been collected from the selected locations using the chosen design, the next step is to estimate the model parameters using the linear geostatistical model [25]. Prediction of p additional locations where representative sample have not been taken denote as $T^{*} = (T(_{x(n+1)}), ..., T(_{x(n+p)}))^{T}$ involves at the third step of the adaptive sampling procedure. This prediction is known as "plug-in prediction". Because all model parameter estimates are plugged in the prediction model.

We used 645 EAs from the EDHS 2016 dataset as the initial inhibitory sample to select additional locations adaptively for the follow-up studies. Based on the exceedance probabilities obtained from the previous prediction model, 50 additional locations were selected adaptively. We have set the minimum distance to be 1500 meters to ensure that sampling locations are not less than 1500 meters apart. This prevents sampling locations from multiple locations where x is highly correlated with corresponding S(x).

3 Results

3.1 Exploratory analysis

3.1.1 Socio-demographic, environmental and behavioral characteristics of study participants

From 645 enumeration areas, 9,361 pregnant women aged 15–49 years were included in the analysis. The average Hgb concentration of the study participants was 131g/l and the average age of pregnant women was 35 years old. 72.9% of the pregnant mothers were not heads of household, and 6,911 (73.8%) lived in rural areas. More than half of the mothers (64.1%) did not have current work, and 5,684 (60.0%) pregnant women did not have formal education.

Approximately, 4,141 (44.2%) of the mothers are in the poorest household index quantile, while 3,907 (41.7%) fall within the richest quantile.

Regarding sanitation-related characteristics, about 36.1%, 34.8%, 15.6, 11.6, and 1.9% of the pregnant women drank piped, well, water truck, surface/river, and bottled water, respectively. The majority (56.2%) of the pregnant women used unsanitary toilets (Table1).

Table 1: Socio-demographic, environmental, and personal characteristics of the study participants in Ethiopia.

Variable	Category	Frequency (n=9361)	Proportion (%)
Sex household	Male	6825	72.9
	Female	2536	27.1
Residency	Urban	2450	26.2
	Rural	6911	73.8
Wealth Index	Middle	1313	14.1
	Poor	4141	44.2
	Riche	3907	41.7
Educational Status	No education	5615	60.0
	Primary education	2540	27.1
	Secondary education	784	8.4
	Higher education	422	4.5
Source of water	Surface/River	1086	11.6
	Piped	3375	36.1
	Bottled water	182	1.9
	Well	3259	34.8
	Water truck	1459	15.6
Type of toilet	Flush	513	5.5
	Pit	5262	56.2
	Unsanitary	3586	38.3
Current working status	Yes	3360	35.8
	No	6001	64.2

3.1.2 Spatial distribution of Hgb among pregnant mothers aged 15–49 years in Ethiopia, EDHS 2016

The lower level of hemoglobin concentration among pregnant mothers aged 15–49 years was observed in Somalia, Harari, Afar, Dire Dawa, and Tigray regions of Ethiopia (Figure 1). Furthermore, there is an imbalance of spatial data within the region of Ethiopia. Most of the data were collected in Amhara, Oromia, and the central region of Ethiopia.

