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Keywords:	Anemia, spatial analysis, multilevel analysis, reproductive age women, women

The Spatial Distribution and Determinant Factors of Maternal Anemia in Ethiopia: A Multilevel and Spatial Analysis

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Abstract

Objective: The aim of this study was to assess the spatial distribution and determinant factors of anemia among reproductive age women in Ethiopia.

Methods: An in depth analysis of the 2016 Ethiopian Demographic and Health Survey data was undertaken. Getis-Ord Gi* statistics were used to identify the hot and cold spot areas for maternal anemia. A multilevel logistic regression model was used to identify independent predictors of maternal anemia.

Results: Women who were older (adjusted odd ratio (AOR) = 0.75; 0.64, 0.96)), with no education (AOR = 1.37; 95 % CI: 1.102–1.72), living in a rural area (AOR=1.29; 95%CI: 1.02, 1.63), lowest wealth quantile (AOR = 1.29; 95 % CI: 1.014-1.60), currently pregnant (AOR=1.28; 95% CI: 1.10, 1.51, currently breastfeeding (AOR =1.09; 95% CI: 1.025, 1.28), with high gravidity (AOR=1.39; 95% CI: 1.13, 1.69), availability of unimproved latrine facilities (AOR = 1.18; 95 % CI: 1.01, 1.39), and HIV positive (AOR= 2.11; 95% CI: 1.59, 2.79) were more likely to have anemia. The spatial analysis indicated that statistically high hotspots of anemia were observed in the eastern (Somali, Dire Dawa and Harari regions) and north-eastern (Afar) parts of the country.

Conclusion: Maternal anemia is not randomly distributed across the country. Significantly high spots /prevalence of anemia was observed in the eastern and north eastern parts of Ethiopia. Anemia prevention strategies need to be targeted on rural residency, women with limited to no education, women who are breastfeeding, areas with poor latrine facilities and women who are HIV positive.

Key words: Anemia, spatial analysis, multilevel analysis, reproductive age women, women

Article Summary

Article focus

- Anemia is a major public health problem of women and nearly a quarter of reproductive women were anemic in Ethiopia.
- Maternal anemia prevalence rates is varied with different factors across different parts of the country while spatial analyses have not been conducted to identify hot spot areas of maternal anemia in Ethiopia.

Key messages

- Considerable geographic disparities of maternal anemia prevalence rate occurs inside Ethiopia

- Maternal anemia was non-random across the country, where significantly high spots of anemia was observed in the eastern and north eastern part of the country
- The occurrence of maternal anemia was associated with rural residence, having no formal education, poorest wealth index, being currently pregnant and breastfeeding, higher gravidity of women, lack of clean water source, and access to an unimproved toilet facility
- The prevention of maternal anemia needs multifaceted intervention approaches like for instance improving economic status of women and teaching women, and improving availability of clean water and toilet facilities

Strength and limitation of this study

- Used large population based data with a large sample size, which is representative to all regions of the country
- A combination of statistical methods (spatial analysis and multilevel logistics analysis) were applied which allows to understand the role of contextual and geographical factors for the occurrence of anemia among women of reproductive age
- The cause effect and temporal relationship could not be established due to cross sectional nature of the data
- Unable to incorporate essential factors such as dietary intake and behavioral factors in the analysis

Introduction

Anemia refers to a low hemoglobin level (<11mg/dl for pregnant women and <12mg/dl for non-pregnant women) [1]. If an individual's hemoglobin level is low, the red blood cells are unable to carry adequate oxygen for the body's physiologic needs [1]. Anemia is a major public health problem in women and children aged under five [2]. Worldwide, 38% of pregnant women, and 29% of non-pregnant women were anemic in 2011 [2]. Pregnant women in low and middle income countries (LMIC) experience high rates of anemia, in which the highest prevalence rates are reported in Central and West Africa (56%), South Asia (52%) and East Africa (36%) [2]. Similarly, a large proportion of non-pregnant women were reportedly anemic in West and Central Africa (48%), South Asia (47%) and East Africa (28%) [2]. Thus, anaemia remains as one of the priority areas at the global level particularly in resource-limited settings [3]. Reducing anemia is taken as an essential part to improving the health of women, and the world health organization (WHO) set a global target of 50% reduction of anemia among women of reproductive age by 2025 [4].

Anemia is a common problem in Ethiopia. The recent Ethiopian Demographic Health Survey (EDHS 2016) reported a 29% prevalence of anemia among pregnant women and 24% among reproductive age women ranging from 16% to 59% across different parts of the country [5]. Likewise, a number of pocket studies from different parts of the country reported varied prevalence rates of anemia among pregnant women ranging from as low as 17% in the north [6], 32% in the south [7] and up to 44% [8] and 57% [9] in eastern Ethiopia. Similarly, different studies reported a 16% [10] prevalence of anemia among non-pregnant women and 29%[11] and 30% [12, 13] among women of reproductive age.

The main cause of anemia is iron deficiency [14], however, deficiencies of other micronutrients (vitamin A, vitamin B12, and folate), chronic bleeding, acute or chronic infections and parasitic infections (hookworm and malaria) are also known to cause anemia [10, 15-17]. Based on the geographic and disease situation in LMIC, about half of anemia cases are attributable to a deficiency of iron and the remainder may be due to diseases like parasitic infections, malaria and human immune deficiency virus (HIV) [18]. A systematic review revealed that the percentage of anemia due to iron deficiency was below 50% in LMIC with regional variations and poor sanitary conditions and subsequent increased occurrence of infections also leading to anemia [19].

In Ethiopia, varied prevalence rates of maternal anemia have been observed with different factors across different parts of the country [6, 9]. For instance, large family size, low education status, rural residence, hookworm infestation and HIV infection were identified as factors of anemia in northern Ethiopia [6, 20], while studies from the eastern area reported that multigravidas, third trimester of pregnancy and intestinal infestation were factors of anemia during pregnancy [8, 21]. The variation in rates of anemia among women in Ethiopia might be due to the presence of diverse contextual and geographically variable factors including diet and the incidence of communicable diseases [3].

To date, spatial analyses have not been conducted to identify hot spot areas of maternal anemia in Ethiopia. Assessing the geographic distributions of anemia and the impact of risk factors on the disease prevalence by area is important to prioritize and design targeted prevention and intervention programmes to address maternal anemia [22]. Mapping the geographical distribution of anemia can also be beneficial for prevention and control of parasitic infections like soil transmitted-helminthiasis, schistosomiasis and malaria; because the control programmes for soil transmitted-helminthiasis and malaria have been evaluated using the burden of anemia as a quantifiable indicator [23].

Thus, the aims of this study was to assess the spatial distribution and determinant factors of anemia among women of reproductive age women in Ethiopia.

Methods

Patient and Public Involvement

As this study used the publicly available data set, the patients and or public were not involved.

Study design and setting

An in depth analysis of the EDHS 2016 data was undertaken for this study. EDHS 2016 is the fourth national survey conducted in all parts of Ethiopia (in nine regional states (Tigray, Afar, Amhara, Oromia, Somali, Benishangul-Gumuz, Southern Nations, Nationalities and Peoples (SNNP), Gambella and Harari) and two city administrations (Addis Ababa and Dire Dawa)) [5]. In Ethiopia the states are administratively further subdivided into Zones, Zones into *Woredas* and *Woredas* further into the lowest unit called *Kebeles.*

Sampling and data measurements

In the 2016 EDHS, stratified and cluster multistage sampling was used and intended to have appropriate demographic and health indicators at nationwide as well as at nine regional states and two city administrations. In the first stage, 645 clusters of enumeration areas (EAs) (202 urban and 443 rural) were identified using probability proportional to the size of EAs. At the second stage, the households were listed in all the selected EAs from September to December 2015 and then a random sample of 18,008 households were selected. Of this, 16,650 were successfully interviewed, resulting in a response rate of 98%. In the interviewed households, 16,583 eligible women were identified for individual interviews. A total of 15,683 women aged 15-49 years were interviewed and haemoglobin levels were measured for 14,923 of them [5]. Data collection took place from January 18, 2016, to June 27, 2016.

The sample size for EDHS was determined based on the multistage sampling procedure and taking into consideration the sampling variation. Standard errors were computed using the Taylor linearization method. The design effect, which is the ratio between the standard error with the given sample design and the standard error that would result if a simple random sample had been used, was determined. The value of the design effect, averaged over all variables, is 1.99. This means that because of multi-stage clustering of the sample, the average standard error is increased by a factor of 1.99 beyond that in an equivalent simple random sample.

Haemoglobin levels of the women were measured using HemoCue and all haemoglobin values were adjusted for both altitude and smoking status. The pregnant women with a haemoglobin value <11g/dl and non-pregnant women with <12g/dl were considered anaemic [1]. Similarly, anemia was classified according to its severity as severe (hemoglobin value < 7 g/dl), moderate (7.0-9.9 g/dl) in all women and mild (10.0 – 10.9 g/dl) in pregnant women and (10.0 – 11.9 g/dl) in non-pregnant women [1].

Explanatory variables

Both individual and community level explanatory factors were used. The individual and community level factors included in this study are presented in Table 1 with their definition and coding. Individual factors included age, religion, marital status, educational status, BMI, birth interval, use of contraceptive, wealth index, family size, iron-folate intake and gravidity of women, while the community level factors were residence (urban, rural), regions, water source and latrine facility type. Community level measures could also be driven by aggregating women level variables. For example, the proportion of women in the community who are in the top quantile of wealth index and proportion of women in the community who have clean water access. Community level factors would describe the group of populations existing in similar living settings.

Table 1 Variables identified for this study with coding

Variable	**Categories**
Age (Age in 5-year groups)	1=15-19; 2=20-29; 3=30-39; 4=40-49
Region	1=Tigray; 2=Afar; 3=Amhara; 4= Oromia; 5=Somali; 6=Benishangul-Gumuz; 7=SNNNP; 8=Gambella; 9=Harari; 10=Addis Ababa; 11=Dire Dawa
Area of residence	1=Urban; 2=Rural
Education level	1=No Education; 2= Primary; 3=Secondary; 4=Higher
Source of drinking water	1=piped water; 2=other improved (public taps, standpipes, tube wells, boreholes, protected dug wells and springs, and rainwater, bottled water); 3=unimproved (river, pond, unprotected spring and well)
Type of toilet facility	1= Improved (flush/pour flush toilets to piped sewer systems, septic tanks, and pit latrines; ventilated improved pit (VIP) latrines; pit latrines with slabs; and composting toilets); 2=Unimproved; 3=Open defecation; 4= Others
Religion	1=Orthodox; 2=Protestant; 3=Muslim; 4= Others (Catholic, traditional, other)
Ethnicity	1=Amhara; 2= Oromo; 3= Tigray; 4= Somali; 5= Sidama; 6=Gurage; 7=Welayta; 8=Hadya; 9=Other
Wealth index	1=Poorest; 2=Poorer; 3=Middle; 4=Richer; 5=Richest

Preceding birth interval (months) (for index child- for youngest child) except the first birth, no interval for 1st birth	1= <24 Months; 2= ≥24 Months
Total children ever born	1=0; 2= 1-3; 3= 4+
Births in past year (number of births in the 12 months (not 0 to 11) prior to the month of interview)	1= 0; 2= 1-2
Currently pregnant	0=No or unsure; 1=Yes
Ever had a terminated pregnancy (miscarriage, abortion, or stillbirth)	1= Yes; 2=No
Births in the last three years (0 to 35 prior to the month of interview)	1= Yes; 2= No
Current contraceptive use	1= Yes; 2 = No
Hemoglobin level adjusted for altitude and smoking (g/dl - 1 decimal)	(g/dl - 1 decimal)
Anemia	1=Anemic (Severe (<7 g/dl), Moderate (7-9.9 g/dl), Mild 10-10.9/11.9 g/dl); 2=Non-Anemic
BMI	1=<18.5; 2=18.5-24.9;3=>=25
Smoking	1=Yes; 2=No
Current marital status	1=Single; 2=Married/Living with partner; 3=Divorced/Widowed/Separated
During pregnancy, given or bought iron tablets/syrup for most recent pregnancy	0=No; 1=Yes; 3= I Don't Know
Drugs for intestinal parasites during pregnancy	0=No; 1=Yes; 3=I Don't Know
Currently breastfeeding	0=No; 1=Yes
Respondent's occupation (grouped)	1= Working; 2= Not working
Have you ever chewed Chat?	0 = No; 1=Yes

Have you ever taken a drink that contains alcohol	0 = No; 1=Yes
HIV test	1= Positive 2 = Negative

Data analysis

Spatial analysis

Spatial analyses were performed using geoda version 1.8.10, QGIS Version 2.18.0 and Arch GIS software version 10.1, and base files of the administrative regions for Ethiopia were obtained from DIVA (diva-gis.org). The spatial analysis was conducted by joining the occurrence of anemia (as proportions) with each cluster to the corresponding geospatial location (survey cluster values). The values of DHS data was merged with the GPS dataset in geoda software and these values were imported into the QGIS software. Anemia proportions were then computed at lower (cluster), Zonal and Regional levels using QGIS.

The spatial pattern of the rate of maternal anemia was visualized and a spatially smoothed proportion was obtained through empirical Bayes estimation methods [24] The smoothed proportions present clearer patterns, where the problem was most severe. The spatial empirical Bayes "smooth" estimates technique was able to deal with spatial heterogeneity. The estimation technique guarantees that estimates of neighbouring states are more alike than estimates of states that are further away [25].

A standardized prevalence rate (SPR), or, the ratio of the observed prevalence rate to a national prevalence rate was determined using Geoda software [25]. Geoda implements this in the form of an excess risk estimate as part of the map. The excess risk rate is the ratio of the observed rate to the average rate computed for all the data [25].

Furthermore, the spatial analysis was performed to identify the clustering of maternal anemia or hotspot areas (the areas that have higher anemia prevalence rates compared to the national average) in different regions of Ethiopia. Spatial analysis is an epidemiological method useful to specify geographic areas with high or low rate of disease occurrence and its variability over the region or country [26]. Getis-Ord Gi* statistics was used for this spatial analysis using ArcGIS version 10.1

software. Local Getis-Ord Gi* statistics [27] is important to identify the hot and cold spot areas for maternal anemia using latitude and longitude coordinate readings of geographic poisoning system (GPS) which was taken at the nearest community centre for EAs or clusters of EDHS 2016 [5].

A local Getis-Ord G-statistic tool in ArcGIS was used to calculate the spatial variability of high and low prevalence rates of maternal anemia. An autocorrelation can be classified into positive and negative correlation through the Local Getis-Ord G statistics [27]. Positive autocorrelation occurs when similar values clustered together on a map (high rates surrounded by nearby high rates or low rates surrounded by nearby low rates). Negative autocorrelation indicates different values clustered together on a map, that is, high values surrounded by nearby low values or low values surrounded by nearby high values. Statistical significance of autocorrelation was determined by z-scores and p-value with a 95 % level of confidence. The distribution and variations of maternal anemia prevalence rate across the country was displayed on the map.

Statistical analysis

The descriptive statistical analysis was performed using SPSS software version 24.0 (www.spss.com). Frequencies, percentage, and standard deviation were used for the descriptive analysis. Since some regions with small populations were oversampled while others with large population are underrepresented, the weighted frequencies and percentages (based on population size of each region) were computed as a correction. The detailed weighting procedure was described in EDHS 2016 report [5]. The mean and standard deviation were computed for blood hemoglobin level. The mean hemoglobin value was also compared across different independent categorical variables using One-way Analysis of Variance (ANOVA) or independent t-test.

Multilevel logistic regression: The Multivariable multilevel logistic regression model was used to determine the effect of different factors on maternal anemia. The analysis was performed by using SAS version 9.4 software (SAS North Carolina State University, www.sas.com). For this multilevel analysis, four models were constructed. The first model is constructed without independent variables to assess the effect of the community variation on maternal anemia. Individual level factors were incorporated in the second model. In the third model the community level factors were included. Finally, both individual and community level factors were included in the fourth model.

The results of fixed effects were presented as odd ratio (OR) with 95% confidence intervals (CIs). An adjusted odds ratio (AOR) with 95% CIs was computed to identify the independent factors of maternal anemia and a p-value <0.05 was used as a measure of statistical significance. The random effects (variation of effects) was measured by intra-cluster correlation coefficient (ICC) (variance partition coefficient) [28], percentage change in variance (PCV) [29] and median odd ratio (MOR) [28, 30] which measure the variability between clusters in the multi-level models. ICC explains the cluster variability while MOR can quantify unexplained cluster variability (heterogeneity). MOR translates cluster variance into OR scale. In the multilevel model, PCV can measure the total variation due to factors at the community and individual level [29]. The ICC, PCV and MOR were determined using the following formula [28, 29].

$$\text{ICC} = \frac{V}{(V + \frac{\pi^2}{3})} \qquad \text{MOR} = \exp\sqrt{2 \times V \times 0.6745} \sim \exp\,(0.95\sqrt{V})]$$

Where V is the estimated variance of clusters

And

$$\text{PCV} = \frac{(V_A - V_B)}{V_B} \times 100$$

Where V_A = variance of the initial model; V_B = variance of the model with more terms

The multilevel analysis model is one of analysis methods, which can correctly handle the correlated data [31]. A multilevel model evaluates how factors at different levels affect the dependent variable. A multilevel model provides correct parameter estimates by correcting the biases introduced from clustering by producing correct standard errors, thus correct CI, and significance tests [31]

Ethical consideration

Publicly available EDHS 2016 data was used for this study. The EDHS 2016 was approved by the National Research Ethics Review Committee (NRERC) of Ethiopia and ICF Macro International. MEASURE DHS approval was obtained to use EDHS 2016. Informed consent was taken from each participant and all identifiers were removed. This analysis was approved by the University of Newcastle Human Research Ethics Committee (approval reference number is H-2018-0045).

Results

Sociodemographic characteristics

The data on 14,923 women were included in this analysis, including 642 clusters nested in 11 regions. The descriptive statistics of the study participants are presented in Table 2. The mean (± standard deviation (sd)) age of the respondents was 28.2 years (±9.2 years). Most of the participants lived in a rural area (78%). Nearly two thirds (66%) of participants were married or living with a partner. Almost half (48%) of the women had no formal education and around 43% were of Orthodox Tewahdo Christian religion. Only 18% of the households had access to a piped water source for drinking, and 15% access to an improved latrine facility (Table 2).

Table 2: Sociodemographic characteristics of study participants included in the analysis, EDHS 2016 (N=14,923)

Variables	**Weighted Frequency**	**Weighted percent**
Age		
15-19	3165	21.2
20-29	5467	36.6
30-39	4078	27.3
40-49	2213	14.8
Place of residence		
Urban	3169	21.2
Rural	11754	78.8
Educational status		
No education	7215	48.3
Primary	5244	35.1
Secondary	1676	11.2
Higher	789	5.3
Marital status		
Single	3758	25.2

Married	9800	65.7
Divorced/widowed/separated	1365	9.1
Religion		
Orthodox	6447	43.2
Protestant	3514	23.5
Muslim	4645	31.1
Other	317	2.1
Region		
Tigray	1073	7.2
Afar	119	0.8
Amhara	3645	24.4
Oromia	5422	36.3
Somali	417	2.8
Benishangul-Gumuz	146	1.0
SNNPR	3124	20.9
Gambella	42	0.3
Harari	32	0.2
Addis Ababa	825	5.5
Dire Dawa	77	0.5
Wealth index		
Poorest	2519	16.9
Poorer	2717	18.2
Middle	2891	19.4
Richer	2979	20.0
Richest	3816	25.6
BMI		
<18.5	3060	22.1
18.5-24.9	9740	70.5
>=25	1018	7.4
Birth interval		
< 24 months	1415	18.3

>= 24 months	6305	81.7
Current use of contraceptive		
Yes	1088	7.3
No	13835	92.7
Iron folate intake during pregnancy		
Yes	3108	42.4
No /don't know	4220	57.6
Gravidity of women (children ever born)		
0	4745	31.8
1-3	4715	31.6
4+	5464	36.6
Children ever born in the preceding 5 years		
0	7595	50.9
1	4475	30.0
2+	2852	19.1
Currently breastfeeding		
Yes	4657	31.2
No	10266	68.8
Currently pregnant		
Yes	1088	7.3
No	13835	92.7
Smoking		
Yes	96	0.6
No	14827	99.4
Birth in the last one year		
0	12474	83.6
1-2	2449	16.4
HIV test		
Positive	187	1.3
Negative	14724	98.7
Water source		

Piped water	2646	17.7
Other improved	6926	46.4
Unimproved	5351	35.9
Latrine facility type		
Improved toilet	2231	14.9
Unimproved toilet	7877	52.8
Open defecation	4414	29.6
Other	401	2.7
Anemia status		
Anemic	3527	23.6
Non-anemic	11396	76.4
Proportion of women in the community who have clean water source , m(se)	64.1 (33.6)	
Proportion of women in the community who have unimproved latrine facility; m(se)	85.1(25.0)	
Proportion of women in the community who are in lowest quantile of wealth index; m(se)	35.1(30.0)	
Percentage of unimproved water per cluster; m(se)	35.9 (33.6)	

BMI= Body mass index; SNNP= Southern nations and nationalities peoples regions; m= mean; se= standard error

Prevalence rate of maternal anemia

Amongst all respondents, the mean (±sd) blood hemoglobin level (adjusted for altitude) was 12.8 g/dl (±1.7 g/dl). The overall prevalence of anemia among women of reproductive age across the country was 23.6% (95% CI: (22.0, 25.3). The prevalence of mild, moderate and severe anemia among all women of reproductive age were 17.8% (16.7-19), 5.0% (4.3-5.8) and 0.8% (0.5-1.2) respectively. There was regional variation of anemia prevalence among women of reproductive age (p= 0.0001) and higher prevalence rates observed in Afar, Somali, Gambella, Dire Dawa and Oromia regions. Lower prevalence of anemia was observed in Addis Ababa, Tigray, and Amhara regions. Rural areas had a higher prevalence [25.4 (23.5, 27.4)] of maternal anemia than urban areas [17.0 (14.4, 20.0)] (p=0.0001). The highest proportion of maternal anemia were found in Somali regional states, while the lowest proportions were found in Addis Ababa city administration (Table 3).

Table 3: The variation of anaemia prevalence rate across different regions and different sociodemographic characteristics of women in Ethiopia, 2016

Region	**Weighted frequency**		**Weighted proportion of anemia (95% CI)**	**p-value**
	Anemic	Non-anemic		
Place of residence				
Urban	538	2630	17.0 (14.4,20.0)	0.0001
Rural	2989	8766	25.4 (23.5, 27.4)	
Region				
Tigray	212	861	19.7 (16.8,23.0)	0.0001
Afar	53	66	44.7 (39.9,49.6)	
Amhara	627	3019	17.2 (14.9,19.7)	

Oromia	1480	3942	27.2 (23.8,31.1)	
Somali	248	169	59.5 (55.2,63.7)	
Benishangul-Gumuz	28	118	19.2 (16.1,22.7)	
SNNP	704	2420	22.5 (19.4,26.0)	
Gambella	11	31	26.1 (21.3,31.5)	
Harari	9	23	27.7 (23.7,32.1)	
Addis Ababa	132	693	16 (13.5,18.8)	
Dire Dawa	23	54	30 (25.8,34.8)	
Education status				
No-education	2002	5212	27.8 (25.4,30.2)	0.0001
Primary	1136	4108	21.7(19.8,23.7)	
Secondary	297	1378	17.8 (14.9,21.0)	
Higher	91	697	11.5(8.2,16.0)	
Wealth index				
Poorest	863	1656	34.3(29.7,39.1)	0.0001
Poorer	688	2028	25.3(22.6,28.3)	
Middle	686	2205	23.7(21.2,26.5)	
Richer	625	2354	21.0(18.6,23.6)	
Richest	664	3152	17.4(15.1,19.9)	
Currently pregnant				
Yes	317	771	29.1 (24.9,33.7)	0.003
No	3210	10625	23.2 (21.6,24.9)	
Currently Breastfeeding				
Yes	1317	3340	28.3 (25.7,31.0)	0.0001
No	2210	8055	21.5 (20.0,23.2)	
Total	3527	11396	23.6 (22.0, 25.3)	

Around 1,080 (7.3%) participants were pregnant at the time of the interview. The mean hemoglobin level among pregnant women was 11.7 g/dl (±1.8 g/dl) and 29.1% (95%CI: 24.9-33.7) of these women were anemic. The prevalence of anemia was higher among pregnant women [29.1 (24.9, 33.7)] than non-pregnant women [23.2 (21.6,24.9)] (p= 0.003) (Table 3). The mean hemoglobin value of women in their second and third trimester was significantly lower compared to women in their first trimester (p = 0.001). The mean hemoglobin levels in pregnant women who had less than 24 months birth interval (for their most recent birth) was significantly lower compared to women who had a birth interval of less than or equal to 24 months (p= 0.0001). Similarly receiving Iron folate supplements during pregnancy improved the mean haemoglobin values among pregnant women (Table 4).

Table 4 Hemoglobin level among pregnant women in Ethiopia, 2016

Variables	**Number**	**Hemoglobin level (g/dl) (mean(sd))**	**P values of ANOVA or independent t test**
Children ever born (CEB)	1,088		0.0001
0	213	12.1(1.7)	
1-3	484	11.7(1.8)	
4+	390	11.5 (1.8)	
Pregnancy stage	1,088		0.0001
1st trimester	226	12.4 (1.7)	
2nd trimester	433	11.6 (1.6)	
3rd trimester	429	11.5 (1.9)	
CEB in last 5 years	1,088		0.0001
0	339	12.1 (1.7)	
1	484	11.7 (1.8)	
2+	265	11.4 (1.9)	
Fe-Fol supplementation	749		0.018
Yes	251	11.8 (1.5)	
No	498	11.5 (1.9)	
Birth interval	702		0.0001
< 2 months	206	11.2 (2.0)	
>= 2 months	497	11.9 (1.5)	

sd = standard deviation, Fe-Fol= Iron-folate, CEB = Children Ever Born

Nearly one-third (n= 4,657; 31.2%) of women were breastfeeding at the time of the survey. The average hemoglobin level among lactating mothers was 12.6 g/dl (±1.7 g/dl) and about 28.3% (95% CI: 25.7-31.0%) of these women were anemic. Lactating women had higher odds of anemia than non-lactating women with AOR 1.09 (95% CI: 1.025 -1.28).

Determinate factors of maternal anemia

Multilevel Analysis (Fixed effect analysis)

The results of multilevel logistic regression for the individual and community level variables are presented in Table 5. In the full model in which all individual and community level factors are included, residence, education, religion, wealth index, pregnancy and breastfeeding status, gravidity of women, and lack of availability of an improved latrine were factors significantly associated with maternal anemia.

Individual factors

The average hemoglobin value was significantly different across age groups (p=0.0001). The highest mean hemoglobin level, 13 g/dl was observed in the youngest (15-19 years) age group while the lowest mean hemoglobin level, 12.71 g/dl in the 30-34 years age group. The general pattern indicated roughly linear decline among the ages of 15-34 years (Figure 1). Women aged 40-49 years old were 25% less likely to be anemic compared to women in the youngest age group (15-19 years old) (AOR= 0.75 (0.64, 0.96). Those women with limited education were 1.37 times more likely to be anemic than women who completed higher education (AOR = 1.37; 95 % CI: 1.102–1.72). The odds of anemia increased by 29% (AOR = 1.29; 95 % CI: 1.014-1.60) when comparing the poorest to the richest women. The odds of anemia was higher in women who were pregnant (AOR=1.28; 95% CI: 1.10, 1.51) compared to those that weren't (non-pregnant). Women who were currently breastfeeding were 9% (AOR =1.09; 95% CI: 1.025, 1.28) more likely to be anemic. The odds of anemia were 39% higher among mothers who had given birth to four or more children (AOR=1.39; 95% CI: 1.13, 1.69). Women who gave birth to two or more children in the preceding five years of the survey were at higher risk of having anemia (AOR =1.31; 95% CI: 1.09,1.57). In this study, women who were HIV positive had a twofold increased odds for anemia compared to women classified as HIV negative (AOR= 2.11; 95% CI: 1.59, 2.79) (Table 5).

Community level factors

Living in a rural area is associated with a 29% higher odds of anemia among women of reproductive age than women of urban residence (AOR=1.29; 95%CI: 1.02, 1.63). Women from households without access to a latrine had 18% higher odds of anemia compared to women from households that had an improved latrine facility (AOR = 1.18; 95 % CI: 1.01, 1.39). The higher odds of anemia was observed in Somali regional state (AOR = 2.163; 95 % CI: 1.58, 2.89) compared to Dire Dawa. However, the odds of maternal anemia were lower in Gambella, Addis Ababa, Amhara and Oromia region compared to Dire Dawa (Table 5).

Multilevel analysis (random effect analysis)

The result of the random effects model is shown in Table 5. The result of the random effect shows that maternal anemia was not random across the communities (t^2=0.88, p=<0.0001).

About 21% of the variance in the odds of maternal anemia could be attributed to community level factors as calculated by the ICC based on estimated intercept component variance. After adjusting for individual and community level factors, the variation in maternal anemia across communities remained statistically significant. About 16% of the odds of maternal anemia variation across communities was observed in the full model (Model 4) (Table 5).

Moreover, the MOR indicated that maternal anemia was attributed to community level factors. The MOR for anemia was 2.44 in the empty model (Model 1); this showed that there is variation between communities (clustering) since MOR is 2.4 times higher than the reference (MOR = 1). The unexplained community variation in maternal anemia decreased to MOR of 2.1 when all factors were added to the null model (empty model). This indicates that when all factors are included, the effect of clustering is still statistically significant in the full model (Table 5).

$$ICC = \frac{V}{(V + \frac{\pi^2}{3})} \qquad MOR = \exp\sqrt{2 \times V \times 0.6745} \sim \exp(0.95\sqrt{V})]$$

Where V is the estimated variance of clusters

And

$$PCV = \frac{(V_A - V_B)}{V_B} \times 100$$

Where V_A = variance of the initial model; V_B = variance of the model with more terms

Table 5: Determinant factors bivariate association between maternal anemia and individual and community contextual characteristics of Ethiopian women, 2016

Variables	**Model 1**	**Model 2 Individual factors**	**Model 3 Community level factors**	**Model 4 Individual + community level factors**
Individual level factors				
Age				
15-19		1		1
20-29		0.93 (0.81,1.07)		0.96 (0.82, 1.19)
30-39		0.89 (0.75,1.10)		0.92 (0.78,1.11)
40-49		0.76 (0.61,0.92)		0.75 (0.64,0.96)
Educational status				
No education		1.41 (1.13,1.76)		1.37 (1.10, 1.72)
Primary		1.22 (0.99,1.51)		1.24 (1.00,1.53)
Secondary		1.22 (0.98,1.5)		1.23(0.98,1.52)
Higher		1		1
Marital status				
Single		0.99 (0.80, 1.22)		0.972 (0.81,1.22)
Married		1.07 (0.92, 1.23)		1.09 (0.91,1.23)
Divorced/widowed/separated		1		1
Religion				
Orthodox		1		
Protestant		1.36 (1.16, 1.58)		1.37 (1.15,1.63)
Muslim		2.04 (1.79, 2.33)		1.36 (1.16, 1.58)
Other		1.49 (1.05, 2.12)		1.525 (1.06, 2.13)
Wealth index				
Poorest		1.73 (1.48, 2.03)		1.29 (1.014,1.60)
Poorer		1.31 (1.10, 1.54)		1.21 (0.96,1.45)
Middle		1.28 (1.08,1.51)		1.22 (0.98,1.50)
Richer		1.04 (0.88,1.24)		1.01(0.82,1.24)

Richest	1		1
Current use of contraceptives			
Yes	0.99 (0.90,1.10)		1.0 (0.91,1.11)
No	1		1
Currently pregnant			
Yes	1.30 (1.11,1.52)		1.28 (1.10,1.51)
no	1		1
Currently breastfeeding			
yes	1.12 (1.00,1.24)		1.09 (1.03,1.28)
No	1		1
Gravidity of women (total children ever born)			
0	1		1
1-3	1.23 (1.03,1.46)		1.22 (1.02,1.44)
4+	1.40 (1.15,1.72)		1.39 (1.13,1.69)
Smoking			
Yes	0.98 (0.64,1.50)		1.05 (0.69,1.61)
No	1		1
Birth in the last 1 year			
0	1		1
1-2	1.20 (1.05,1.37)		1.15 (1.01,1.32)
Children ever born in preceding 5 year			
0	1		1
1	1.12 (0.96,1.29)		1.10 (0.95,1.27)
2+	1.39 (1.16,1.66)		1.31 (1.09,1.57)
HIV test			
Positive	2.19 (1.65, 2.91)		2.11 (1.59, 2.79)
Negative	1		1
Community level factors			
Place of residence			
Urban		1	1
Rural		1.67 (1.35,2.05)	1.29(1.02,1.63)

Region				
Tigray			0.39(0.28,0.53)	0.52(0.38, 0.72)
Afar			1.25 (0.91,1.7)	1.14 (0.83,1.56)
Amhara			0.30 (0.22,0.41)	0.39 (0.28,0.54)
Oromia			0.55 (0.41,0.75)	0.57 (0.42,0.78)
Somali			2.40 (1.78,3.27)	2.16 (1.58,2.90)
Benishangul-Gumuz			0.36 (0.25,0.50)	0.37 (0.26,0.52)
SNNPR			0.40 (0.29,0.54)	0.41(0.29,0.57)
Gambella			0.63 (0.45,0.87)	0.63(0.45,0.89)
Harari			0.74 (0.53,1.04)	0.76(0.54,1.04)
Addis Ababa			0.54 (0.39,0.73)	0.67(0.49,0.91)
Dire Dawa			1	1
Water source				
Piped water			1	1
Other improved			1.15 (0.95,1.39)	1.04 (0.86,1.26)
Un-improved			1.18 (0.95,1.44)	1.03 (0.83,1.27)
Latrine facility type				
Improved toilet			1	1
Unimproved toilet			1.12 (0.97,1.29)	1.08 (0.94,1.25)
Open defecation			1.33 (1.15,1.55)	1.18 (1.00,1.39)
Other			0.86 (0.64,1.17)	0.94 (0.69,1.27)
Random effects (effect of variation/ measure of variation for maternal anemia)				
Community level variance (SE)	0.888 (0.07)	0.46(0.05)	0.32(0.04)	0.31(0.035)
P- value	0.001	0.001	0.001	0.001
DIC(-2log likelihood)	7926.056	7749.25	7720.74	7613.56
ICC (%)	21.25	16.1	18.3	15.86
Explained variation –PCV (%)	Reference	40.95	21.0	43.1

MOR	2.44	2.13	2.3	2.1

Note: Model 1= empty model (without the predictors); Model 2= adjusted for individual factors; Model 3 = adjusted for community level factors; Model 4 = adjusted for both community and individual level factors; DIC = Deviance information criterion; ICC= Intra-cluster correlation coefficient; MOR= Median Odd Ratio; PCV = percentage change in variance; SE= Standard Error; SNNPR=Southern Nations and nationalities region

Spatial data analysis

The spatial analysis helps to visualize anemia prevalence rates across Ethiopia on a map. In addition it helps to test whether the anemia prevalence rate is randomly distributed or not; to test this we can use the global and local spatial autocorrelation using Getis-Ord Gi statistics. Figure 2 displays the empirical Bayes smoothed proportion estimate of maternal anemia across regions in Ethiopia. The higher/severe prevalence (≥40%) of anemia among women was observed in Afar and Somali regional states. Likewise, moderate prevalence rates (20-40%) of anemia was occurred in Oromia, Gambella, SNNPR, Harari and Dire Dawa regional states. In contrast, the proportion of anemic women classified as mild was lowest (<20%) in Tigray and Amhara regional state as well Addis Ababa City Administration.

Similarly, the standardized prevalence ratio by regions (standardized to the national average prevalence of 23.6%), ranging from 0.63 to 2.39, was overlayed (Figure 3). Higher prevalence ratio of maternal anemia was observed in Somali (2.39), Afar (1.8) Oromia (1.17), Dire Dawa 1.15, Gambella (1.12) regional states (Figure 3); whereas, lower prevalence ratio of anemia occurred in other regional states - Addis Ababa (0.64), Amhara (0.76), Benishangul-Gumuz (0.79), SNNPR (0.96), Tigray (0.85)

Figure 4 displays the smoothed anemia prevalence rates at Zonal level where higher anemia rates were observed in all zones of Afar and Somali regions as well as in some zones of Oromia. Likewise, the higher standardize ratio of maternal anemia was observed in all zones of Afar and Somali regions as well as in some zones of Oromia (Figure 5).

The spatial distributions of maternal anemia at the lower level (cluster level) is displayed in figure 6. The spatial investigation at the cluster level indicated that statistically high hotspots of anemia were observed in the eastern (Somali, Dire Dawa and Harari regions) and in north-eastern (Afar) parts of the country, while low spots of anemia were observed in the northern (Tigray, Amhara), central (Addis Ababa, Oromia) and western (Benishangul-Gumuz and Gambella) parts of the country (Figure. 6).

Discussion

Approximately a quarter of women of reproductive age were anemic in the current study, indicating that anemia is a moderate public health problem at the national level in Ethiopia [1]. However, geographic differences demonstrated that anemia is a particularly serious public health problem in 5 of the 11 Ethiopian states. A higher number of anemia cases were observed in the eastern and north-eastern parts of the country, which are less developed compared to other Ethiopian states in terms of economy, gender, health care facility and food shortage [32]. The geographical disparity of anaemia across the regional states might be attributable to the regional variations in food consumption preferences [33, 34], the occurrence of communicable diseases [35], and availability of health care facilities [36]. The altitude has effect on the hemoglobin level [1] which results a disparity of anemia occurrence across the country. In addition, lack of clean water access and unimproved latrine facility would increase the occurrence of soil transmitted infection [37] which could lead to anemia [38], might be the reasons for the observed geographical differences.

According to the final model, both individual and community level factors were responsible for about 43% of the disparity of anemia prevalence rates among women of reproductive age in Ethiopia. After adjusting for all factors in the model, the likelihood of having anemia was higher among those of younger age, with lower levels of education, living in rural areas, in the lowest wealth quantile, who were currently pregnant or breastfeeding, with high gravidity, and having birthed in the year prior to the survey and without access to an improved latrine facility.

Women aged 40-49 years had a lower likelihood of being anemic compared to women aged between 15-19 years. This finding is in line with other study findings from Ethiopia [10, 13] and Benin [39]. This could be due to the fact that low fertility rates occurred in this age group [5]. But, findings from Iran [40] reported that women aged 20-24 were less likely to be anemic compared to those aged 45-49, however, this might be a result of Iran having a targeted intervention for younger women or women of reproductive age.

This study found that women who did not have formal education had higher odds of anemia than those with higher education. This is consistent with the studies conducted in developing countries[18] including in Ethiopia [10], Timor-Leste [41], Benin [39] and India [42, 43] which reports that low education was associated with the higher odds of anemia among women of reproductive age. Formal education might assist the women to get knowledge that in turn helps them to follow better lifestyle behaviours like good nutrition, better health-seeking habit and hygiene practices that can prevent maternal anemia.

The likelihood of having anemia was higher in rural residence compared to the urban residence. This is in agreement with the study conducted in low income countries that revealed living in rural areas were identified as determinant factors to anemia [18]. The lowest wealth quantile compared to highest quantile was associated with higher risk of maternal anemia. Results of this study show that women who had poorest wealth quintile were 30% more likely to be anemic than women who belongs to the richest quintile, which is in line with the results of the studies conducted in other developing countries [18] like Benin [39] and India [43, 44]. This might be due to the fact that low income leads to poor dietary intake [45, 46], which in turn leads to inadequate nutrient intake and nutritional status [47]. More than 38 % of the Ethiopian population belongs to the poor and poorest wealth quintile, which indicates a large percentage of women who are at risk for anemia because of low socioeconomic position [5].

The role of pregnancy as a disposing factor for anemia is also explicit in this current study. Pregnant mothers were 28% more likely to have anemia than non-pregnant women. Pregnancy predisposes the women to low haemoglobin which results in anemia. The studies conducted in Nepal [48] and India [49] reported similar findings that pregnant women were more likely to be anemic than non-pregnant women.

The findings of this study clearly show the role of women's fertility in anemia. An increased odds of anemia was associated with high gravidity, births in the past five years of the survey and having a birth in the last year. Similar studies in Ethiopia [10], Iran [40] and Timor-Leste [41] also document this association between parity and risk of anemia. The study results from Pakistan [50, 51] and Iran [40] reported that women with parity of four or more were found to be at increased odds of anaemia than women with lower parity. And so, emphasis needs to be given for the family planning services.

The recent report illustrated that more than half of the Ethiopian population had access to unimproved toilet facilities [52]. Our study findings revealed that women from households with unimproved latrine facility were more likely to be anemic than women from households with improved latrine facility which is in agreement with other research findings [39, 53]. The possible justification might be the unimproved latrine facility would expose the women to helminthic infections [37], which in turn resulted in anemia in women [38]. Increased odds of anemia was observed in women with HIV positive. In this study, women with HIV positive had a twofold increased odds for anemia.