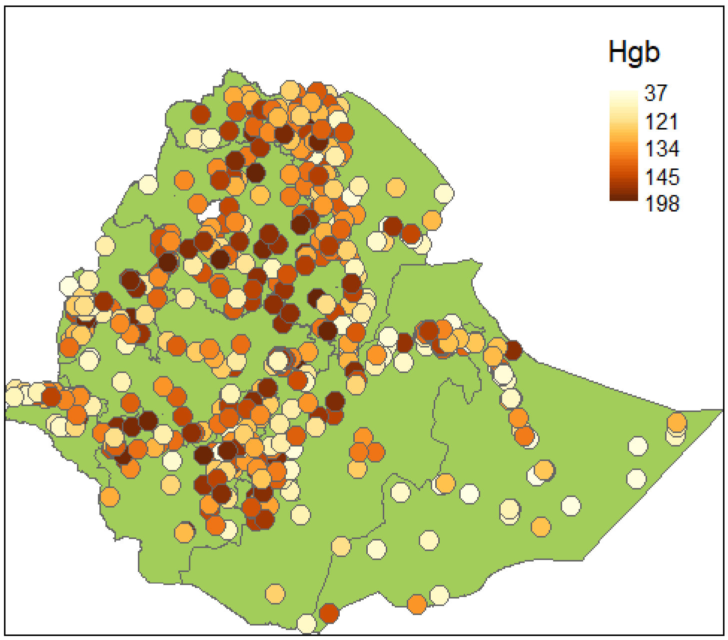

Figure 1: Point-map of hemoglobin concentration among pregnant women in Ethiopia

3.2 Variogram analysis

Figure 2 and 3 show the empirical variogram of Hgb concentrations together with a 95% tolerance band derived from 1,000 random permutations. Diagnostic check results using the variogram to test the presence of spatial correlation without covariates (figure 2) and with covariates (figure 3). The empirical variogram of the data is represented by the solid line, while the shaded areas indicate 95% tolerance bands assuming spatial independence. The empirical variogram falls outside this tolerance region, indicating the presence of a significant spatial correlation within the data. The variogram shown in Figure 3 was fitted to the residuals obtained from the model with predictors. Compared to the variogram from the null model, it shows a reduction in range parameters. This indicates that the covariates included in the model explain a portion of the spatial variation. Some of this variation still falls outside 95% tolerance bands, which indicates the existence of spatial correlation, with the empirical variogram falling outside the tolerance envelope at distances up to about 5 kilometers.

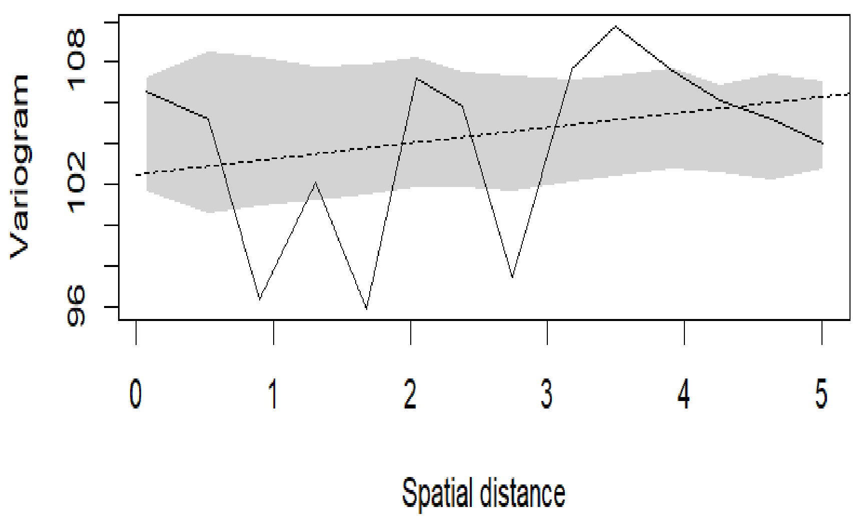

Figure 2: Semi-variogram for the null model

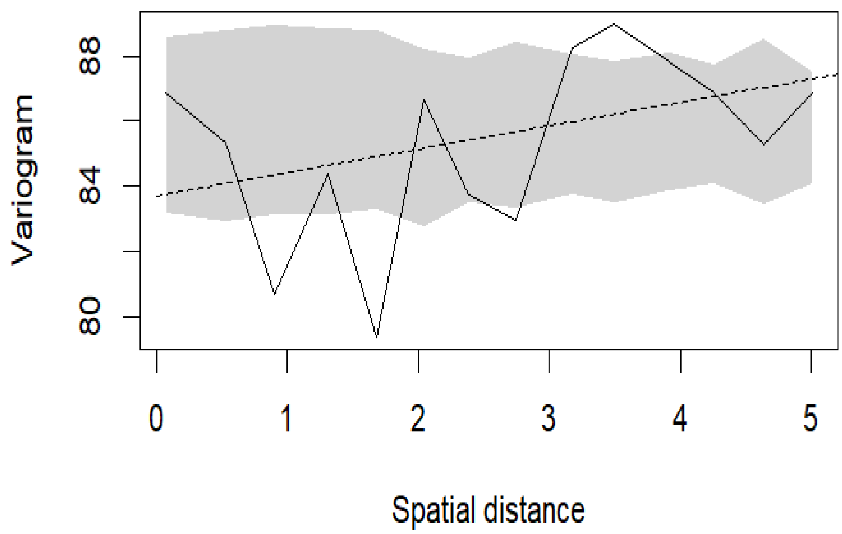

Figure 3: Semi-variogram for the models with covariates

3.3 Linear geostatistical model

We fitted the model for each variable and kept the variables with nominal p-values less than 0.25 to be included in the multivariable analysis. Table 2 reports MCML estimates with corresponding p-values for model parameters. The results showed that residence, sex of household, wealth index, BMI, and age of pregnant women were significantly associated with a reduction in Hgb at a 5% level of significance. Regarding the explanation of spatial dependence, the residence of the respondents explains more than the other variables in the bi-variable analysis. However, the sex of the household and toilet type explain less spatial correlation. The variance of the Gaussian process (σ^2) and the variance of the individual unexplained variation (ω^2) are almost the same for all variables. In the bivariable analysis, the corresponding estimates for each variable are not adjusted to the effect of other variables on pregnant women's hemoglobin concentration levels.

Therefore, multivariable analysis was used to adjust the effect of other covariates. we started from the null model and then added the most significant variables one after the other based on the bi-variable analysis. We determined the better model based on the likelihood ratio test.

Table 2: Maximum likelihood estimates for the bi-variable model fitted to the 2016 EDHS data. In the model column, we presented the list of variables included in each analysis.

Model	$\log(\sigma^2)(Se)$	$\log(\phi)(Se)$	$\log(\omega^2)(Se)$	p-value
Age	5.2777 (0.2172)	2.5688 (0.2486)	5.6275 (0.4347)	< 0.0001
BMI	5.2843 (0.2316)	2.6633 (0.2626)	5.6261 (0.4635)	< 0.0001
wealth index	5.1098 (0.1377)	2.7076 (0.2719)	5.6300 (0.4804)	< 0.0001
Source water	5.10976 (0.1377)	2.6500 (0.2607)	5.68418(0.2755)	0.093
Residence	5.2971 (0.2571)	2.8190 (0.2860)	5.6270 (0.5144)	< 0.0001
Education	5.10682 (0.1345)	2.6105 (0.2544)	5.68366 (0.2691)	0.467
Toilet Type	5.0821 (0.1363)	1.8917 (0.1693)	5.6837 (0.2728)	0.645
Sex of household	5.1339 (0.1329)	1.8576(0.1656)	5.6835 (0.2660)	< 0.0001

The maximum likelihood estimates of the model parameters are in Table 3. The results include point estimates, standard errors, and confidence intervals of the regression coefficients. Among the pregnant women in Ethiopia, residence, head of the household, wealth index, and BMI were identified as the most important variables associated with reducing Hgb concentration levels. In the linear geostatistical regression analysis, the proportion of pregnant women who lived in rural areas, the proportion of pregnant women who had been head of household, the proportion of women with low BMI, and younger pregnant women were considered important predictors for Hgb reduction in the linear geostatistical model, as it was statistically significant in the multivariable linear geostatistical analysis. We found that pregnant women from the wealthiest and middle-income households had a lower risk of anemia compared to women from the poorest households, although the difference for the middle-income group was not statistically significant.

Table 3: Maximum likelihood estimates with corresponding standard errors and confidence intervals for coefficients of the geostatistical model

Parameter	Estimate	Standard error	95%CI
β_0	116.49	4.96	(106.77,126.21)
β_1	-5.85	0.74	(-7.29, -4.34)
β_2	1.49	0.42	(0.67, 2.31)
β_3	0.075	0.02	(0.04, 0.11)
β_4	0.31	0.05	(0.21, 0.41)
β_5	-1.16	0.59	(-2.32,-0.004)
β_6	1.10	0.63	(-0.14,2.33)
$\log(\sigma^2)$	5.31	0.27	(4.78, 5.84)
$\log(\phi)$	2.88	0.30	(2.29 3.47)
$\log(\omega^2)$	5.62	0.54	(4.56,6.68)

Notes: β_0: Intercept; β_1: Residence (=1 if rural; =0 urban (ref)); β_2: Sex of household (=1 if female; =0 male (ref)); β_3: Age in years; β_4: body mass index (kg/m^2); β_5 and β_6; wealth index (=0 middle(ref); 1=poor; 2=rich) σ^2: variance of Gaussian process; ϕ: scale of spatial correlation; ω^2: variance of the individual unexplained variation; CI: confidence interval.