Strength and Limitations

This study used large population based data with a large sample size, which is representative to all regions of Ethiopia. Furthermore, a combination of statistical methods (spatial analysis and multilevel logistics analysis) were applied for this study which allows the understanding of the role of contextual and geographical factors for the occurrence of anemia among women of reproductive age. Because of the cross sectional nature of the EDHS dada, the cause effect and temporal relationship could not be established based on these study findings. Similarly, essential factors such as dietary intake and behavioural factors were not available in EDHS survey so that it could not be possible to incorporate these variables in the analysis. Furthermore, EDHS was a questionnaire based survey and relied on the memory of the respondent, and as a result recall bias might be a threat for this study.

Conclusion

This study indicates that considerable geographic disparities of maternal anemia prevalence rate occurs inside Ethiopia. The results of this study revealed that maternal anemia was non-random across the country, where significantly high spots of anemia was observed in the eastern and north eastern part of the country while low spots of anemia were observed in northern and western part of the country. About 43% of the disparity in maternal anemia occurrence across the communities was attributable to both individual and community level factors. The increased occurrence of maternal anemia was associated with the individual and community level factors. Being rural residence, having no formal education, being in the poorest wealth index, either currently pregnant or breastfeeding, and higher gravidity for the woman were factors that increased the odds of maternal anemia at the individual level, whereas lack of clean water source, and access to an unimproved toilet facility were factors significantly associated with maternal anemia.

Accordingly, the prevention of maternal anemia needs multifaceted intervention approaches like for instance improving economic status of women and teaching women, and improving availability of clean water and toilet facilities. Anemia prevention strategies have to be targeted on the identified factors. Priority should be given for those states or areas which have high hotspots of occurrence of maternal anemia. Particularly, any intervention programs needs to be prioritized for pregnant women, women with recent births, those with lower education, and women living in rural areas. The regions with the greatest numbers of anemic women (Afar and Somali) should be prioritized, as the burden of anemia is higher in which more than 50% of women in these region are anemic.

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Authors' contributions

Formulating the research question (s) KTK CC DL EG; designing the study KTK CC DL EG; analysed the data and interpreted the results KTK CC DL EG; drafted, wrote, reviewed and approved the final manuscript KTK CC DL EG.

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Conflicts of interest

Authors declare that they have no any conflicting interests.

Data sharing statement

The dataset is available at measure DHS program website (http://www.measuredhs.com)

Figure 1: Average hemoglobin value with 95% CI at different age groups, Ethiopia, 2016

Figure 2. Spatial Empirical Bayesian smoothed (SEBS) percentage of maternal anemia across regions

Figure 3. Standardized prevalence ratio for anemia among women of reproductive age across the regions in Ethiopia (standardized to national prevalence of 23.6%).

Figure 4 Spatial Empirical Bayesian smoothed (SEBS) percentage of maternal anemia across Zones

Figure 5. Standardized prevalence ratio for anemia among women of reproductive age across Zones in Ethiopia (standardized to national prevalence of 23.6%).

Figure 6. Spatial pattern of hot spots and cold spots of maternal anemia rate at cluster level in Ethiopia, EDHS, 2016

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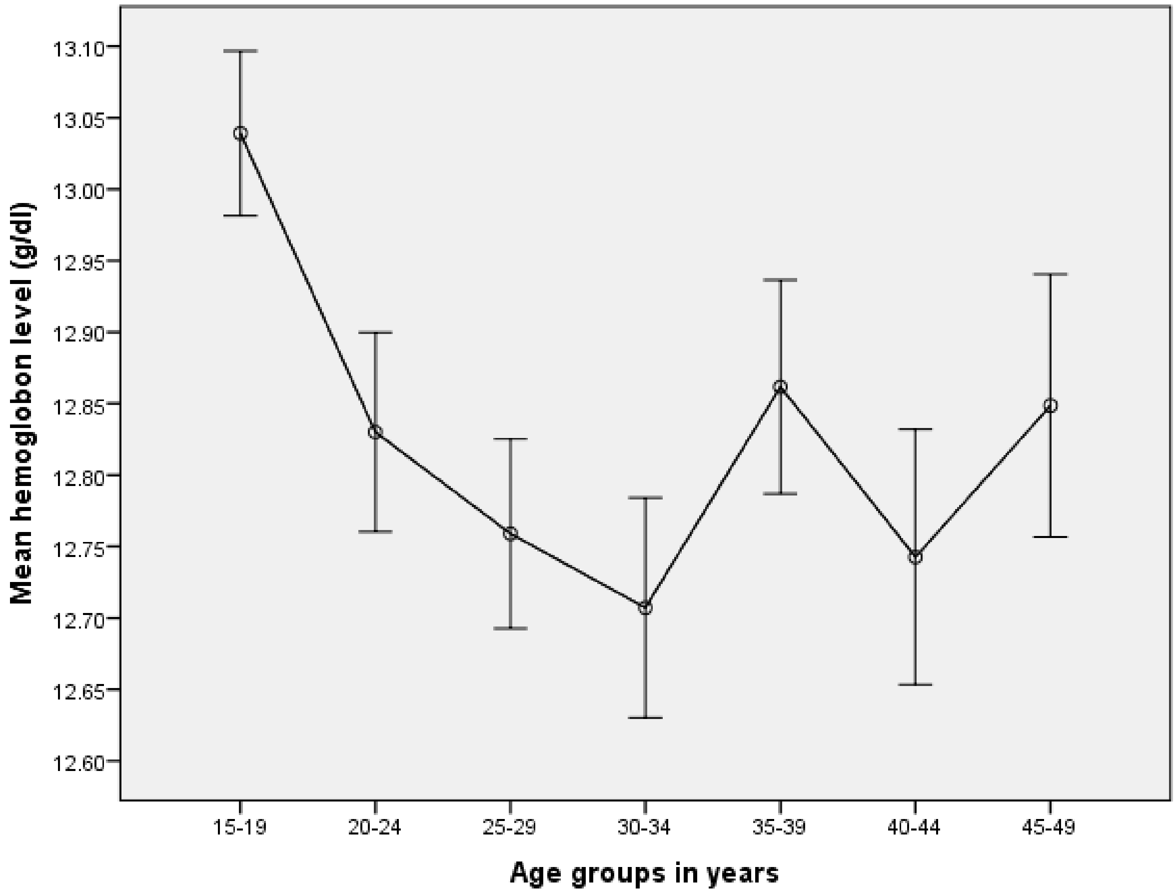

Figure 1: Average hemoglobin value with 95% CI at different age groups, Ethiopia, 2016

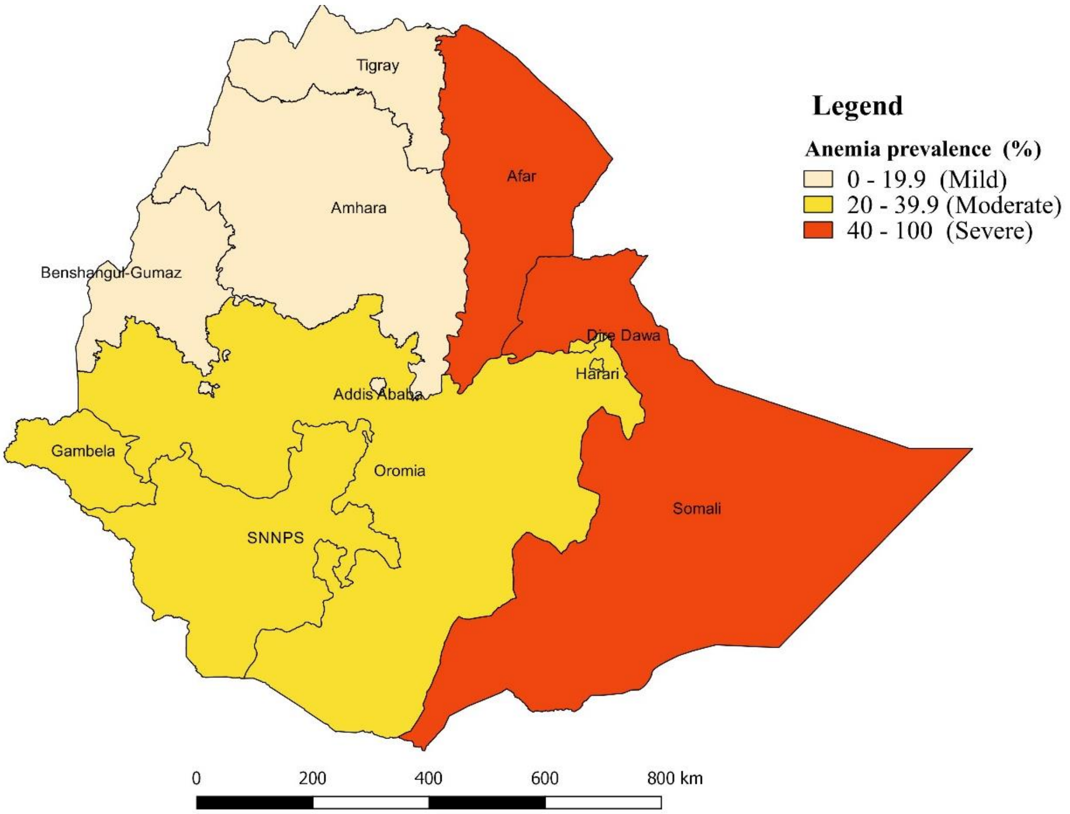

Figure 2. Spatial Empirical Bayesian smoothed (SEBS) percentage of maternal anemia across regions

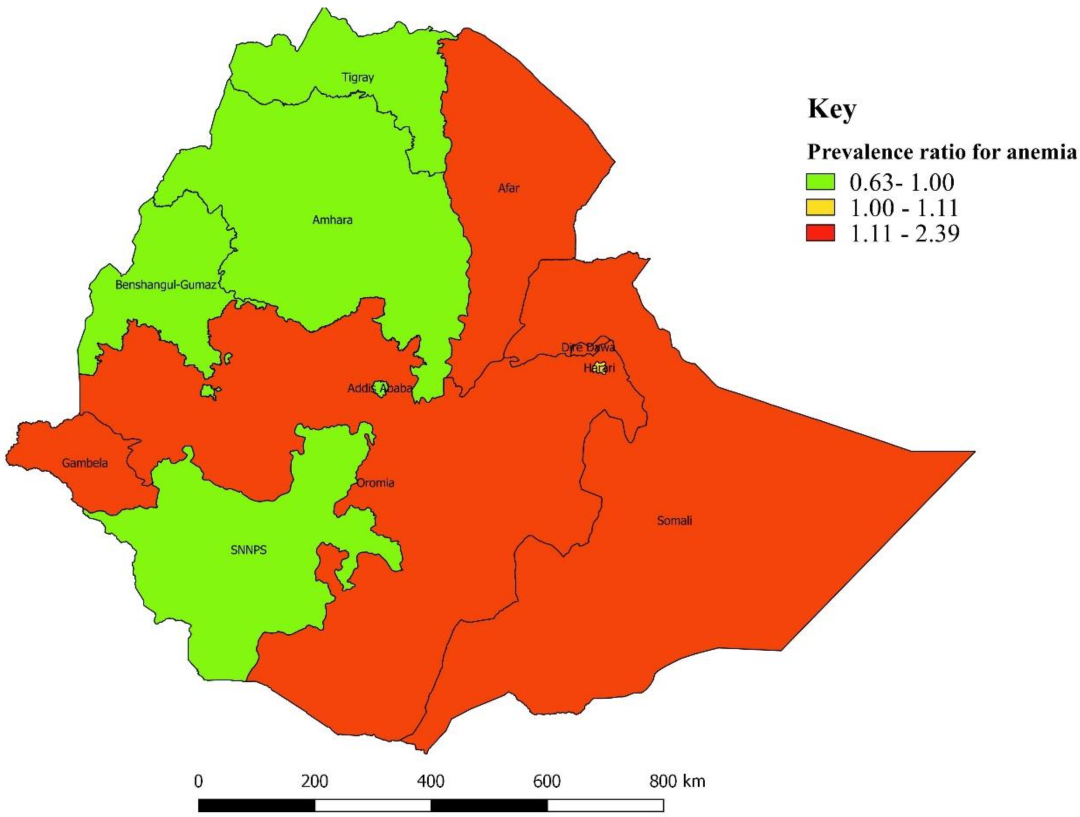

Figure 3. Standardized prevalence ratio for anemia among women of reproductive age across the regions in Ethiopia (standardized to national prevalence of 23.6%).

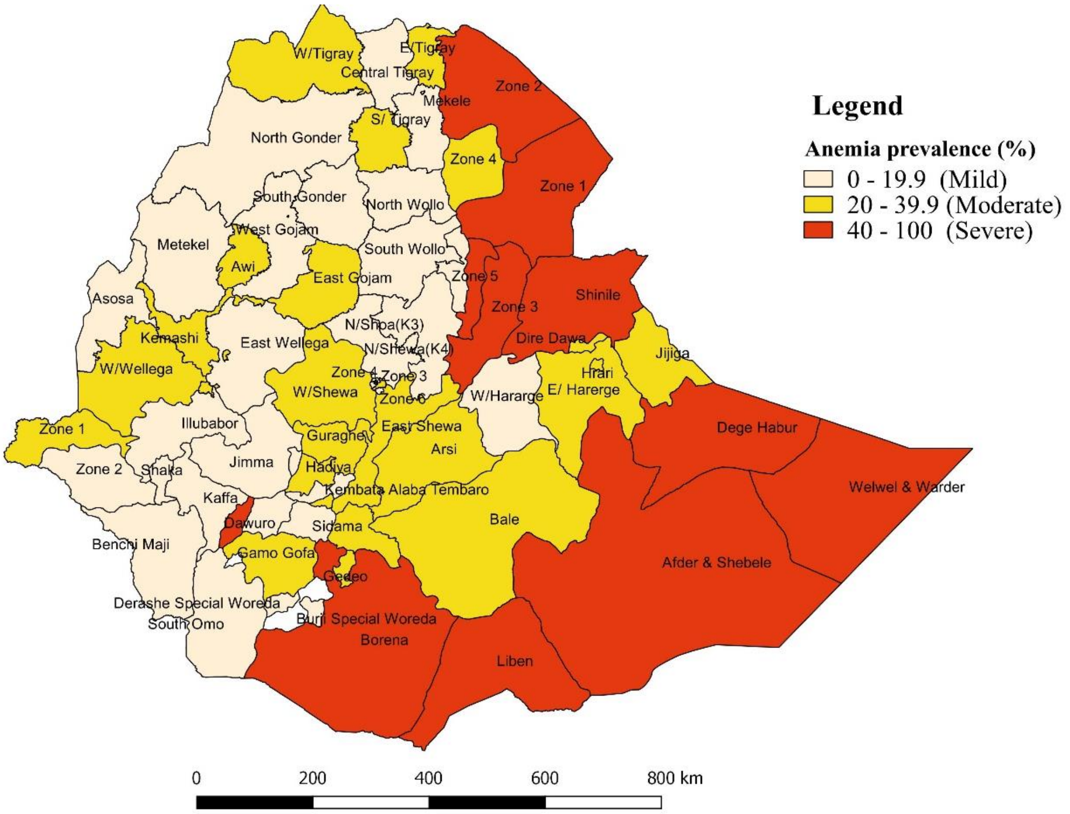

Figure 4 Spatial Empirical Bayesian smoothed (SEBS) percentage of maternal anemia across Zones

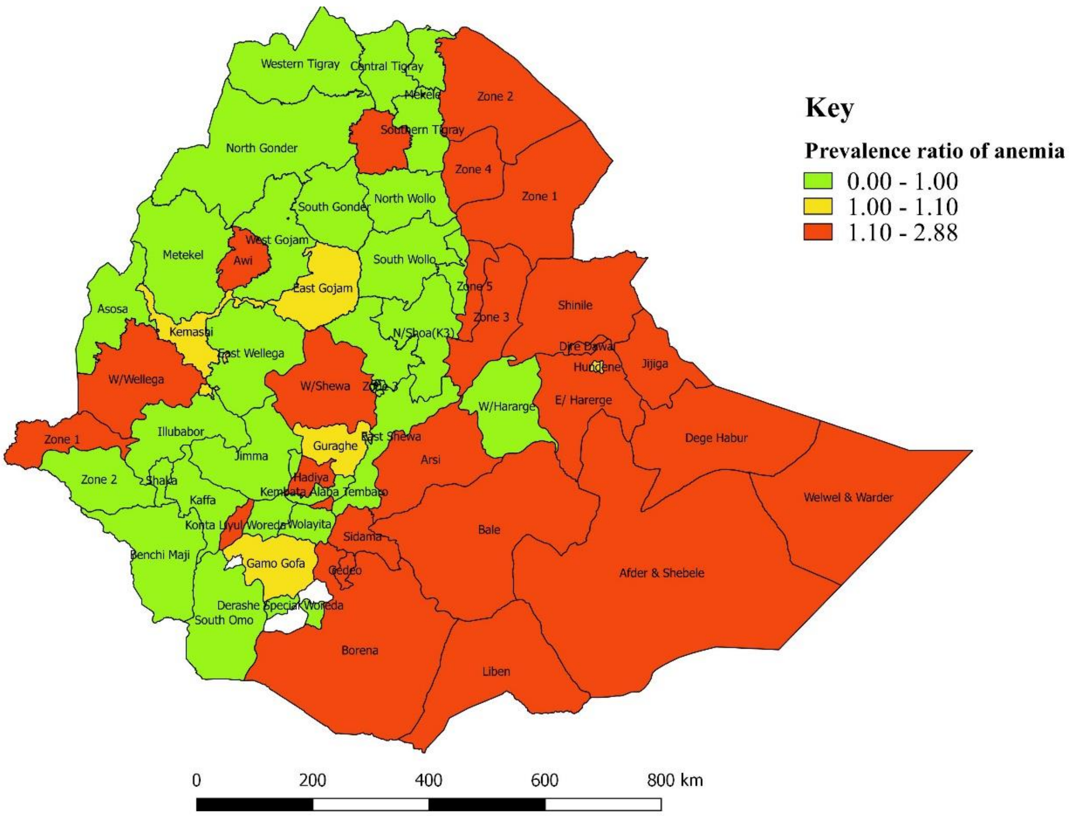

Figure 5. Standardized prevalence ratio for anemia among women of reproductive age across Zones in Ethiopia (standardized to national prevalence of 23.6%).

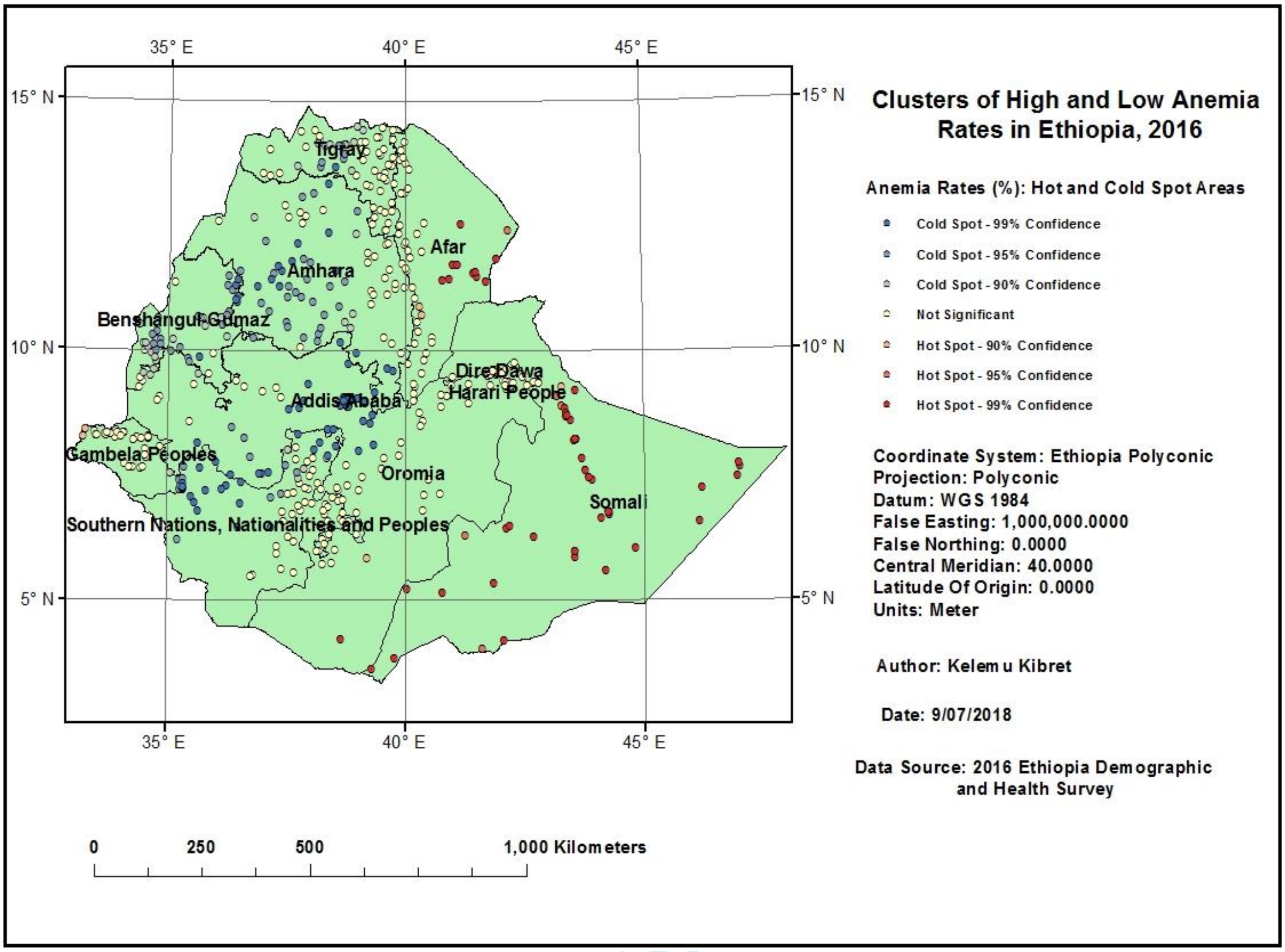

Figure 6. Spatial pattern of hot spots and cold spots of maternal anemia rate at cluster level in Ethiopia, EDHS, 2016.

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The Spatial Distribution and Determinant Factors of Anemia among Women of Reproductive Age in Ethiopia: A Multilevel and Spatial Analysis

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The Spatial Distribution and Determinant Factors of Anemia among Women of Reproductive Age in Ethiopia: A Multilevel and Spatial Analysis

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Abstract

Objective: The aim of this study was to assess the spatial distribution and determinant factors of anemia among reproductive age women in Ethiopia.

Methods: An in depth analysis of the 2016 Ethiopian Demographic and Health Survey data was undertaken. Getis-Ord Gi* statistics were used to identify the hot and cold spot areas for maternal anemia. A multilevel logistic regression model was used to identify independent predictors of maternal anemia.

Results: Older age (adjusted odds ratio (AOR) = 0.75; 0.64, 0.96)), no education (AOR = 1.37; 95 % CI: 1.102–1.72), lowest wealth quantile (AOR = 1.29; 95 % CI: 1.014-1.60), currently pregnant (AOR=1.28; 95% CI: 1.10, 1.51, currently breastfeeding (AOR =1.09; 95% CI: 1.025, 1.28), high gravidity (AOR=1.39; 95% CI: 1.13, 1.69), and HIV positive (AOR= 2.11; 95% CI: 1.59, 2.79) are individual factors associated with the occurrence of anemia. Likewise, living in a rural area (AOR=1.29; 95%CI: 1.02, 1.63), and availability of unimproved latrine facilities (AOR = 1.18; 95 % CI: 1.01, 1.39) are community level factors associated with higher odds of anemia. The spatial analysis indicated that statistically high hotspots of anemia were observed in the eastern (Somali, Dire Dawa and Harari regions) and north-eastern (Afar) parts of the country.

Conclusion: The prevalence rate of anemia among women of reproductive age is varied across the country. Significantly hotspots /high prevalence of anemia was observed in the eastern and north-eastern parts of Ethiopia. Anemia prevention strategies need to be targeted on rural residents, women with limited to no education, women who are breastfeeding, areas with poor latrine facilities and women who are HIV positive.

Key words: Anemia, spatial analysis, multilevel analysis, reproductive age women, women

Strength and limitation of this study

- Used large population-based data with a large sample size, which is representative of all regions of the country
- A combination of statistical methods (spatial analysis and multilevel logistics analysis) were applied which allows understanding of the role of contextual and geographical factors in the occurrence of anemia among women of reproductive age
- The cause effect and temporal relationship could not be established due to the cross sectional nature of the data
- Unable to incorporate essential factors such as dietary intake and behavioral factors in the analysis

Introduction

Anemia refers to a low hemoglobin level (<11mg/dl for pregnant women and <12mg/dl for non-pregnant women) [1]. If an individual's hemoglobin level is low, the red blood cells are unable to carry adequate oxygen for the body's physiologic needs [1]. Consequently, a low hemoglobin level can adversely affect women's health in the following ways: maternal mortality and severe morbidity [2], depression [3, 4], raised blood pressure [5, 6], as well as low birth weight and preterm birth [7].

Anemia is a major public health problem in women and children under five years of age [8]. Worldwide, 38% of pregnant women, and 29% of non-pregnant women were anemic in 2011 [8]. Pregnant women in low and middle income countries (LMIC) experience high rates of anemia, in which the highest prevalence rates are reported in Central and West Africa (56%), South Asia (52%) and East Africa (36%) [8]. Similarly, a large proportion of non-pregnant women were reportedly anemic in West and Central Africa (48%), South Asia (47%) and East Africa (28%) [8]. Thus, anaemia remains one of the global health priority areas at the global level, particularly in resource-limited settings [9]. Reducing anemia is considered as an essential part of improving the health of women, and the World Health Organization (WHO) has set a global target of 50% reduction of anemia among women of reproductive age by 2025 [10].

Anemia is also a common problem in Ethiopia; the recent Ethiopian Demographic Health Survey (EDHS 2016) reported 29% prevalence of anemia among pregnant women and 24% among women of reproductive age; the figure ranging from 16% to 59% across different parts of the country [11]. Likewise, in several pocket studies from different parts of the country researchers reported varied anemia prevalence rates among pregnant women, which ranged from 17% in the north. [12], 32% in the south [13] and up to 44% [14] and 57% [15] in the eastern part of Ethiopia. Similarly, in different studies there was reported to be a 16% [16] prevalence of anemia among non-pregnant women and 29% [17] and 30% [18, 19] among women of reproductive age.

Different factors are responsible for anemia, even though iron deficiency is the main cause of the disease [20]. Other micronutrients (vitamin A, vitamin B12, and folate), chronic bleeding, acute or chronic infections and parasitic infections (hookworm and malaria) are also known to cause anemia [16, 21-23]. Based on the geographic and disease situation in LMIC, about half of anemia cases are attributable to a deficiency of iron and the remainder may be due to diseases like parasitic infections, malaria and Human Immune Deficiency Virus (HIV) [24]. In a systematic review, it was revealed that the proportion of anemia caused by iron deficiency was below 50% in LMIC, with regional variations, poor sanitary conditions and subsequent increased occurrence of infections also leading to anemia [25].

In Ethiopia, varied prevalence rates of maternal anemia have been observed with different factors across different parts of the country [12, 15]. For instance, large family size, low education status, rural residence, hookworm infestation and HIV infection were identified as factors of anemia in northern Ethiopia [12, 26], while in studies from the eastern area it was reported that multigravidas, third trimester of pregnancy and intestinal infestation were factors for anemia during pregnancy [14, 27]. The variation in rates of anemia among women in Ethiopia might be due to the presence of diverse contextual and geographically variable factors including diet and the incidence of communicable diseases [9].

To date, spatial analyses have not been conducted to identify areas with hotspots (high prevalence rates) of maternal anemia in Ethiopia. Assessing the geographic distributions of anemia and the impact of risk factors on disease prevalence by area is important to prioritize and design targeted prevention and intervention programmes to address maternal anemia [28]. In addition, the burden of anemia has been used as a measureable indicator of soil transmitted-helminthiasis, so understanding the geographical distribution of anemia can help target prevention and control mechanisms for parasitic infections such as these [29].

Thus, the aims of this study were to assess the spatial distribution and determinant factors of anemia among women of reproductive age women in Ethiopia.

Methods

Patient and Public Involvement

As this study used the publicly available data set, no patients or members of the public were involved. The participants of this study were women of reproductive age (15-49). The mean (± standard deviation (sd)) age of the respondents was 28.2 years (±9.2 years). The majority (78%) of the participants were rural residents and nearly two thirds (66%) were married or living with a partner. Almost half (48%) of the participants had no formal education.

Study design and setting

An in depth analysis of the EDHS 2016 data was undertaken for this study. EDHS 2016 was a population based cross sectional study conducted across the country. It is the fourth national survey conducted in all parts of Ethiopia (in nine regional states (Tigray, Afar, Amhara, Oromia, Somali, Benishangul-Gumuz, Southern Nations, Nationalities and Peoples' Region (SNNP), Gambella and Harari) and two city administrations (Addis Ababa and Dire Dawa)) [11]. In Ethiopia the states are administratively further subdivided into Zones, Zones into *Woredas* and *Woredas* further into the lowest unit called *Kebeles.*

Sampling and data measurements

In the 2016 EDHS, stratified and cluster multistage sampling was used and it was intended to have appropriate demographic and health indicators at nationwide and regional states. In the first stage, 645 clusters of enumeration areas (EAs) (202 urban and 443 rural) were identified using probability proportional to the size of EAs. In the second stage, a random sample of 18,008 households was selected from all the identified EAs. A total of 15,683 women aged 15-49 years were interviewed and haemoglobin levels were measured for 14,923 of them [11] (Figure 1). Data collection took place from January 18, 2016, to June 27, 2016.

The sample size for EDHS was determined based on the multistage sampling procedure, taking into consideration the sampling variation. Standard errors were computed using the Taylor linearization method. The design effect, which is the ratio between the standard error with the given sample design and the standard error that would result if a simple random sample had been used, was determined [11].

Haemoglobin levels of the women were measured using HemoCue, which is the standard test used in the EDHS 2016, and all haemoglobin values were adjusted for both altitude and smoking status [11]. Pregnant women with a haemoglobin value <11g/dl and non-pregnant women with <12g/dl were considered anaemic [1]. Similarly, anemia was classified according to its severity as severe (hemoglobin value < 7 g/dl), moderate (7.0-9.9 g/dl) in all women and mild (10.0 – 10.9 g/dl) in pregnant women and (10.0 – 11.9 g/dl) in non-pregnant women [1].

Explanatory variables (Determinant factors)

Both individual and community level factors were used. The individual and community level factors included in this study are presented in Supplemental Table 1 with their definition and coding. The variables were selected based on the literature review for factors affecting anemia based on this sociodemographic, maternal as well as community level factors identified as important factors for the occurrence of anemia. Therefore, all the available variables in the data set were included for the analysis. Individual factors included were age, religion, marital status, educational status, BMI, birth interval, use of contraceptives, wealth index, family size, iron-folate intake and gravidity of women, while the community level factors were residence (urban, rural), region, water source and latrine facility type. Community level measures could also be driven by aggregating individual level variables, for example, the proportion of women in the community who are in the top quantile of wealth index and proportion of women in the community who have clean water access. Community level factors describe the group of populations living in similar settings.

The assumption of independence of observation has been taken as a basis to determine which variables are analysed at individual and community level. If the observations at the individual level are independent, variables were treated as individual level factors. Whereas, if the observations were clustered into higher levels of units and if several women have shared features such as place of residence, types of water source, latrine facility and region that could have the same effect on maternal anemia in the locality, then variables are analysed at the community level.

Data analysis

Spatial analysis

Spatial analyses were performed using Geoda version 1.8.10, QGIS Version 2.18.0 and Arch GIS software version 10.1, and base files of the administrative regions for Ethiopia were obtained from DIVA (diva-gis.org). The spatial analysis was conducted by joining the occurrence of anemia (as proportions) with each cluster to the corresponding geospatial location (survey cluster values). The values of DHS data were merged with the GPS dataset in Geoda software and these values were imported into the QGIS software. Anemia proportions were then computed at lower (cluster), zonal and regional levels using QGIS.

The spatial pattern of the rate of maternal anemia was visualized and a spatially smoothed proportion was obtained through empirical Bayes estimation methods [30] The smoothed proportions present clearer patterns, where the problem was most severe. The spatial empirical Bayes "smooth" estimates technique was able to deal with spatial heterogeneity. The estimation technique guarantees that estimates of neighbouring states are more alike than estimates of states that are further away [31].

A standardized prevalence rate (SPR), or the ratio of the observed prevalence rate to a national prevalence rate, was determined using Geoda software [31]. Geoda implements this in the form of an excess risk estimate as part of the map. The excess risk rate is the ratio of the observed rate to the average rate computed for all the data [31].

Furthermore, a spatial analysis was performed to identify the clustering of maternal anemia or hotspot areas (the areas that have higher anemia prevalence rates compared to the national average) in different regions of Ethiopia. Spatial analysis is an epidemiological method useful to specify geographic areas with high or low rates of disease occurrence and variability over the region or country [32]. Getis-Ord Gi* statistics was used for this spatial analysis. Local Getis-Ord Gi* statistics [33] are important to identify the hot and cold spot areas for maternal anemia using geographic poisoning system (GPS) latitude and longitude coordinate readings which were taken at the nearest community centre for EAs or EDHS 2016 clusters [11]. An anemia hotspot refers to the occurrence of high prevalence rates of anemia clustered together on the map, whereas cold spots refers to the occurrence of low prevalence rates of anemia clustered together on the map [33].

A local Getis-Ord G-statistic tool in ArcGIS was used to calculate the spatial variability of high and low prevalence rates of maternal anemia. An autocorrelation can be classified into positive and negative correlation through the Local Getis-Ord G statistics [33]. Positive autocorrelation occurs when similar values clustered together on a map (high rates surrounded by nearby high rates or low rates surrounded by nearby low rates). Negative autocorrelation indicates different values clustered together on a map, that is, high values surrounded by nearby low values or low values surrounded by nearby high values. Statistical significance of autocorrelation was determined by z-scores and p-value with a 95 % level of confidence. The distribution and variations of maternal anemia prevalence rates across the country were displayed on the map.

Statistical analysis

The descriptive statistical analysis was performed using SPSS software version 24.0 (www.spss.com) by complex sample analysis. Frequencies, percentage, and standard deviation were used for the descriptive analysis. Since some regions with small populations were oversampled, while others with large population were underrepresented, the weighted frequencies and percentages (based on population size of each region) were computed as a correction. The detailed weighting procedure was described in EDHS 2016 report [11]. The mean and standard deviation were computed for blood hemoglobin level. The mean hemoglobin value was also compared across different independent categorical variables using One-way Analysis of Variance (ANOVA) or independent t-test.

Multilevel logistic regression: The Multivariable multilevel logistic regression model was used to determine the effect of different factors on maternal anemia. The analysis was performed by using SAS version 9.4 software (SAS North Carolina State University, www.sas.com) using Proc Glimmix with Laplace's method. For this multilevel analysis, four models were constructed. The first model was constructed without independent variables to assess the effect of community variation on maternal anemia. Individual level factors were incorporated in the second model. In the third model, community level factors were included. Finally, both individual and community level factors were included in the fourth model.

The results of fixed effects were presented as odds ratio (OR) with 95% confidence intervals (CIs). An adjusted odds ratio (AOR) with 95% CIs was computed to identify the independent factors of maternal anemia and a p-value <0.05 was used as a measure of statistical significance. A muliticollinearity test was done in order to rule out a significant correlation between variables. If the values of variance inflation factor (VIF) was lower than 10, then the collinearity problem was considered as less likely. The random effects (variation of effects) were measured by intra-cluster correlation coefficient (ICC) (variance partition coefficient) [34], percentage change in variance (PCV) [35] and median odds ratio (MOR) [34, 36] which measure the variability between clusters in the multi-level models. ICC explains the cluster variability while MOR can quantify unexplained cluster variability (heterogeneity). MOR translates cluster variance into OR scale. In the multilevel model, PCV can measure the total variation due to factors at the community and individual level [35]. The ICC, PCV and MOR were determined using the estimated variance of clusters utilising the following formula [34, 35].

$$\text{ICC} = \frac{V}{(V + \frac{\pi^2}{3})} \qquad \text{MOR} = \exp\sqrt{2 \times V \times 0.6745} \sim \exp\,(0.95\sqrt{V})]$$

Where V is the estimated variance of clusters

And

$$\text{PCV} = \frac{(V_A - V_B)}{V_B} \times 100$$

Where V_A = variance of the initial model; V_B = variance of the model with more terms

The multilevel analysis model is one of the analysis methods which can correctly handle the correlated data [37]. A multilevel model evaluates how factors at different levels affect the dependent variable. A multilevel model provides correct parameter estimates by correcting the biases introduced from clustering by producing correct standard errors, thus producing correct CI, and significance tests [37]

Ethical consideration

Publicly available EDHS 2016 data was used for this study. The EDHS 2016 was approved by the National Research Ethics Review Committee (NRERC) of Ethiopia and ICF Macro International. MEASURE DHS approval was obtained to use EDHS 2016. Informed consent was taken from each participant and all identifiers were removed. This analysis was approved by the University of Newcastle Human Research Ethics Committee (approval reference number H-2018-0045).

Results

Sociodemographic characteristics

The data on 14,923 women were included in this analysis, including 642 clusters nested in 11 regions. The descriptive statistics of the study participants are presented in Table 1. The mean (± sd) age of the respondents was 28.2 years (±9.2 years). Most of the participants lived in a rural area (78%). Nearly two-thirds (66%) of participants were married or living with a partner. Almost half (48%) of the women had no formal education and around 43% were of the Orthodox Tewahdo Christian religion. Only 18% of the households had access to a piped water source for drinking, and 15% had access to an improved latrine facility. Nearly one-third (n= 4,657; 31.2%) of women were breastfeeding at the time of the survey (Table 1). The average haemoglobin level among lactating mothers was 12.6 g/dl (±1.7 g/dl) and about 28.3% (95% CI: 25.7-31.0%) of these women were anemic.

Table 1: Sociodemographic and other health-related characteristics of study participants included in the analysis, EDHS 2016 (N=14,923)

Variables	**Weighted Frequency**	**Weighted percent**
Age		
15-19	3165	21.2

20-29	5467	36.6
30-39	4078	27.3
40-49	2213	14.8
Place of residence		
Urban	3169	21.2
Rural	11754	78.8
Educational status		
No education	7215	48.3
Primary	5244	35.1
Secondary	1676	11.2
Higher	789	5.3
Marital status		
Single	3758	25.2
Married	9800	65.7
Divorced/widowed/separated	1365	9.1
Religion		
Orthodox	6447	43.2
Protestant	3514	23.5
Muslim	4645	31.1
Other	317	2.1
Region		
Tigray	1073	7.2
Afar	119	0.8
Amhara	3645	24.4
Oromia	5422	36.3
Somali	417	2.8
Benishangul-Gumuz	146	1.0
SNNPR	3124	20.9
Gambella	42	0.3
Harari	32	0.2
Addis Ababa	825	5.5
Dire Dawa	77	0.5
Wealth index		

Poorest	2519	16.9
Poorer	2717	18.2
Middle	2891	19.4
Richer	2979	20.0
Richest	3816	25.6
BMI		
<18.5	3060	22.1
18.5-24.9	9740	70.5
>=25	1018	7.4
Birth interval		
< 24 months	1415	18.3
>= 24 months	6305	81.7
Current use of contraceptives		
Yes	1088	7.3
No	13835	92.7
Iron folate intake during pregnancy (n = 7328)		
Yes	3108	42.4
No /don't know	4220	57.6
Gravidity of women (children ever born)		
0	4745	31.8
1-3	4715	31.6
4+	5464	36.6
Children ever born in the preceding 5 years		
0	7595	50.9
1	4475	30.0
2+	2852	19.1
Currently breastfeeding		
Yes	4657	31.2
No	10266	68.8
Currently pregnant		
Yes	1088	7.3
No	13835	92.7
Smoking		

Yes	96	0.6
No	14827	99.4
Birth in the last year		
0	12474	83.6
1-2	2449	16.4
HIV test		
Positive	187	1.3
Negative	14724	98.7
Water source		
Piped water	2646	17.7
Other improved	6926	46.4
Unimproved	5351	35.9
Latrine facility type		
Improved toilet	2231	14.9
Unimproved toilet	7877	52.8
Open defecation	4414	29.6
Other	401	2.7
Anemia status		
Anemic	3527	23.6
Non-anemic	11396	76.4
Proportion of women in the community who have clean water source , m(se)	64.1 (33.6)	
Proportion of women in the community who have unimproved latrine facility; m(se)	85.1(25.0)	
Proportion of women in the community who are in lowest quantile of wealth index; m(se)	35.1(30.0)	
Percentage of unimproved water per cluster; m(se)	35.9 (33.6)	

BMI= Body mass index; SNNP= Southern Nations, Nationalities and Peoples' Region; m= mean; se= standard error

Prevalence rate of maternal anemia

Amongst all respondents, the mean (±sd) blood hemoglobin level (adjusted for altitude) was 12.8 g/dl (±1.7 g/dl). The overall prevalence of anemia among women of reproductive age across the country was 23.6% (95% CI: 22.0, 25.3). The prevalence of mild, moderate and severe anemia among all women of reproductive age were 17.8% (95% CI: 16.7-19), 5.0% (95% CI: 4.3-5.8) and 0.8% (95% CI: 0.5-1.2) respectively. There was regional variation in anemia prevalence among women of reproductive age (p= 0.0001) and higher prevalence rates observed in Afar, Somali, Gambella, Dire Dawa and Oromia regions. Lower prevalence of anemia was observed in Addis Ababa, Tigray, and Amhara regions. Rural areas had a higher prevalence, 25.4 (95% CI: 23.5, 27.4) of maternal anemia than urban areas, 17.0 (95% CI: 14.4, 20.0) (p=0.0001). The highest proportion of maternal anemia were found in Somali Regional States, while the lowest proportions were found in Addis Ababa city administration (Table 2).