3.4 Spatial predictions for the target population

In Figure 4, spatial predictions were carried out based on the null model (without covariates). Upper panel: predicted surfaces of Hemoglobin concentration. Lower panel; maps of the predictive probability that Hgb lies below the threshold of 110 g/l (risk of anemia).

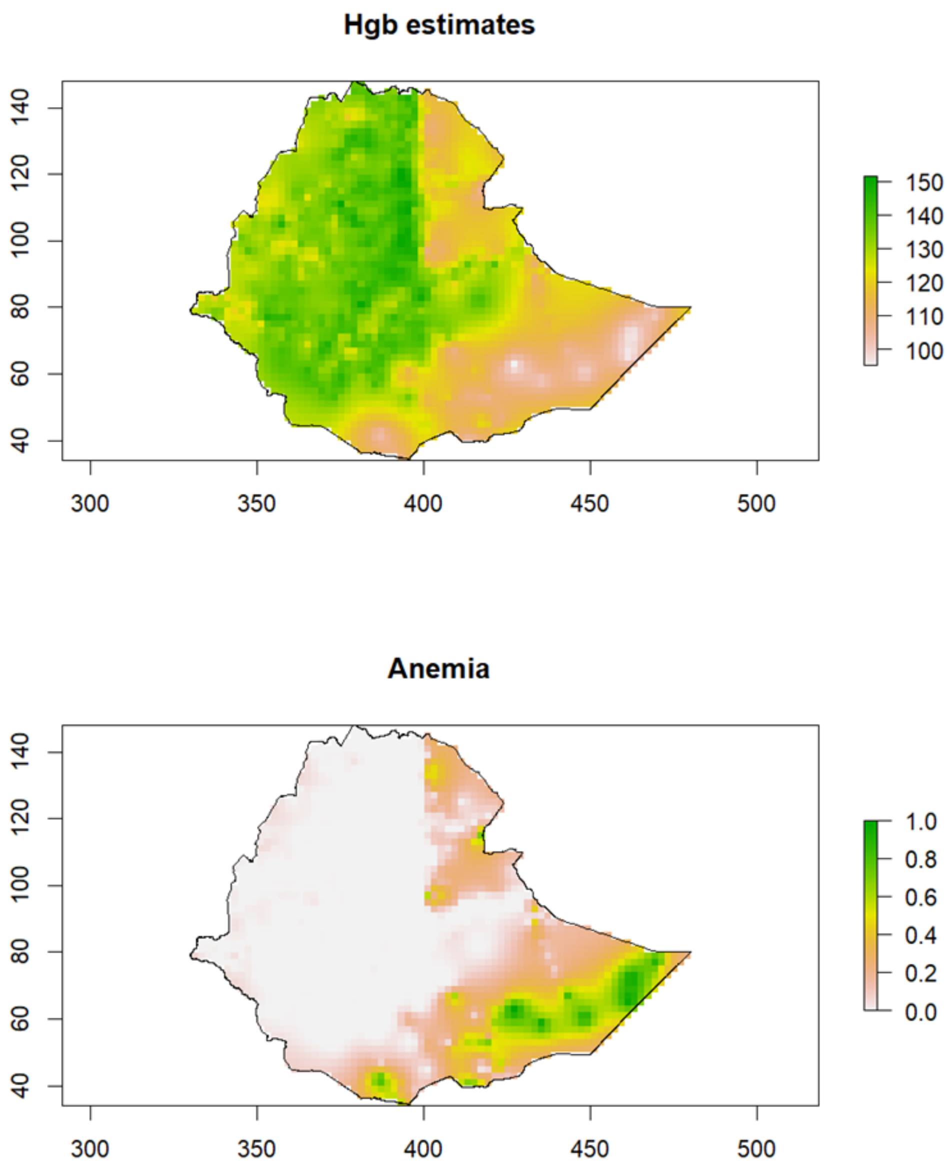

Figure 4: Maps of the predicted Hgb concentration (upper panel) and exceedance probability of Hgb$<110g/l$ (lower panel) in Ethiopia from the null model

Our fitted model for these data includes covariates that are properties of a person at a location, rather than of a location itself. It follows that predictive maps can only be constructed under hypothetical scenarios about the people who live at an unsampled location.

We suppose that our target population for prediction, T(x), are Hgb of 35 (average) years pregnant women, living in rural areas, having 20 kg/m^2 BMI (average), from a poor household, and being head of household. Hence,

$$T(x) = \beta_0 + \beta_1 + \beta_2 + \beta_3 * 35 + \beta_4 * 20 + S(x), x \in \mathcal{G} \tag{7}$$

where $\mathcal{G}$ is a regular grid covering the whole area of Ethiopia. The contour plot in figure 5 shows the probability of Hgb is below 110 g/l, taking into account significant covariates in the model, formally expressed as we observe the presence of a small hotspot of anemia risk in northeastern Ethiopia and a high risk of anemia in eastern Ethiopia. where $\rho(x)$ reaches a maximum value of about 90%, while in the rest of the country $\rho(x)$ is close to zero.

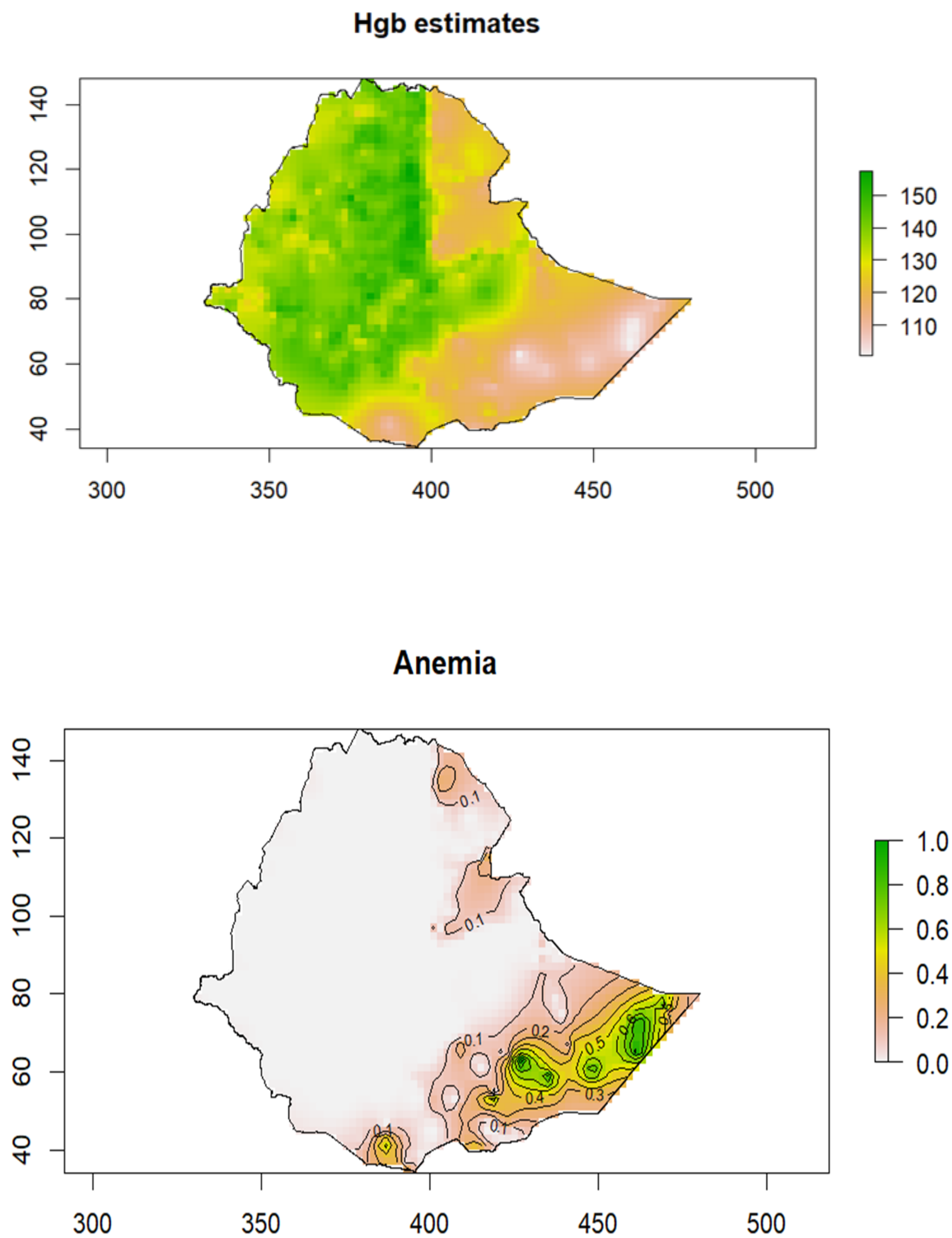

Figure 5: Maps of predicted Hgb concentration (upper panel) and exceedance probability of Hgb$<$ $110g/l$ (lower panel) in Ethiopia from the model with covariates. Contours of $Hgb <$ $110g/l$ (Anemia) and of 25% and 75% exceedance probabilities are also shown.