Table 2: The variation of anaemia prevalence rates across different regions and different sociodemographic characteristics of women in Ethiopia, 2016

Region	**Weighted frequency**		**Weighted proportion of anemia (95% CI)**	**p-value**
	Anemic	Non-anemic		
Place of residence				
Urban	538	2630	17.0 (14.4,20.0)	0.0001
Rural	2989	8766	25.4 (23.5, 27.4)	
Region				
Tigray	212	861	19.7 (16.8,23.0)	0.0001
Afar	53	66	44.7 (39.9,49.6)	
Amhara	627	3019	17.2 (14.9,19.7)	
Oromia	1480	3942	27.2 (23.8,31.1)	
Somali	248	169	59.5 (55.2,63.7)	
Benishangul-Gumuz	28	118	19.2 (16.1,22.7)	

SNNP	704	2420	22.5 (19.4,26.0)	
Gambella	11	31	26.1 (21.3,31.5)	
Harari	9	23	27.7 (23.7,32.1)	
Addis Ababa	132	693	16 (13.5,18.8)	
Dire Dawa	23	54	30 (25.8,34.8)	
Education status				
No education	2002	5212	27.8 (25.4,30.2)	0.0001
Primary	1136	4108	21.7(19.8,23.7)	
Secondary	297	1378	17.8 (14.9,21.0)	
Higher	91	697	11.5(8.2,16.0)	
Wealth index				
Poorest	863	1656	34.3(29.7,39.1)	0.0001
Poorer	688	2028	25.3(22.6,28.3)	
Middle	686	2205	23.7(21.2,26.5)	
Richer	625	2354	21.0(18.6,23.6)	
Richest	664	3152	17.4(15.1,19.9)	
Currently pregnant				
Yes	317	771	29.1 (24.9,33.7)	0.003
No	3210	10625	23.2 (21.6,24.9)	
Currently breastfeeding				
Yes	1317	3340	28.3 (25.7,31.0)	0.0001
No	2210	8055	21.5 (20.0,23.2)	
Total	3527	11396	23.6 (22.0, 25.3)	

Around 1,080 [7.3% (95% CI: 6.6, 8.1)] participants were pregnant at the time of the interview. The mean hemoglobin level among pregnant women was 11.7 g/dl (±1.8 g/dl) and 29.1% (95% CI: 24.9-33.7) of these women were anemic. The prevalence of anemia was higher among pregnant women, 29.1 (95% CI: 24.9, 33.7) than non-pregnant women, 23.2 (95% CI: 21.6, 24.9) (p= 0.003) (Table 2). The mean hemoglobin value of women in their second and third trimester was significantly lower compared to women in their first trimester (p = 0.001). The mean hemoglobin levels in pregnant women who had less than a 24 month birth interval (for their most recent birth) was significantly lower compared to women who had a birth interval of less than or equal to 24 months (p= 0.0001). Similarly receiving Iron folate supplements during pregnancy improved the mean haemoglobin values in pregnant women (Table 3).

Table 3: Hemoglobin level among pregnant women in Ethiopia, 2016

Variables	Number	Hemoglobin level (g/dl) (mean(sd))	P values of ANOVA or independent t test
Children ever born (CEB)	1,088		0.0001
0	213	12.1(1.7)	
1-3	484	11.7(1.8)	
4+	390	11.5 (1.8)	
Pregnancy stage	1,088		0.0001
1st trimester	226	12.4 (1.7)	
2nd trimester	433	11.6 (1.6)	
3rd trimester	429	11.5 (1.9)	
CEB in last 5 years	1,088		0.0001
0	339	12.1 (1.7)	
1	484	11.7 (1.8)	
2+	265	11.4 (1.9)	
Fe-Fol supplementation	749		0.018
Yes	251	11.8 (1.5)	
No	498	11.5 (1.9)	
Birth interval	702		0.0001
< 24 months	206	11.2 (2.0)	
>= 24 months	497	11.9 (1.5)	

sd = standard deviation, Fe-Fol= Iron-folate, CEB = Children Ever Born

Determinate factors of maternal anemia

Multilevel Analysis (Fixed effect analysis)

The results of multilevel logistic regression for the individual and community level variables are presented in Table 4. In the full model in which all individual and community level factors are included, residence, education, religion, wealth index, pregnancy and breastfeeding status, gravidity of women, and lack of availability of an improved latrine were factors significantly associated with maternal anemia. The results of the muliticollinearity test indicated that no collinearity problem existed, since the VIF value of all variables is lower than 10.

Individual factors

The average hemoglobin value was significantly different across age groups (p=0.0001). The highest mean hemoglobin level, 13 g/dl was observed in the youngest (15-19 years) age group while the lowest mean hemoglobin level, 12.71 g/dl, in the 30-34 years age group. The general pattern indicated roughly linear decline among women aged 15-34 years (Figure 2). Women aged 40-49 years old were 25% less likely to be anemic compared to women in the youngest age group (15-19 years old) (AOR= 0.75 (0.64, 0.96). Those women with limited education were 1.37 times more likely to be anemic than women who completed higher education (AOR = 1.37; 95 % CI: 1.102–1.72). The odds of anemia increased by 29% (AOR = 1.29; 95 % CI: 1.014-1.60) when comparing the poorest to the richest women. The odds of anemia were higher in women who were pregnant (AOR=1.28; 95% CI: 1.10, 1.51) compared to those who were not non-pregnant. Women who were currently breastfeeding were 9% (AOR =1.09; 95% CI: 1.025, 1.28) more likely to be anemic. The odds of anemia were 39% higher among mothers who had given birth to four or more children (AOR=1.39; 95% CI: 1.13, 1.69). Women who gave birth to two or more children in the preceding five years of the survey were at higher risk of having anemia (AOR =1.31; 95% CI: 1.09,1.57). In this study, women who were HIV positive had a twofold increased odds of having anemia compared to women classified as HIV negative (AOR= 2.11; 95% CI: 1.59, 2.79) (Table 4).

Community level factors

Living in a rural area was associated with a 29% higher odds of anemia among women of reproductive age than women who were urban residents (AOR=1.29; 95%CI: 1.02, 1.63). Women from households without access to a latrine had 18% higher odds of anemia compared to women from households that had an improved latrine facility (AOR = 1.18; 95 % CI: 1.01, 1.39). Higher odds of anemia were observed in Somali regional state (AOR = 2.16; 95 % CI: 1.58, 2.90) compared to Dire Dawa. However, the odds of maternal anemia were lower in Gambella, Addis Ababa, Amhara and Oromia region compared to Dire Dawa (Table 4).

Multilevel analysis (random effect analysis)

The results of the random effects model is shown in Table 4. The results of the random effect shows that the prevalence rate of anemia varied across communities (t^2=0.88, p=<0.0001). In other words, the anemia prevalence rate was not similarly distributed across the communities. About 21% of the variance in the odds of maternal anemia could be attributed to community level factors, as calculated by the ICC based on estimated intercept component variance. After adjusting for individual and community level factors, the variation in maternal anemia across communities remained statistically significant. About 16% of the odds of maternal anemia variation across communities was observed in the full model (Model 4) (Table 4).

Moreover, the MOR indicated that maternal anemia was attributed to community level factors. The MOR for anemia was 2.44 in the empty model (Model 1); this showed that there was variation between communities (clustering) since MOR was 2.4 times higher than the reference (MOR = 1). The unexplained community variation in maternal anemia decreased to MOR of 2.1 when all factors were added to the null model (empty model). This indicates that when all factors are included, the effect of clustering is still statistically significant in the full model (Table 4).

Table 4: Determinant factors bivariate association between maternal anemia and individual and community contextual characteristics of Ethiopian women, 2016

Variables	Model 1	Model 2 Individual factors	Model 3 Community level factors	Model 4 Individual + community level factors
Individual level factors				
Age				
15-19		1		1
20-29		0.93 (0.81,1.07)		0.96 (0.82, 1.19)
30-39		0.89 (0.75,1.10)		0.92 (0.78,1.11)
40-49		0.76 (0.61,0.92)		0.75 (0.64,0.96)
Educational status				
No education		1.41 (1.13,1.76)		1.37 (1.10, 1.72)
Primary		1.22 (0.99,1.51)		1.24 (1.00,1.53)
Secondary		1.22 (0.98,1.5)		1.23(0.98,1.52)
Higher		1		1

Marital status		
Single	0.99 (0.80, 1.22)	0.972 (0.81,1.22)
Married	1.07 (0.92, 1.23)	1.09 (0.91,1.23)
Divorced/widowed/separated	1	1
Religion		
Orthodox	1	
Protestant	1.36 (1.16, 1.58)	1.37 (1.15,1.63)
Muslim	2.04 (1.79, 2.33)	1.36 (1.16, 1.58)
Other	1.49 (1.05, 2.12)	1.525 (1.06, 2.13)
Wealth index		
Poorest	1.73 (1.48, 2.03)	1.29 (1.014,1.60)
Poorer	1.31 (1.10, 1.54)	1.21 (0.96,1.45)
Middle	1.28 (1.08,1.51)	1.22 (0.98,1.50)
Richer	1.04 (0.88,1.24)	1.01(0.82,1.24)
Richest	1	1
Current using contraceptives		
Yes	0.99 (0.90,1.10)	1.0 (0.91,1.11)
No	1	1
Currently pregnant		
Yes	1.30 (1.11,1.52)	1.28 (1.10,1.51)
no	1	1
Currently breastfeeding		
yes	1.12 (1.00,1.24)	1.09 (1.03,1.28)
No	1	1
Gravidity of women (total children ever born)		
0	1	1
1-3	1.23 (1.03,1.46)	1.22 (1.02,1.44)
4+	1.40 (1.15,1.72)	1.39 (1.13,1.69)
Smoking		
Yes	0.98 (0.64,1.50)	1.05 (0.69,1.61)
No	1	1
Birth in the last 1 year		

0	1		1
1-2	1.20 (1.05,1.37)		1.15 (1.01,1.32)
Children ever born in preceding 5 years			
0	1		1
1	1.12 (0.96,1.29)		1.10 (0.95,1.27)
2+	1.39 (1.16,1.66)		1.31 (1.09,1.57)
HIV test			
Positive	2.19 (1.65, 2.91)		2.11 (1.59, 2.79)
Negative	1		1
Community level factors			
Place of residence			
Urban		1	1
Rural		1.67 (1.35,2.05)	1.29(1.02,1.63)
Region			
Tigray		0.39(0.28,0.53)	0.52(0.38, 0.72)
Afar		1.25 (0.91,1.7)	1.14 (0.83,1.56)
Amhara		0.30 (0.22,0.41)	0.39 (0.28,0.54)
Oromia		0.55 (0.41,0.75)	0.57 (0.42,0.78)
Somali		2.40 (1.78,3.27)	2.16 (1.58,2.90)
Benishangul-Gumuz		0.36 (0.25,0.50)	0.37 (0.26,0.52)
SNNPR		0.40 (0.29,0.54)	0.41(0.29,0.57)
Gambella		0.63 (0.45,0.87)	0.63(0.45,0.89)
Harari		0.74 (0.53,1.04)	0.76(0.54,1.04)
Addis Ababa		0.54 (0.39,0.73)	0.67(0.49,0.91)
Dire Dawa		1	1
Water source			
Piped water		1	1
Other improved		1.15 (0.95,1.39)	1.04 (0.86,1.26)
Un-improved		1.18 (0.95,1.44)	1.03 (0.83,1.27)
Latrine facility type			
Improved toilet		1	1
Unimproved toilet		1.12 (0.97,1.29)	1.08 (0.94,1.25)

Open defecation			1.33 (1.15,1.55)	1.18 (1.00,1.39)
Other			0.86 (0.64,1.17)	0.94 (0.69,1.27)
Random effects (effect of variation/ measure of variation for maternal anemia**)**				
Community level variance (SE)	0.888 (0.07)	0.46(0.05)	0.32(0.04)	0.31(0.035)
P- value	0.001	0.001	0.001	0.001
DIC(-2log likelihood)	7926.056	7749.25	7720.74	7613.56
ICC (%)	21.25	16.1	18.3	15.86
Explained variation –PCV (%)	Reference	40.95	21.0	43.1
MOR	2.44	2.13	2.3	2.1

Note: Model 1= empty model (without the predictors); Model 2= adjusted for individual factors; Model 3 = adjusted for community level factors; Model 4 = adjusted for both community and individual level factors; DIC = Deviance Information Criterion; ICC= Intra-cluster Correlation Coefficient; MOR= Median Odds Ratio; PCV = Percentage Change in Variance; SE= Standard Error; SNNPR=Southern Nations, Nationalities and Peoples' Region

Spatial data analysis

Figure 3 displays the empirical Bayes smoothed proportion estimate of maternal anemia across regions in Ethiopia. A severe anemia prevalence rate (≥40%) among women of reproductive age was observed in Afar and Somali Regional States. Likewise, a moderate anemia prevalence rate (20-40%) occurred in Oromia, Gambella, SNNPR, Harari and Dire Dawa Regional States. Whereas, and a mild anemia prevalence rate (<20%) was observed in Tigray and Amhara Regional Sates and Addis Ababa.

Similarly, the standardized prevalence ratio by regions (standardized to the national average prevalence of 23.6%), ranging from 0.63 to 2.39, was displayed on the map (Figure 3). A higher prevalence ratio of maternal anemia was observed in Somali (2.39), Afar (1.8) Oromia (1.17), Dire Dawa 1.15, Gambella (1.12) regional states (Figure 4); whereas, a lower prevalence ratio of anemia occurred in other regional states - Addis Ababa (0.64), Amhara (0.76), Benishangul-Gumuz (0.79), SNNPR (0.96), Tigray (0.85)

Figure 5 displays the smoothed anemia prevalence rates at zonal level where higher anemia rates were observed in all zones in Afar and Somali regions, as well as in some zones in Oromia. Likewise, the higher standardized ratio of maternal anemia was observed in all zones in Afar and Somali regions as well as in some zones in Oromia (Figure 6).

The spatial distributions of maternal anemia at the lower level (cluster level) is displayed in figure 6. The spatial investigation at the cluster level indicated that statistically high hotspots of anemia were observed in the eastern (Somali, Dire Dawa and Harari regions) and in north-eastern (Afar) parts of the country, while cold spots of anemia were observed in the northern (Tigray, Amhara), central (Addis Ababa, Oromia) and western (Benishangul-Gumuz and Gambella) parts of the country (Figure 7).

Discussion

Approximately a quarter of women of reproductive age were anemic in the current study, indicating that anemia is a moderate public health problem at the national level in Ethiopia [1]. However, geographic differences demonstrated that anemia is a particularly serious public health problem in 5 of the 11 Ethiopian states. A higher proportion of anemia cases was observed in the eastern and north-eastern parts of the country, which are less developed compared to other Ethiopian states in terms of economy, gender, health care facility and food availability [38]. The geographical difference of anaemia across the regional states might be attributable to the regional variation of food consumption preferences [39, 40], the occurrence of communicable diseases [41], and differences in availability of health care facilities [42]. The altitude also has an effect on the hemoglobin level [1] which results in a disparity of anemia occurrence across the country. In addition, lack of clean water and unimproved latrine facilities would increase the occurrence of soil transmitted infection [43] which in turn could lead to anemia [44]; these might explain some of the observed geographical differences.

According to the final model, both individual and community level factors were responsible for about 43% of the disparity of anemia prevalence rates among women of reproductive age in Ethiopia. After adjusting for all factors in the model, the likelihood of having anemia was higher among those of younger age, with lower levels of education, living in rural areas, in the lowest wealth quantile, who were currently pregnant or breastfeeding, with high gravidity, who had given birth in the year prior to the survey and who were without access to an improved latrine facility.

Women aged 40-49 years had a lower likelihood of being anemic compared to women aged between 15-19 years. This finding is in line with other study findings from Ethiopia [16, 19] and Benin [45]. This could be due to the fact that low fertility rates occurred in this age group (40-49) [11]. However, in Iran [46] it has been reported that women aged 20-24 were less likely to be anemic compared to those aged 45-49; this might be a result of Iran having a targeted intervention for younger women or women of reproductive age [46].

In this study, it was found that there is variation of the anemia rate in terms of education status of the women. A higher proportion of anemic cases were observed among women with no education. It was found that women who did not have formal education had higher odds of anemia than those with higher education. This is consistent with other studies conducted in developing countries [24] including in Ethiopia [16], Timor-Leste [47], Benin [45] and India [48, 49] in which it was reported that a low level of education was associated with higher odds of anemia among women of reproductive age. Formal education might assist women to obtain knowledge that in turn helps them to follow better lifestyle behaviours like good nutrition, and to form better health-seeking habits and hygiene practices that can prevent maternal anemia.

A higher proportion of anemic cases were observed among women in the poorest wealth quantile. The lowest wealth quantile compared to highest quantile was associated with a higher risk of maternal anemia. Results of this study show that women who were in the poorest wealth quintile were 30% more likely to be anemic than women who belong to the richest quintile; this is in line with the results of other studies conducted in other developing countries [24] like

Benin [45] and India [49, 50]. This might be due to the fact that having a low income would mean having less money to buy nutritious foods or have a balanced diet [51, 52], which in turn leads to inadequate nutrient intake and nutritional status [53]. More than 38 % of the Ethiopian population belongs to the poor and poorest wealth quintile, which indicates a large percentage of women are at risk for anemia because of low socioeconomic position [11].

Lactating mothers were 9% more likely to have anemia than non- lactating mothers. Lactating may predispose women to low haemoglobin, which results in anemia. In a study conducted in India [54], a similar finding was reported, that lactating mothers were more likely to be anemic than non-lactating women.

The findings of our study clearly show the role of women's fertility in anemia. Increased odds of anemia was associated with high gravidity, births in the past five years of the survey and having a birth in the last year. Similar studies in Ethiopia [16], Iran [46] and Timor-Leste [47] also document this association between parity and risk of anemia. The study results from Pakistan [55, 56] and Iran [46] indicate that women with a parity of four or more were found to be at increased risk of anaemia than women with lower parity. This might be explained by that fact that the more the women give birth, the more they are exposed to blood loss which in turn results in low hemoglobin levels in the blood [57]. Similarly, prior births may deplete maternal iron stores due to the increased nutritional demands of pregnancy and puerperal blood loss [58]. Consequently, emphasis needs to be placed on family planning services. Increased odds of anemia were observed in women who were HIV positive. In this study, women who were HIV positive had twofold increased odds for anemia. This could be due to the direct effects of the HIV infection on the bone marrow and depletion of hemoglobin levels in the blood [59]. Many of the opportunistic infections to which HIV patients are susceptible might also lead to anemia [59].

This study revealed there to be a significant difference in the proportion of anemic cases according to place of residence (urban/rural). The likelihood of having anemia was higher for rural residents compared to urban residents. This is in agreement with a study conducted in low income countries in which it was revealed that living in a rural area was a determinant factor for anemia [24]. A recent report illustrated that more than half of the Ethiopian population had access to unimproved toilet facilities [60]. Our study findings revealed that women from households with unimproved latrine facilities were more likely to be anemic than women from households with improved latrine facilities, which is in agreement with other research findings

[45, 61]. The possible justification might be that an unimproved latrine facility would expose women to helminthic infections [43], which in turn resulted them developing anemia [44].