3.5 Spatially adaptive sampling

Complete enumeration of households in the study area and recording their geographic coordinates using GPS are involved in the first stage of geostatistical design. The data collected from EAs households in 2016 EDHS data act as initial sampling. The locations of all households included in the analysis to select new locations are shown in figure 6.

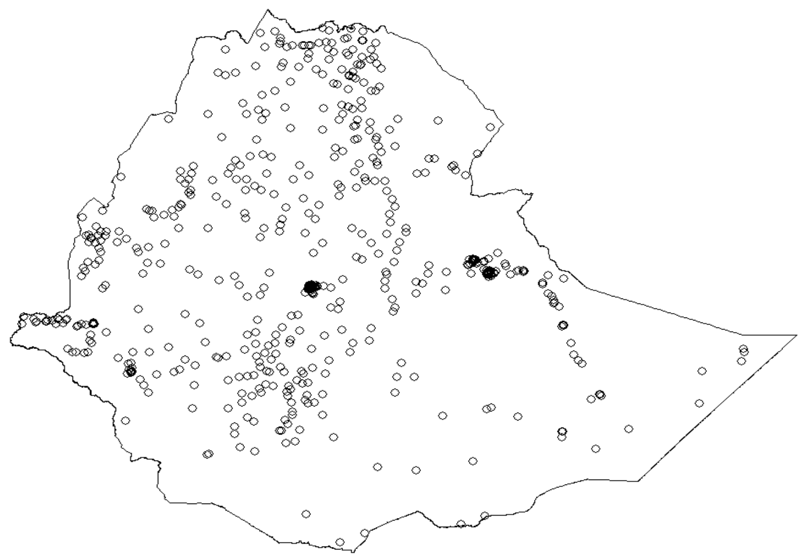

Figure 6: Locations of the all available household in Ethiopia, 2016 EDHS dataset

The maps of exceedance probabilities with 110g/l low Hgb concentration probabilities in Ethiopia and contours of 25% and 75% exceedance probabilities for regular grid were shown in figure 5 to show if and where areas with high risk are located in Ethiopia using 2016 EDHS data. The map shows the areas in the northeast, southeast, and east, as highlighted green have low Hgb concentration probabilities of less than 110g/l. Therefore, these areas are considered high-risk areas of anemia. On the other hand, the exceedance probabilities between 25% and 75% are considered a zone of uncertainty in which the stakeholders could collect additional data for further investigation.

Based on the exceedance probabilities from section 3.4, we select an adaptive sample of 50 additional areas. The results are presented in figure 7 with δ= 1500 meters. Blue dots ($n_0 =$ 645) are the selected areas from the EDHS 2016 data set, for visualization we select only 100 of them, and red dots ($n_a = 50$) are additional samples selected adaptively after analyzing the data from the initial design. Therefore, the stakeholders can collect an additional 50 new locations depending on these results.