Strength and Limitations

This study used large population-based data with a large sample size, which is representative of all regions of Ethiopia. Furthermore, a combination of statistical methods (spatial analysis and multilevel logistics analysis) were applied for this study which allows for the understanding of the role of contextual and geographical factors in the occurrence of anemia among women of reproductive age. Because of the cross sectional nature of the EDHS data, the cause/effect and temporal relationship could not be established based on these study findings. Similarly, essential factors such as dietary intake and behavioural factors were not available in the EDHS survey so that it was not possible to incorporate these variables in the analysis. Furthermore, EDHS was a questionnaire based survey and relied on the memory of the respondents, and as such, recall bias in the results might be a weakness for this study.

Conclusion

This study indicates that considerable geographic disparities in maternal anemia prevalence rate occur within Ethiopia. The results of this study revealed that maternal anemia was non-random across the country; significant anemia hotspots were observed in the eastern and north eastern part of the country while anemia cold spots were observed in the northern and western parts of the country. About 43% of the disparity in maternal anemia occurrence across communities was attributable to both individual and community level factors. The increased occurrence of maternal anemia was associated with individual and community level factors. For women, being of rural residence, having no formal education, being in the poorest wealth index, either currently pregnant or breastfeeding, and higher gravidity were factors that increased the odds of maternal anemia at the individual level, whereas lack of a clean water source, and access to an unimproved toilet facility were factors significantly associated with maternal anemia.

Accordingly, the prevention of maternal anemia requires multifaceted intervention approaches, for instance, improving the economic and educational status of women, and improving the availability of clean water and toilet facilities. Anemia prevention strategies must be targeted on the identified factors. Priority should be given for those states or areas which have maternal anemia hotspots. Particularly, any intervention programs need to be prioritized for pregnant women, women having a recent birth, those with lower levels of education, and women living in rural areas. The regions with the greatest numbers of anemic women (Afar and Somali) should be prioritized, as the burden of anemia is higher in these areas, with more than 50% of women being anemic.

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Authors' contributions

Formulating the research question(s): KTK CC DL EG; designing the study: KTK CC DL EG; analysing the data: KTK Interpreting the results: KTK CC DL EG; drafting, writing, reviewing and approving the final manuscript: KTK CC DL EG.

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Conflicts of interest

The authors declare that they have no conflicting interests.

Data sharing statement

This study was an in depth analysis of publicly available dataset from the Demographic and Health Surveys Program (DHS Program). The dataset is available at the DHS program website (http://www.measuredhs.com)

Figure 1: Selection of the Sample in the 2016 EDH Survey

Figure 2: Average hemoglobin value with 95% CI at different age groups, Ethiopia, 2016

Figure 3. Spatial Empirical Bayesian smoothed (SEBS) percentage of maternal anemia across regions

Figure 4. Standardized prevalence ratio for anemia among women of reproductive age across the regions in Ethiopia (standardized to national prevalence of 23.6%).

Figure 5. Spatial Empirical Bayesian smoothed (SEBS) percentage of maternal anemia across Zones

Figure 6. Standardized prevalence ratio for anemia among women of reproductive age across Zones in Ethiopia (standardized to national prevalence of 23.6%).

Figure 7. Spatial pattern of hotspots and cold spots of maternal anemia rate at cluster level in Ethiopia, EDHS, 2016

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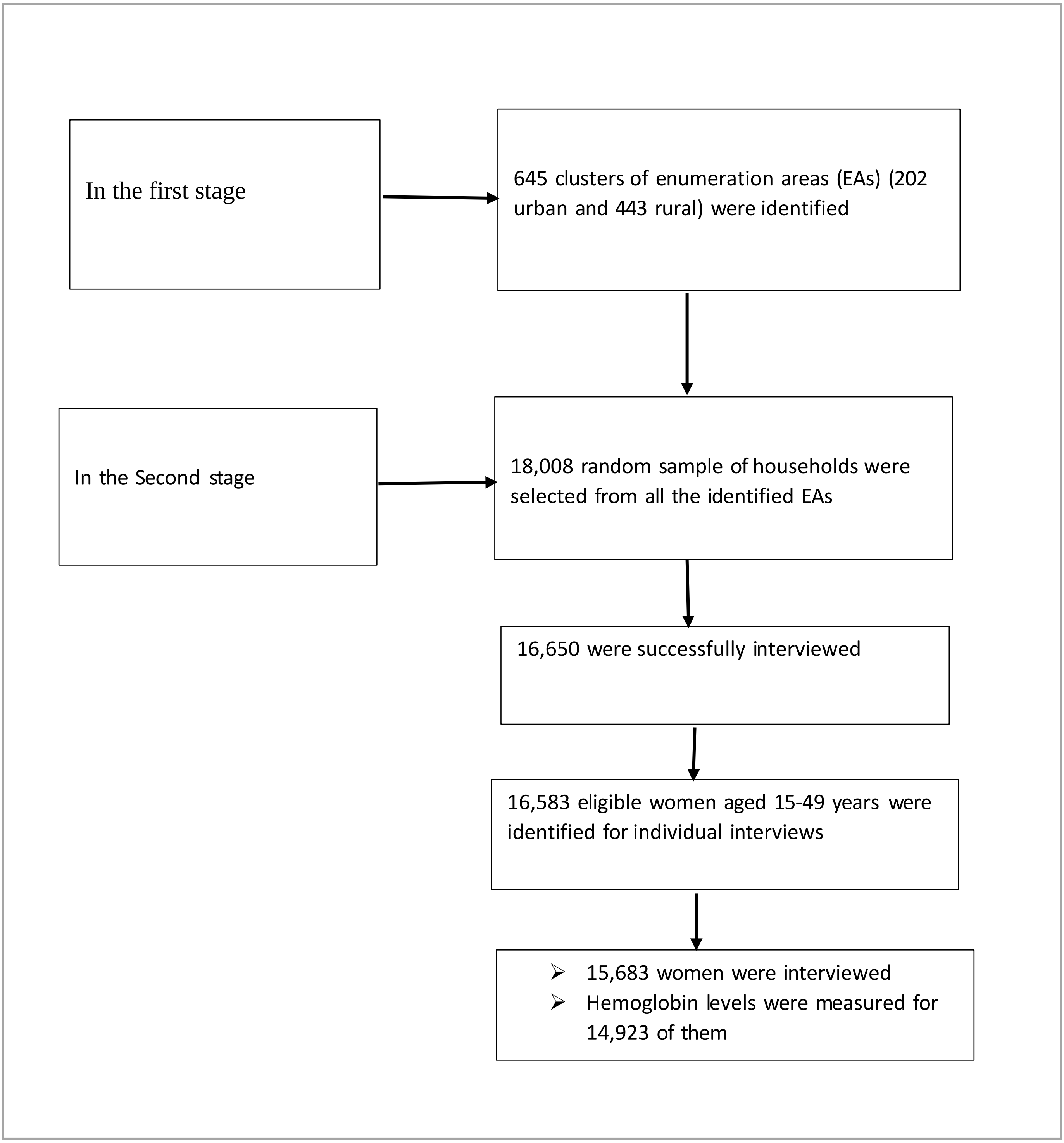

Figure 1: Selection of sample in the 2016 EDH Survey

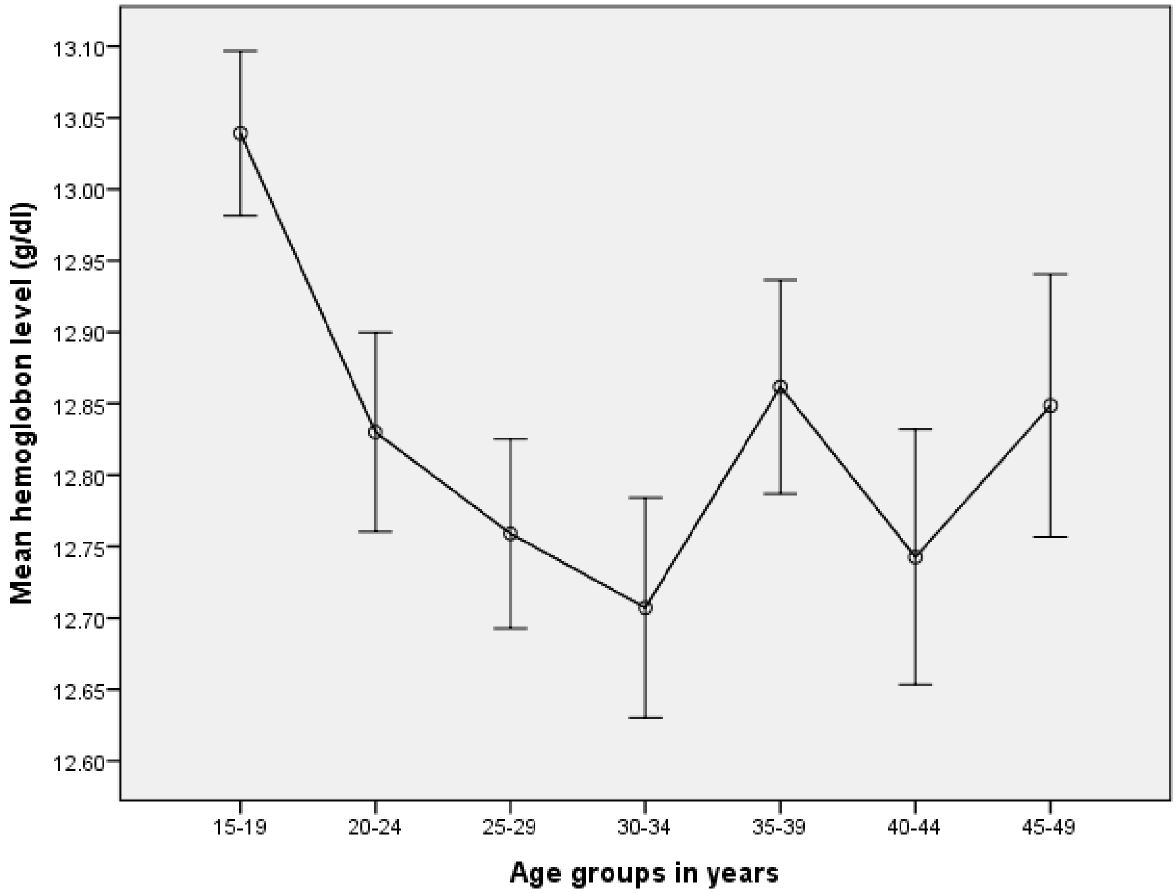

Figure 2: Average hemoglobin value with 95% CI at different age groups, Ethiopia, 2016

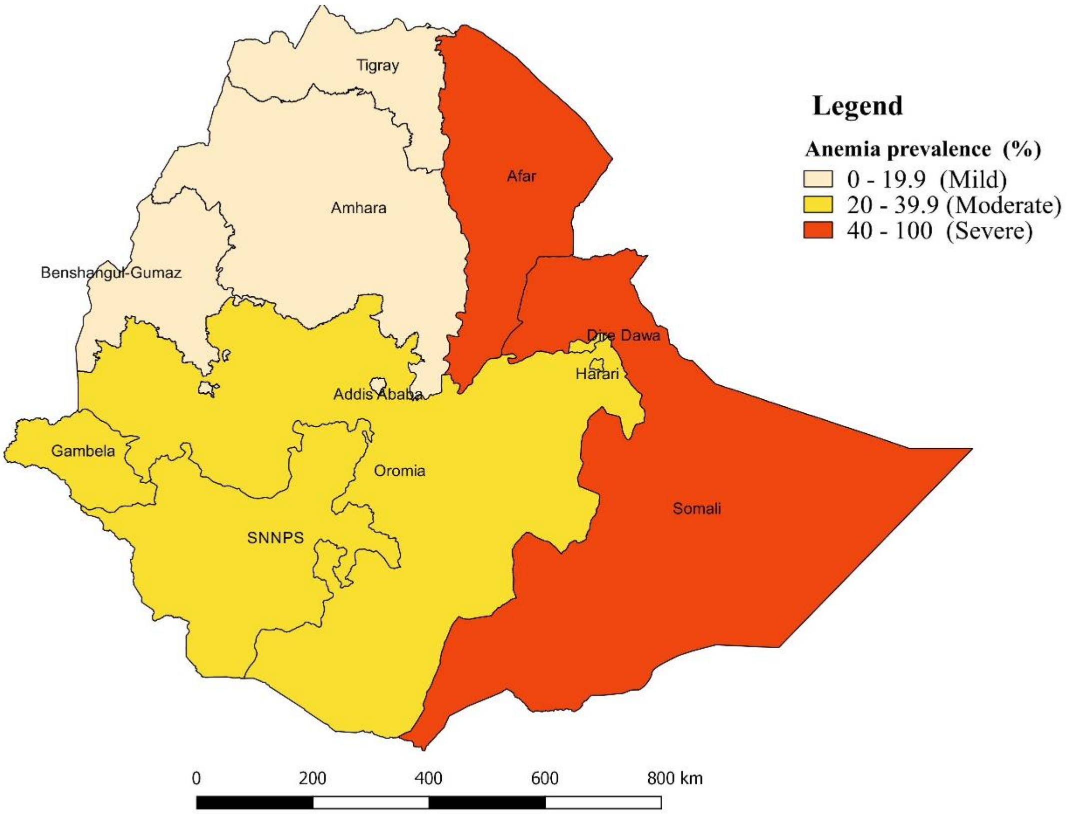

Figure 3. Spatial Empirical Bayesian smoothed (SEBS) percentage of maternal anemia across regions

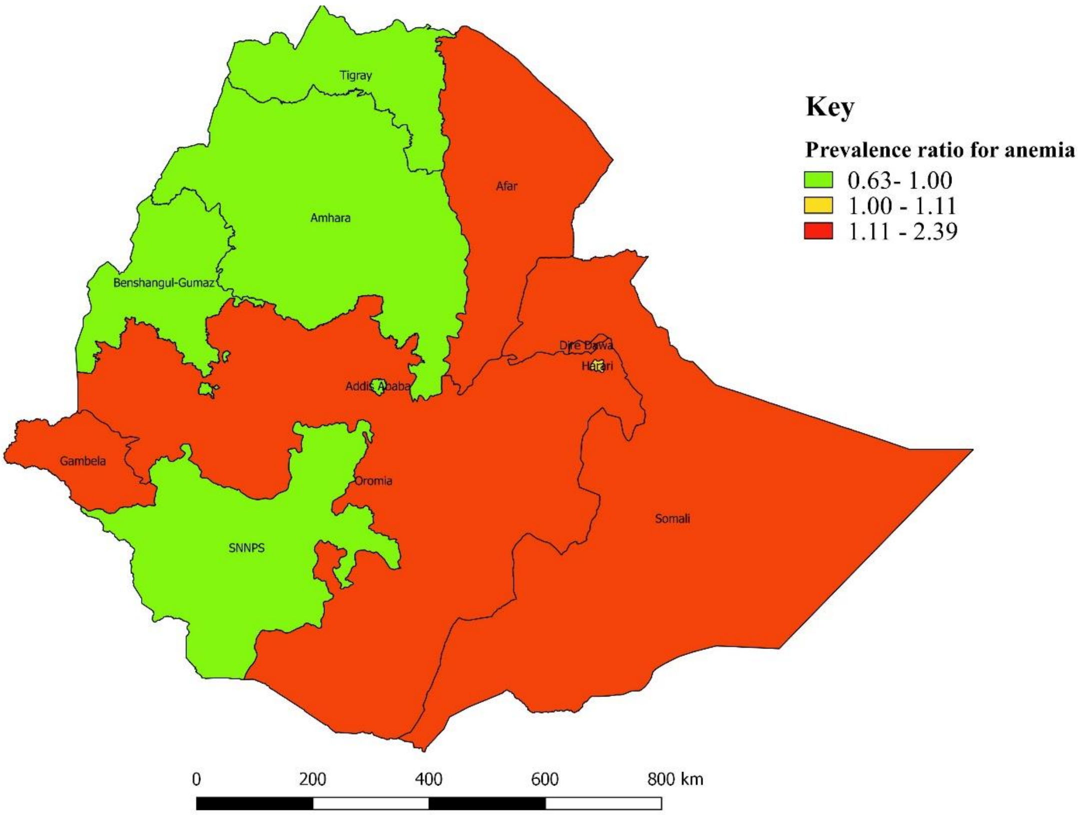

Figure 4. Standardized prevalence ratio for anemia among women of reproductive age across the regions in Ethiopia (standardized to national prevalence of 23.6%).

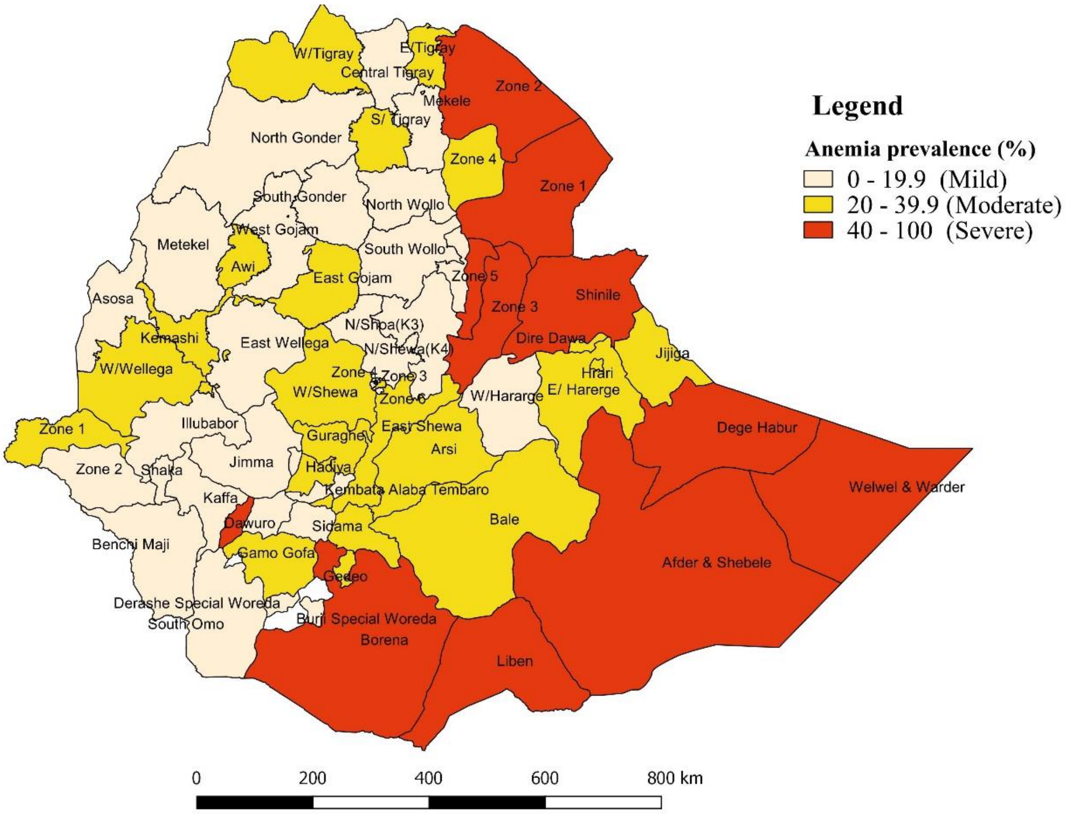

Figure 5. Spatial Empirical Bayesian smoothed (SEBS) percentage of maternal anemia across Zones

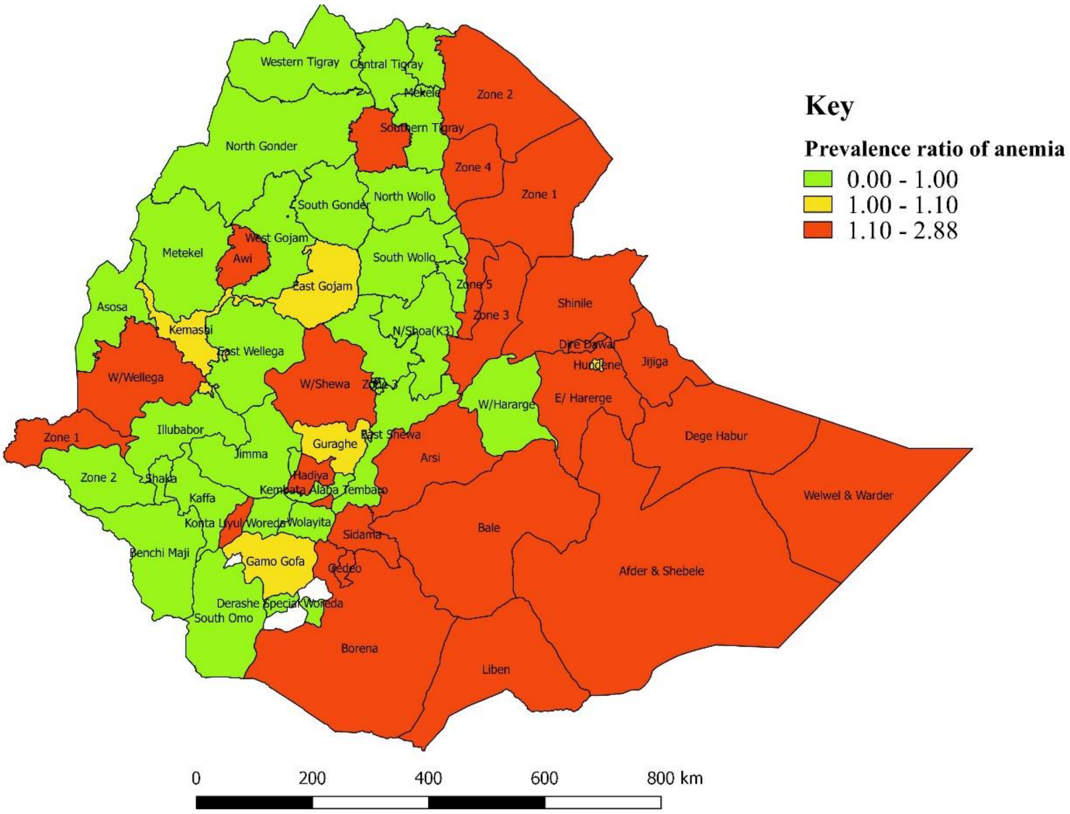

Figure 6. Standardized prevalence ratio for anemia among women of reproductive age across Zones in Ethiopia (standardized to national prevalence of 23.6%).

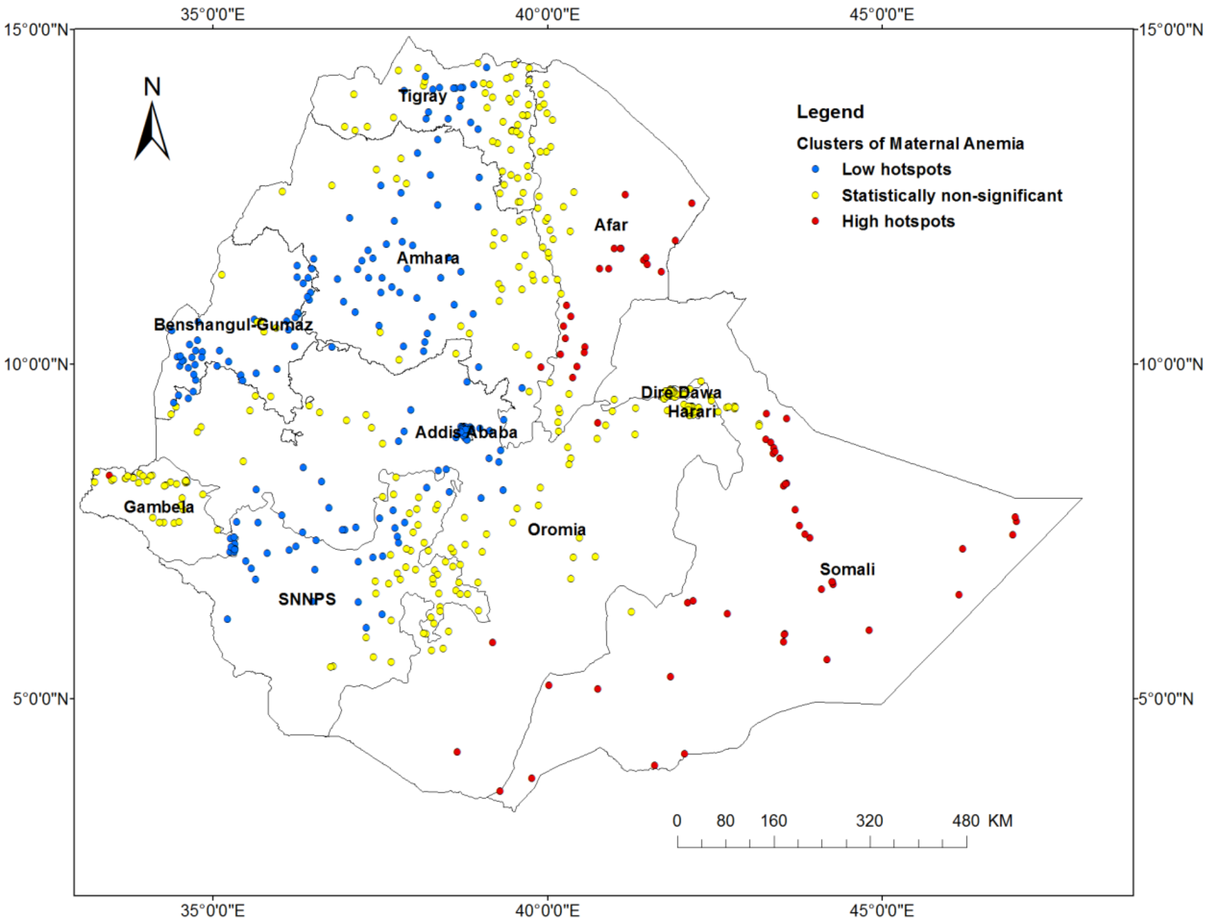

Figure 7. Spatial pattern of hot spots and cold spots of maternal anemia rate at cluster level in Ethiopia, EDHS, 2016.

Table 1 Variables identified for this study with coding

Variable	Categories
Age (Age in 5-year groups)	1=15-19; 2=20-29; 3=30-39; 4=40-49
Region	1=Tigray; 2=Afar; 3=Amhara; 4= Oromia; 5=Somali; 6=Benishangul-Gumuz; 7=SNNNP; 8=Gambella; 9=Harari; 10=Addis Ababa; 11=Dire Dawa
Area of residence	1=Urban; 2=Rural
Education level	1=No Education; 2= Primary; 3=Secondary; 4=Higher
Source of drinking water	1=piped water; 2=other improved (public taps, standpipes, tube wells, boreholes, protected dug wells and springs, and rainwater, bottled water); 3=unimproved (river, pond, unprotected spring and well)
Type of toilet facility	1= Improved (flush/pour flush toilets to piped sewer systems, septic tanks, and pit latrines; ventilated improved pit (VIP) latrines; pit latrines with slabs; and composting toilets); 2=Unimproved; 3=Open defecation; 4= Others
Religion	1=Orthodox; 2=Protestant; 3=Muslim; 4= Others (Catholic, traditional, other)
Ethnicity	1=Amhara; 2= Oromo; 3= Tigray; 4= Somali; 5= Sidama; 6=Gurage; 7=Welayta; 8=Hadya; 9=Other
Wealth index	1=Poorest; 2=Poorer; 3=Middle; 4=Richer; 5=Richest
Preceding birth interval (months) (for index child- for youngest child) except the first birth, no interval for 1st birth	1= <24 Months; 2= ≥24 Months
Total children ever born	1=0; 2= 1-3; 3= 4+
Births in past year (number of births in the 12 months (not 0 to 11) prior to the month of interview)	1= 0; 2= 1-2
Currently pregnant	0=No or unsure; 1=Yes

Variable	Categories
Age (Age in 5-year groups)	1=15-19; 2=20-29; 3=30-39; 4=40-49
Region	1=Tigray; 2=Afar; 3=Amhara; 4= Oromia; 5=Somali; 6=Benishangul-Gumuz; 7=SNNNP; 8=Gambella; 9=Harari; 10=Addis Ababa; 11=Dire Dawa
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Preceding birth interval (months) (for index child- for youngest child) except the first birth, no interval for 1st birth	1= <24 Months; 2= ≥24 Months
Total children ever born	1=0; 2= 1-3; 3= 4+
Births in past year (number of births in the 12 months (not 0 to 11) prior to the month of interview)	1= 0; 2= 1-2
Currently pregnant	0=No or unsure; 1=Yes

Births in the last three years (0 to 35 prior to the month of interview)	1= Yes; 2= No
Current contraceptive use	1= Yes; 2 = No
Hemoglobin level adjusted for altitude and smoking (g/dl - 1 decimal)	(g/dl - 1 decimal)
Anemia	1=Anemic (Severe (<7 g/dl), Moderate (7-9.9 g/dl), Mild 10-10.9/11.9 g/dl); 2=Non-Anemic
BMI	1=<18.5; 2=18.5-24.9;3=>=25
Smoking	1=Yes; 2=No
Current marital status	1=Single; 2=Married/Living with partner; 3=Divorced/Widowed/Separated
During pregnancy, given or bought iron tablets/syrup for most recent pregnancy	0=No; 1=Yes; 3= I Don't Know
Currently breastfeeding	0=No; 1=Yes
HIV test	1= Positive 2 = Negative

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

Title: The Spatial Distribution and Determinant Factors of Anemia among Women of Reproductive Age in Ethiopia: A Multilevel and Spatial Analysis

	Item No	Recommendation	Page numbers
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4,5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7,8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	9

Outcome data	15*	Report numbers of outcome events or summary measures	9,10,11,12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15,16,1718
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	21
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	24
Generalisability	21	Discuss the generalisability (external validity) of the study results	22,23
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

The Spatial Distribution and Determinant Factors of Anemia among Women of Reproductive Age in Ethiopia: A Multilevel and Spatial Analysis

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	Anemia, spatial analysis, multilevel analysis, reproductive age women, women

The Spatial Distribution and Determinant Factors of Anemia among Women of Reproductive Age in Ethiopia: A Multilevel and Spatial Analysis

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Abstract

Objective: The aim of this study was to assess the spatial distribution and determinant factors of anemia among reproductive age women in Ethiopia.

Methods: An in depth analysis of the 2016 Ethiopian Demographic and Health Survey data was undertaken. Getis-Ord Gi* statistics were used to identify the hot and cold spot areas for anemia among women of reproductive age. A multilevel logistic regression model was used to identify independent predictors of anemia among women of reproductive age.

Results: Older age (adjusted odds ratio (AOR) = 0.75; 0.64, 0.96)), no education (AOR = 1.37; 95 % CI: 1.102–1.72), lowest wealth quantile (AOR = 1.29; 95 % CI: 1.014-1.60), currently pregnant (AOR=1.28; 95% CI: 1.10, 1.51, currently breastfeeding (AOR =1.09; 95% CI: 1.025, 1.28), high gravidity (AOR=1.39; 95% CI: 1.13, 1.69), and HIV positive (AOR= 2.11; 95% CI: 1.59, 2.79) are individual factors associated with the occurrence of anemia. Likewise, living in a rural area (AOR=1.29; 95%CI: 1.02, 1.63), and availability of unimproved latrine facilities (AOR = 1.18; 95 % CI: 1.01, 1.39) are community level factors associated with higher odds of anemia. The spatial analysis indicated that statistically high hotspots of anemia were observed in the eastern (Somali, Dire Dawa and Harari regions) and north-eastern (Afar) parts of the country.

Conclusion: The prevalence rate of anemia among women of reproductive age varied across the country. Significant hotspots/high prevalence of anemia was observed in the eastern and north-eastern parts of Ethiopia. Anemia prevention strategies need to be targeted on rural residents, women with limited to no education, women who are breastfeeding, areas with poor latrine facilities and women who are HIV positive.

Key words: Anemia, spatial analysis, multilevel analysis, reproductive age women, women

Strength and limitation of this study

- Used large population-based data with a large sample size, which is representative of all regions of the country
- A combination of statistical methods (spatial analysis and multilevel logistics analysis) were applied which allows understanding of the role of contextual and geographical factors in the occurrence of anemia among women of reproductive age
- The cause effect and temporal relationship could not be established due to the cross sectional nature of the data
- Essential factors such as dietary intake and behavioral factors were unable to be incorporated in the analysis

Introduction

Anemia refers to a low hemoglobin level (<11mg/dl for pregnant women and <12mg/dl for non-pregnant women) [1]. If an individual's hemoglobin level is low, the red blood cells are unable to carry adequate oxygen for the body's physiologic needs [1]. Anemia is a major public health problem in women and children under five years of age [2]. Worldwide, 38% of pregnant women, and 29% of non-pregnant women were anemic in 2011 [2]. Pregnant women in low and middle income countries (LMIC) experience high rates of anemia, in which the highest prevalence rates are reported in Central and West Africa (56%), South Asia (52%) and East Africa (36%) [2]. Similarly, a large proportion of non-pregnant women were reportedly anemic in West and Central Africa (48%), South Asia (47%) and East Africa (28%) [2]. Anemia can have negative effects on a woman's health including maternal mortality and severe morbidity [3], depression [4, 5], raised blood pressure [6, 7], as well as negative influences on the infant including low birth weight and preterm birth [8]. Thus, anemia remains one of the global health priority areas at the global level, particularly in resource-limited settings [9]. Reducing anemia is considered as an essential part of improving the health of women, and the World Health Organization (WHO) has set a global target of achieving 50% reduction of anemia among women of reproductive age by 2025 [10].

Anemia is also a common problem in Ethiopia; the recent Ethiopian Demographic Health Survey (EDHS 2016) reported 29% prevalence of anemia among pregnant women and 24% among women of reproductive age; these prevalence statistics ranging from 16% to 59% across different parts of the country [11]. Likewise, in several pocket studies from different parts of the country researchers reported varied anemia prevalence rates among pregnant women, which ranged from 17% in the north. [12], 32% in the south [13] and up to 44% [14] and 57% [15] in the eastern part of Ethiopia. Similarly, in different studies there was reported to be a 16% [16] prevalence of anemia among non-pregnant women and 29% [17] and 30% [18, 19] among women of reproductive age.

There are a number of different factors contributing to the burden of anemia, with iron deficiency the main cause of the disease [20]. Other micronutrients (vitamin A, vitamin B12, and folate), chronic bleeding, acute or chronic infections and parasitic infections (hookworm and malaria) are also known to cause anemia [16, 21-23]. Based on the geographic distribution and disease burden in LMIC, about half of anemia cases are attributable to a deficiency of iron and the remainder may be due to diseases like parasitic infections, malaria and Human Immune Deficiency Virus (HIV) [24]. A recent systematic review revealed that the proportion of anemia caused by iron deficiency was below 50% in LMIC, with regional variations, poor sanitary conditions and subsequent increased occurrence of infections also contributing to anemia [25].

In Ethiopia, varied prevalence rates of anemia among women have been observed with different factors across different parts of the country [12, 15]. For instance, large family size, low education status, rural residence, hookworm infestation and HIV infection were identified as factors contributing to anemia in northern Ethiopia [12, 26], while in studies from the eastern area it was reported that multigravidas, third trimester of pregnancy and intestinal infestation were factors contributing to anemia during pregnancy [14, 27]. The variation in rates of anemia among women in Ethiopia might be due to the presence of diverse contextual and geographically variable factors including diet and the incidence of communicable diseases [9].

To date, spatial analyses have not been conducted to identify areas with hotspots (high prevalence rates) of anemia among reproductive age women in Ethiopia. Assessing the geographic distributions of anemia and the impact of risk factors on disease prevalence by area is important to prioritize and design targeted prevention and intervention programmes to address anemia in women [28]. In addition, the burden of anemia has been used as a measureable indicator of soil transmitted-helminthiasis, so understanding the geographical distribution of anemia can help target prevention and control mechanisms for parasitic infections such as these [29].

Thus, the aims of this study were to assess the spatial distribution and determinant factors of anemia among women of reproductive age women in Ethiopia.

Methods

Patient and Public Involvement

This study used a publicly available data set (EDHS 2016), therefore there were no patients or members of the public involved. The participants of this study were women of reproductive age (15-49 years). The mean (± standard deviation (sd)) age of the respondents was 28.2 years (±9.2 years). The majority (78%) of the participants were rural residents and nearly two thirds (66%) were married or living with a partner. Almost half (48%) of the participants had no formal education.

Study design and setting

An in depth analysis of the EDHS 2016 data was undertaken for this study. EDHS 2016 was a population based cross sectional study conducted across the country. It is the fourth national survey conducted in all parts of Ethiopia (in nine regional states (Tigray, Afar, Amhara, Oromia, Somali, Benishangul-Gumuz, Southern Nations, Nationalities and Peoples' Region (SNNP), Gambella and Harari) and two city administrations (Addis Ababa and Dire Dawa)) [11]. In Ethiopia the states are administratively further subdivided into Zones, Zones into *Woredas* and *Woredas* further into the lowest unit called *Kebeles.*

Sampling and data measurements

In the 2016 EDHS, stratified and cluster multistage sampling was used and it was intended to be representative at the regional and national level in terms of appropriate demographic and health indicators. In the first stage, 645 clusters of enumeration areas (EAs) (202 urban and 443 rural) were identified using probability proportional to the size of EAs. In the second stage, a random sample of 18,008 households were selected from all the identified EAs. A total of 15,683 women aged 15-49 years were interviewed and haemoglobin levels were measured for 14,923 of them [11] (Figure 1). Data collection took place from January 18, 2016, to June 27, 2016.

The sample size for EDHS was determined based on the multistage sampling procedure, taking into consideration the sampling variation. Standard errors were computed using the Taylor linearization method. The design effect, which is the ratio between the standard error with the given sample design and the standard error that would result if a simple random sample had been used, was determined [11].

Haemoglobin levels of the women were measured using HemoCue, which is the standard test used in the EDHS 2016, and all hemoglobin values were adjusted for both altitude and smoking status [11]. Pregnant women with a haemoglobin value <11g/dl and non-pregnant women with a haemoglobin value <12g/dl were considered anaemic [1]. Similarly, anemia was classified according to its severity as severe (hemoglobin value < 7 g/dl), moderate (7.0-9.9 g/dl) in all women and mild (10.0 – 10.9 g/dl) in pregnant women and non-pregnant women (10.0 – 11.9 g/dl) [1].

Explanatory variables (Determinant factors)

Both individual and community level factors were used. The individual and community level factors included in this study are presented in Supplemental Table 1 with their definition and coding. The variables were selected based on the literature review for factors affecting anemia [12, 14, 26, 27]; and sociodemographic, maternal as well as community level factors were identified as important factors for the occurrence of anemia. Therefore, all the available variables in the data set were included for the analysis. Individual factors included age, religion, marital status, educational status, body mass index (BMI), birth interval, use of contraceptives, wealth index, family size, iron-folate intake and gravidity of women, while the community level factors were residence (urban, rural), region, water source and latrine facility type. Community level measures could also be driven by aggregating individual level variables, for example, the proportion of women in the community who are in the top quantile of wealth index and proportion of women in the community who have clean water access. Community level factors describe the group of populations living in similar settings.

The assumption of independence of observation has been taken as a basis to determine which variables are analysed at individual and community level. If the observations at the individual level are independent, variables were treated as individual level factors. Whereas, if the observations were clustered into higher levels of units and if several women have shared features such as place of residence, types of water source, latrine facility and region that could have the same effect on anemia among women in the locality, then variables are analysed at the community level.

Data analysis

Spatial analysis

Spatial analyses were performed using Geoda version 1.8.10 (geodacenter.github.ib), QGIS Version 2.18.0 (qgis.org) and Arch GIS software version 10.1 (arcgis.com), and base files of the administrative regions for Ethiopia were obtained from DIVA (diva-gis.org). The spatial analysis was conducted by joining the occurrence of anemia (as proportions) with each cluster to the corresponding geospatial location (survey cluster values). The values of DHS data were merged with the GPS dataset in Geoda software and these values were imported into the QGIS software. Anemia proportions were then computed at lower (cluster), zonal and regional levels using QGIS.

The spatial pattern of the rate of anemia among women of reproductive age was visualized and a spatially smoothed proportion was obtained through empirical Bayes estimation methods [30]. The smoothed proportions present clearer patterns, where the problem was most severe. The spatial empirical Bayes "smooth" estimates technique was able to deal with spatial heterogeneity. The estimation technique guarantees that estimates of neighbouring states are more alike than estimates of states that are further away [31].

A standardized prevalence rate (SPR), or the ratio of the observed prevalence rate to a national prevalence rate, was determined using Geoda software [31]. Geoda implements this in the form of an excess risk estimate as part of the map. The excess risk rate is the ratio of the observed rate to the average rate computed for all the data [31].

Furthermore, a spatial analysis was performed to identify the clustering of anemia in women or hotspot areas (the areas that have higher anemia prevalence rates compared to the national average) in different regions of Ethiopia. Spatial analysis is an epidemiological method useful to specify geographic areas with high or low rates of disease occurrence and variability over the region or country [32]. Getis-Ord Gi* statistics was used for this spatial analysis. Local Getis-Ord Gi* statistics [33] are important to identify the hot and cold spot areas for anemia in reproductive age women using geographic poisoning system (GPS) latitude and longitude coordinate readings which were taken at the nearest community centre for EAs or EDHS 2016 clusters [11]. An anemia hotspot refers to the occurrence of high prevalence rates of anemia clustered together on the map, whereas cold spots refers to the occurrence of low prevalence rates of anemia clustered together on the map [33].