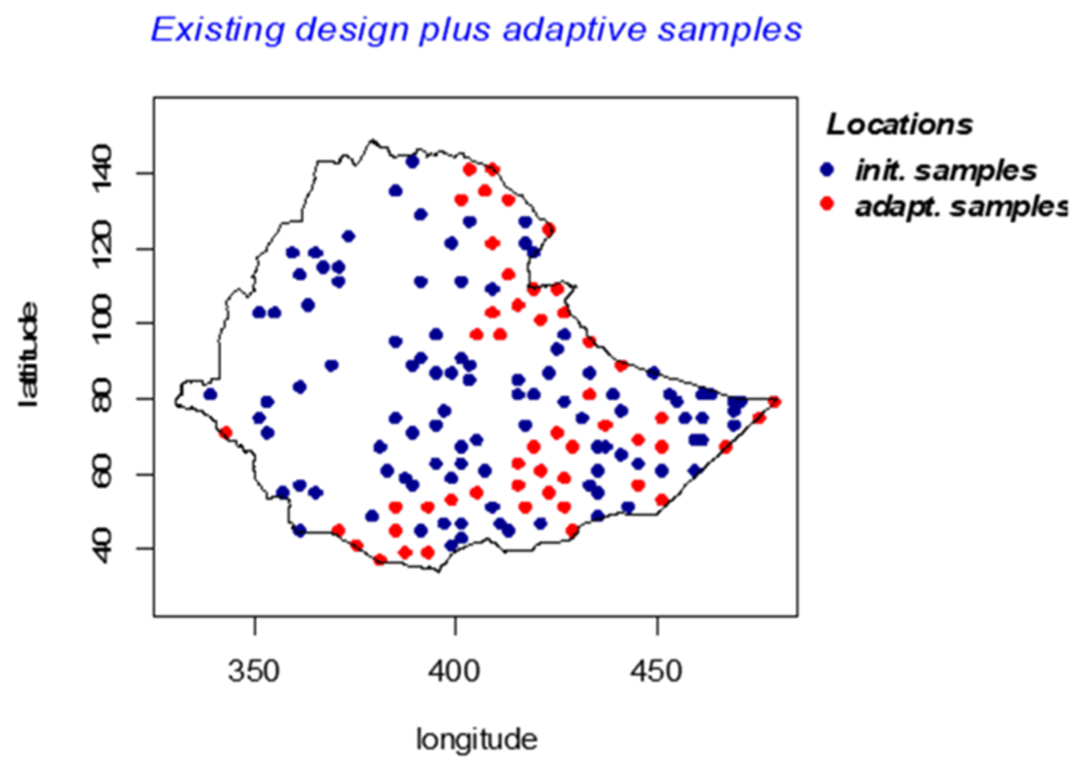

Figure 7: Adaptive sampling design $\delta = 1500$m and initial sampling household are represented by blue dots (only 100 locations from the EDHS dataset are visualized), red dots ($n_a = 50$) are adaptive samples

4 Discussion

DHS reports that in 2016 the prevalence of anemia among pregnant women aged 15–49 years was 28.55%, with the highest prevalences found in the Afar (44.7%) and Somalia (59.5%) regions of Ethiopia. These values are higher than those reported in studies from Ghana [1] and China [30].

Anemia significantly burdens the health care system in Ethiopia, despite the WHO's combined strategies to reduce anemia, such as infectious disease management and iron supplementation during pregnancy, and improving personal and community hygiene [28, 57].

Among the pregnant women aged 15–49 years, there was systematic (non-random) spatial distribution of anemia across Ethiopia. We found the hotspot areas (high risk of anemia) in Somalia, Dire Dawa, Harari, Tigray, and Afar regions of Ethiopia. This may be explained by the high prevalence of chronic diseases like chronic kidney disease and autoimmune disorders, excessive bleeding during pregnancy, iron and folate deficiencies, and inadequate nutrient intake of pregnant women in Ethiopia [21]. Due to poor sanitation, and environmental conditions in the eastern part of the country, many people are affected by infectious diseases like hookworms, Schistosoma, malaria, and visceral leishmaniasis that facilitate the transmission and spread of parasites [29, 61, 46, 54].

Using geostatistical modeling, we estimated the mean Hgb concentration for pregnant women and examined spatial variation in Hgb concentration and the risk of anemia. Residence, household sex, wealth index, BMI, and age of respondents were significant covariates associated with the reduction of Hgb concentration levels of pregnant mothers. As opposed to other studies [60, 10], our study found that drinking water sources and toilet facilities were not significantly associated with reducing Hgb concentration among pregnant women in Ethiopia.

Anemia in pregnant women is often associated with poor nutritional status, wasting, and stunting. This has predominantly happened with pregnant mothers in the context of endemic infections and unfavorable socioeconomic conditions [58].

In our study, the wealth index had a statistically significant effect on the reduction of Hgb concentration levels in pregnant women aged 15–49 years. The study revealed that respondents

from wealthier and middle-income households had better hemoglobin concentration (lower risk of anemia) compared to those from the poorest households. This finding aligns with other studies conducted in developing countries [51], Ethiopia [10, 38], Tanzania [56], Benin [3], and India [12, 1]. As it was explained above, poor economic status is strongly associated with various health-related problems, particularly increasing the risk of intestinal infections like ascariasis, amoebiasis, and hookworm, which in turn leads to a high risk of anemia among pregnant women from the poorest households [45]. It may also be possible that pregnant women from the poorest households cannot afford to buy nutritious foods and maintain a balanced diet [37], leading to insufficient nutrient intake and poor nutritional status [35].
Based on the CSA report, over 38% of Ethiopians fall into the poor wealth quantile, suggesting that a high proportion of pregnant women is at risk of anemia due to their poor socioeconomic status [52].

In this study, the age of the pregnant women was positively associated with their hemoglobin concentration level, indicating that the reduction of Hgb concentration was higher among adolescent pregnant women compared to young pregnant mothers. Our finding is supported by other studies conducted in Ethiopia [6, 59]. Though anemia affects the whole population, women are more prone to it, particularly teenage pregnant girls. Adolescents are particularly vulnerable due to the high demands of iron for their rapid growth. Consequently, pregnancy increases their nutritional demand, leading adolescents to be at higher risk of anemia than young pregnant women [15].

Maternal education has been reported as another important determinant of anemia among pregnant women, with a higher prevalence of anemia observed among women who have no formal education [11, 6, 3]. In this study, maternal education was not statistically associated with the risk of anemia among pregnant women. This difference may be attributed to the methods applied to assess predictors associated with anemia among pregnant women in Ethiopia.

The finding of our study revealed that the residence of the respondent was significantly associated with the reduction of Hgb concentration level of pregnant women in Ethiopia. Pregnant mothers living in rural areas are at higher risk of anemia as compared to pregnant mothers from urban areas. Our finding is in agreement with previous studies [7, 6, 10]. This may be due to pregnant women from rural areas often having inadequate health care services, unsanitary environments, and being uneducated, leading to less awareness about the consequences of anemia during pregnancy. Additionally, these pregnant women are from the poorest households and unable to maintain a balanced diet, resulting in a high risk of anemia.

Our study also showed that being the head of household increases the risk of anemia among pregnant women in Ethiopia. Our finding is in agreement with previous studies conducted in sub-Saharan countries [60]. The possible reason may be, that pregnant mothers who are heads of households may experience higher stress levels and greater economic and caregiving responsibilities. These factors can adversely affect their nutritional status and overall health, leading to lower hemoglobin concentrations (higher risk of anemia) [19]. Additionally, these women might have reduced access to healthcare resources and support, which can further contribute to decreased hemoglobin levels [41].

5 Strengths and weakness of the study

This study used well-documented EDHS data and utilized a rigorous statistical method, allowing for the generalization of findings at the national level. The findings of this study can give insights for Ethiopian public health institutes and other policymakers to design geographically targeted health interventions to control and prevent anemia among Ethiopian pregnant women.

It is important to note that the study has limitations that should be considered for further follow-up studies. For instance, essential predictors like temperature, underlying medical conditions, drought, malaria status, HIV/AIDS, etc., were not included in the analysis due to their unavailability in the EDHS 2016 data at the individual level. Furthermore, Since DHS data were collected through a cross-sectional study design, we cannot draw causal relationships between the reduction of Hgb concentration levels and the possible predictor variables included in the study. Lastly, the exact locations of the EAs areas were displaced by two kilometers for urban areas and ten kilometers for rural enumeration areas to secure the privacy of the study participants. This displacement could potentially affect the estimated cluster effect in the geostatistical regression analysis.

6 Conclusion and future work

Socio-economic statuses like wealth index, head of household, age of pregnant women, residency, body mass index, access to pure water, hygiene, and sanitation service were important predictors that affect the spatial variation of anemia among pregnant women aged 15–49 years in Ethiopia, and other sub-Saharan countries. In the 2016 DHS program, not enough data were collected from Afar, Harari, Somalia, Diren Dawa, and the eastern Tigray part of Ethiopia. This omission impacts the certainty of our exceedance probability predictions. Based on the adaptive sampling technique, we recommend that stakeholders and researchers in Ethiopia collect data from an additional location within these regions to improve the accuracy and reliability of future studies. However, it is important to consider the current socio-political and security issues in Ethiopia when planning data collection efforts. These challenges may affect accessibility and the safety of both researchers and participants. Therefore, a comprehensive risk assessment should be developed to address these issues while ensuring that the data collection process is as inclusive and representative as possible.

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