A local Getis-Ord G-statistic tool in ArcGIS was used to calculate the spatial variability of high and low prevalence rates of anemia among women of reproductive age. An autocorrelation can be classified into positive and negative correlation through the Local Getis-Ord G statistics [33]. Positive autocorrelation occurs when similar values clustered together on a map (high rates surrounded by nearby high rates or low rates surrounded by nearby low rates). Negative autocorrelation indicates different values clustered together on a map, that is, high values surrounded by nearby low values or low values surrounded by nearby high values. Statistical significance of autocorrelation was determined by z-scores and p-value with a 95 % level of confidence. The distribution and variations of anemia prevalence rates among women across the country were displayed on the map.

Statistical analysis

The descriptive statistical analysis was performed using SPSS software version 24.0 (www.spss.com) by complex sample analysis. Frequencies, percentage and standard deviation were used for the descriptive analysis. Since some regions with small populations were oversampled, while others with large population were underrepresented, the weighted frequencies and percentages (based on population size of each region) were computed as a correction. The detailed weighting procedure was described in EDHS 2016 report [11]. The mean and standard deviation were computed for blood hemoglobin level. The mean hemoglobin value was also compared across different independent categorical variables using One-way Analysis of Variance (ANOVA) or independent t-test.

The Multivariable multilevel logistic regression model was used to determine the effect of different factors on anemia among women. The analysis was performed by using SAS version 9.4 software (SAS North Carolina State University, www.sas.com) using Proc Glimmix with Laplace's method. For this multilevel analysis, four models were constructed. The first model was constructed without independent variables to assess the effect of community variation on anemia among women. Individual level factors were incorporated in the second model. In the third model, community level factors were included. Finally, both individual and community level factors were included in the fourth model.

The results of fixed effects were presented as odds ratio (OR) with 95% confidence intervals (CIs). An adjusted odds ratio (AOR) with 95% CIs was computed to identify the independent factors of anemia among women and a p-value <0.05 was used as a measure of statistical significance. A muliticollinearity test was done in order to rule out a significant correlation between variables. If the values of variance inflation factor (VIF) was lower than 10, then the collinearity problem was considered as less likely. The random effects (variation of effects) were measured by intra-cluster correlation coefficient (ICC) (variance partition coefficient) [34], percentage change in variance (PCV) [35] and median odds ratio (MOR) [34, 36] which measure the variability between clusters in the multi-level models. ICC explains the cluster variability while MOR can quantify unexplained cluster variability (heterogeneity). MOR translates cluster variance into OR scale. In the multilevel model, PCV can measure the total variation due to factors at the community and individual level [35]. The ICC, PCV and MOR were determined using the estimated variance of clusters utilising the following formula [34, 35].

$$\text{ICC} = \frac{V}{(V + \frac{\pi^2}{3})} \qquad \text{MOR} = \exp\sqrt{2 \times V \times 0.6745} \sim \exp\,(0.95\sqrt{V})]$$

Where V is the estimated variance of clusters

And

$$\text{PCV} = \frac{(V_A - V_B)}{V_B} \times 100$$

Where V_A = variance of the initial model; V_B = variance of the model with more terms

The multilevel analysis model is one of the analysis methods which can correctly handle the correlated data [37]. A multilevel model evaluates how factors at different levels affect the dependent variable. A multilevel model provides correct parameter estimates by correcting the biases introduced from clustering by producing correct standard errors, thus producing correct CI, and significance tests [37]

Ethical consideration

Publicly available EDHS 2016 data was used for this study. The EDHS 2016 was approved by the National Research Ethics Review Committee (NRERC) of Ethiopia and ICF Macro International. MEASURE DHS approval was obtained to use EDHS 2016. Informed consent was taken from each participant and all identifiers were removed. This analysis was approved by the University of Newcastle Human Research Ethics Committee (H-2018-0045).

Results

Sociodemographic characteristics

The data on 14,923 women were included in this analysis, including 642 clusters nested in 11 regions. The descriptive statistics of the study participants are presented in Table 1. The mean (± sd) age of the respondents was 28.2 years (±9.2 years). The majority of participants lived in a rural area (78%). Nearly two-thirds (66%) of participants were married or living with a partner. Almost half (48%) of the women had no formal education and around 43% were of the Orthodox Tewahdo Christian religion. Only 18% of the households had access to a piped water source for drinking, and 15% had access to an improved latrine facility. Nearly one-third (N=4,657; 31.2%) of women were breastfeeding at the time of the survey (Table 1). The average haemoglobin level among lactating mothers was 12.6 g/dl (±1.7 g/dl) and about 28.3% (95% CI: 25.7-31.0%) of these women were anemic.

Table 1: Sociodemographic and other health-related characteristics of study participants included in the analysis, EDHS 2016 (N=14,923)

Variables	Weighted Frequency	Weighted percent
Age		
15-19	3165	21.2
20-29	5467	36.6

30-39	4078	27.3
40-49	2213	14.8
Place of residence		
Urban	3169	21.2
Rural	11754	78.8
Educational status		
No education	7215	48.3
Primary	5244	35.1
Secondary	1676	11.2
Higher	789	5.3
Marital status		
Single	3758	25.2
Married	9800	65.7
Divorced/widowed/separated	1365	9.1
Religion		
Orthodox	6447	43.2
Protestant	3514	23.5
Muslim	4645	31.1
Other	317	2.1
Region		
Tigray	1073	7.2
Afar	119	0.8
Amhara	3645	24.4
Oromia	5422	36.3
Somali	417	2.8
Benishangul-Gumuz	146	1.0
SNNPR	3124	20.9
Gambella	42	0.3
Harari	32	0.2
Addis Ababa	825	5.5
Dire Dawa	77	0.5
Wealth index		
Poorest	2519	16.9

Poorer	2717	18.2
Middle	2891	19.4
Richer	2979	20.0
Richest	3816	25.6
BMI		
<18.5	3060	22.1
18.5-24.9	9740	70.5
>=25	1018	7.4
Birth interval		
< 24 months	1415	18.3
>= 24 months	6305	81.7
Current use of contraceptives		
Yes	1088	7.3
No	13835	92.7
Iron folate intake during pregnancy (n = 7328)		
Yes	3108	42.4
No /don't know	4220	57.6
Gravidity of women (children ever born)		
0	4745	31.8
1-3	4715	31.6
4+	5464	36.6
Children ever born in the preceding 5 years		
0	7595	50.9
1	4475	30.0
2+	2852	19.1
Currently breastfeeding		
Yes	4657	31.2
No	10266	68.8
Currently pregnant		
Yes	1088	7.3
No	13835	92.7
Smoking		
Yes	96	0.6

No	14827	99.4
Birth in the last year		
0	12474	83.6
1-2	2449	16.4
HIV test		
Positive	187	1.3
Negative	14724	98.7
Water source		
Piped water	2646	17.7
Other improved	6926	46.4
Unimproved	5351	35.9
Latrine facility type		
Improved toilet	2231	14.9
Unimproved toilet	7877	52.8
Open defecation	4414	29.6
Other	401	2.7
Anemia status		
Anemic	3527	23.6
Non-anemic	11396	76.4
Proportion of women in the community who have clean water source , m(se)	64.1 (33.6)	
Proportion of women in the community who have unimproved latrine facility; m(se)	85.1(25.0)	
Proportion of women in the community who are in lowest quantile of wealth index; m(se)	35.1(30.0)	
Percentage of unimproved water per cluster; m(se)	35.9 (33.6)	

BMI= Body mass index; SNNP= Southern Nations, Nationalities and Peoples' Region; m= mean; se= standard error

Prevalence rate of anemia among women

Amongst all respondents, the mean (±sd) blood hemoglobin level (adjusted for altitude) was 12.8 g/dl (±1.7 g/dl). The overall prevalence of anemia among women of reproductive age across the country was 23.6% (95% CI: 22.0, 25.3). The prevalence of mild, moderate and severe anemia among all women of reproductive age were 17.8% (95% CI: 16.7-19), 5.0% (95% CI: 4.3-5.8) and 0.8% (95% CI: 0.5-1.2) respectively. There was regional variation in anemia prevalence among women of reproductive age (p= 0.0001) and higher prevalence rates observed in Afar, Somali, Gambella, Dire Dawa and Oromia regions. Lower prevalence of anemia was observed in Addis Ababa, Tigray, and Amhara regions. Rural areas had a higher prevalence, 25.4 (95% CI: 23.5, 27.4) of anemia in women than urban areas, 17.0 (95% CI: 14.4, 20.0) (p=0.0001). The highest proportion of anemia among women were found in Somali Regional States, while the lowest proportions were found in Addis Ababa city administration (Table 2).

Table 2: The variation of anaemia prevalence rates across different regions and different sociodemographic characteristics of women in Ethiopia, 2016

Region	**Weighted frequency**		**Weighted proportion of anemia (95% CI)**	**p-value**
	Anemic	Non-anemic		
Place of residence				
Urban	538	2630	17.0 (14.4,20.0)	0.0001
Rural	2989	8766	25.4 (23.5, 27.4)	
Region				
Tigray	212	861	19.7 (16.8,23.0)	0.0001
Afar	53	66	44.7 (39.9,49.6)	
Amhara	627	3019	17.2 (14.9,19.7)	
Oromia	1480	3942	27.2 (23.8,31.1)	
Somali	248	169	59.5 (55.2,63.7)	
Benishangul-Gumuz	28	118	19.2 (16.1,22.7)	
SNNP	704	2420	22.5 (19.4,26.0)	

Gambella	11	31	26.1 (21.3,31.5)	
Harari	9	23	27.7 (23.7,32.1)	
Addis Ababa	132	693	16 (13.5,18.8)	
Dire Dawa	23	54	30 (25.8,34.8)	
Education status				
No education	2002	5212	27.8 (25.4,30.2)	0.0001
Primary	1136	4108	21.7(19.8,23.7)	
Secondary	297	1378	17.8 (14.9,21.0)	
Higher	91	697	11.5(8.2,16.0)	
Wealth index				
Poorest	863	1656	34.3(29.7,39.1)	0.0001
Poorer	688	2028	25.3(22.6,28.3)	
Middle	686	2205	23.7(21.2,26.5)	
Richer	625	2354	21.0(18.6,23.6)	
Richest	664	3152	17.4(15.1,19.9)	
Currently pregnant				
Yes	317	771	29.1 (24.9,33.7)	0.003
No	3210	10625	23.2 (21.6,24.9)	
Currently breastfeeding				
Yes	1317	3340	28.3 (25.7,31.0)	0.0001
No	2210	8055	21.5 (20.0,23.2)	
Total	3527	11396	23.6 (22.0, 25.3)	

Around 1,080 [7.3% (95% CI: 6.6, 8.1)] participants were pregnant at the time of the interview. The mean hemoglobin level among pregnant women was 11.7 g/dl (±1.8 g/dl) and 29.1% (95% CI: 24.9-33.7) of these women were anemic. The prevalence of anemia was higher among pregnant women, 29.1 (95% CI: 24.9, 33.7) than non-pregnant women, 23.2 (95% CI: 21.6, 24.9) (p= 0.003) (Table 2). The mean hemoglobin value of women in their second and third trimester was significantly lower compared to women in their first trimester (p = 0.001). The mean hemoglobin levels in pregnant women who had less than a 24 month birth interval (for their most recent birth) was significantly lower compared to women who had a birth interval of less than or equal to 24 months (p= 0.0001). Similarly receiving iron folate supplements during pregnancy improved the mean haemoglobin values in pregnant women (Table 3).

Table 3: Hemoglobin level among pregnant women in Ethiopia, 2016

Variables	**Number**	**Hemoglobin level (g/dl) (mean(sd))**	**P values of ANOVA or independent t test**
Children ever born (CEB)	1,088		0.0001
0	213	12.1(1.7)	
1-3	484	11.7(1.8)	
4+	390	11.5 (1.8)	
Pregnancy stage	1,088		0.0001
1st trimester	226	12.4 (1.7)	
2nd trimester	433	11.6 (1.6)	
3rd trimester	429	11.5 (1.9)	
CEB in last 5 years	1,088		0.0001
0	339	12.1 (1.7)	
1	484	11.7 (1.8)	
2+	265	11.4 (1.9)	
Fe-Fol supplementation	749		0.018
Yes	251	11.8 (1.5)	
No	498	11.5 (1.9)	
Birth interval	702		0.0001
< 24 months	206	11.2 (2.0)	
>= 24 months	497	11.9 (1.5)	

sd = standard deviation, Fe-Fol= Iron-folate, CEB = Children Ever Born

Determinant factors of anemia among women of reproductive age

Multilevel Analysis (Fixed effect analysis)

The results of multilevel logistic regression for the individual and community level variables are presented in Table 4. In the full model in which all individual and community level factors are included, residence, education, religion, wealth index, pregnancy and breastfeeding status, gravidity of women, and lack of availability of an improved latrine were factors significantly associated with anemia in women. The results of the muliticollinearity test indicated that no collinearity problem existed, since the VIF value of all variables is lower than 10.

Individual factors

The average hemoglobin value was significantly different across age groups (p=0.0001). The highest mean hemoglobin level, 13 g/dl was observed in the youngest (15-19 years) age group while the lowest mean hemoglobin level, 12.71 g/dl, in the 30-34 years age group. The general pattern indicated roughly linear decline among women aged 15-34 years (Figure 2). Women aged 40-49 years old were 25% less likely to be anemic compared to women in the youngest age group (15-19 years old) (AOR= 0.75 (0.64, 0.96). Those women with limited education were 1.37 times more likely to be anemic than women who completed higher education (AOR = 1.37; 95 % CI: 1.102–1.72). The odds of anemia increased by 29% (AOR = 1.29; 95 % CI: 1.014-1.60) when comparing the poorest to the richest women. The odds of anemia were higher in women who were pregnant (AOR=1.28; 95% CI: 1.10, 1.51) compared to those who were not pregnant. Women who were currently breastfeeding were 9% (AOR =1.09; 95% CI: 1.025, 1.28) more likely to be anemic. The odds of anemia were 39% higher among mothers who had given birth to four or more children (AOR=1.39; 95% CI: 1.13, 1.69). Women who gave birth to two or more children in the preceding five years of the survey were at higher risk of having anemia (AOR =1.31; 95% CI: 1.09,1.57). In this study, women who were HIV positive had a twofold increased odds of having anemia compared to women classified as HIV negative (AOR= 2.11; 95% CI: 1.59, 2.79) (Table 4).

Community level factors

Living in a rural area was associated with a 29% higher odds of anemia among women of reproductive age than women who were urban residents (AOR=1.29; 95%CI: 1.02, 1.63). Women from households without access to a latrine had 18% higher odds of anemia compared to women from households that had an improved latrine facility (AOR = 1.18; 95 % CI: 1.01, 1.39). Higher odds of anemia were observed in Somali regional state (AOR = 2.16; 95 % CI:

1.58, 2.90) compared to Dire Dawa. However, the odds of anemia among women were lower in Gambella, Addis Ababa, Amhara and Oromia region compared to Dire Dawa (Table 4).

Multilevel analysis (random effect analysis)

The results of the random effects model is shown in Table 4. Prevalence rate of anemia varied across communities (t^2=0.88, p=<0.0001). In other words, the anemia prevalence rate was not similarly distributed across the communities. About 21% of the variance in the odds of anemia in women could be attributed to community level factors, as calculated by the ICC based on estimated intercept component variance. After adjusting for individual and community level factors, the variation in anemia across communities remained statistically significant. About 16% of the odds of anemia variation across communities was observed in the full model (Model 4) (Table 4).

Moreover, the MOR indicated that anemia was attributed to community level factors. The MOR for anemia was 2.44 in the empty model (Model 1); this showed that there was variation between communities (clustering) since MOR was 2.4 times higher than the reference (MOR = 1). The unexplained community variation in anemia decreased to MOR of 2.1 when all factors were added to the null model (empty model). This indicates that when all factors are included, the effect of clustering is still statistically significant in the full model (Table 4).

Table 4: Determinant factors bivariate association between anemia and individual and community contextual characteristics of Ethiopian women, 2016

Variables	**Model 1**	**Model 2 Individual factors**	**Model 3 Community level factors**	**Model 4 Individual + community level factors**
Individual level factors				
Age				
15-19		1		1
20-29		0.93 (0.81,1.07)		0.96 (0.82, 1.19)
30-39		0.89 (0.75,1.10)		0.92 (0.78,1.11)
40-49		0.76 (0.61,0.92)		0.75 (0.64,0.96)
Educational status				
No education		1.41 (1.13,1.76)		1.37 (1.10, 1.72)
Primary		1.22 (0.99,1.51)		1.24 (1.00,1.53)

Secondary	1.22 (0.98,1.5)	1.23(0.98,1.52)
Higher	1	1
Marital status		
Single	0.99 (0.80, 1.22)	0.972 (0.81,1.22)
Married	1.07 (0.92, 1.23)	1.09 (0.91,1.23)
Divorced/widowed/separated	1	1
Religion		
Orthodox	1	
Protestant	1.36 (1.16, 1.58)	1.37 (1.15,1.63)
Muslim	2.04 (1.79, 2.33)	1.36 (1.16, 1.58)
Other	1.49 (1.05, 2.12)	1.525 (1.06, 2.13)
Wealth index		
Poorest	1.73 (1.48, 2.03)	1.29 (1.014,1.60)
Poorer	1.31 (1.10, 1.54)	1.21 (0.96,1.45)
Middle	1.28 (1.08,1.51)	1.22 (0.98,1.50)
Richer	1.04 (0.88,1.24)	1.01(0.82,1.24)
Richest	1	1
Current using contraceptives		
Yes	0.99 (0.90,1.10)	1.0 (0.91,1.11)
No	1	1
Currently pregnant		
Yes	1.30 (1.11,1.52)	1.28 (1.10,1.51)
no	1	1
Currently breastfeeding		
yes	1.12 (1.00,1.24)	1.09 (1.03,1.28)
No	1	1
Gravidity of women (total children ever born)		
0	1	1
1-3	1.23 (1.03,1.46)	1.22 (1.02,1.44)
4+	1.40 (1.15,1.72)	1.39 (1.13,1.69)
Smoking		
Yes	0.98 (0.64,1.50)	1.05 (0.69,1.61)

No	1		1
Birth in the last 1 year			
0	1		1
1-2	1.20 (1.05,1.37)		1.15 (1.01,1.32)
Children ever born in preceding 5 years			
0	1		1
1	1.12 (0.96,1.29)		1.10 (0.95,1.27)
2+	1.39 (1.16,1.66)		1.31 (1.09,1.57)
HIV test			
Positive	2.19 (1.65, 2.91)		2.11 (1.59, 2.79)
Negative	1		1
Community level factors			
Place of residence			
Urban		1	1
Rural		1.67 (1.35,2.05)	1.29(1.02,1.63)
Region			
Tigray		0.39(0.28,0.53)	0.52(0.38, 0.72)
Afar		1.25 (0.91,1.7)	1.14 (0.83,1.56)
Amhara		0.30 (0.22,0.41)	0.39 (0.28,0.54)
Oromia		0.55 (0.41,0.75)	0.57 (0.42,0.78)
Somali		2.40 (1.78,3.27)	2.16 (1.58,2.90)
Benishangul-Gumuz		0.36 (0.25,0.50)	0.37 (0.26,0.52)
SNNPR		0.40 (0.29,0.54)	0.41(0.29,0.57)
Gambella		0.63 (0.45,0.87)	0.63(0.45,0.89)
Harari		0.74 (0.53,1.04)	0.76(0.54,1.04)
Addis Ababa		0.54 (0.39,0.73)	0.67(0.49,0.91)
Dire Dawa		1	1
Water source			
Piped water		1	1
Other improved		1.15 (0.95,1.39)	1.04 (0.86,1.26)
Un-improved		1.18 (0.95,1.44)	1.03 (0.83,1.27)
Latrine facility type			

Improved toilet			1	1
Unimproved toilet			1.12 (0.97,1.29)	1.08 (0.94,1.25)
Open defecation			1.33 (1.15,1.55)	1.18 (1.00,1.39)
Other			0.86 (0.64,1.17)	0.94 (0.69,1.27)
Random effects (effect of variation/ measure of variation for anemia**)**				
Community level variance (SE)	0.888 (0.07)	0.46(0.05)	0.32(0.04)	0.31(0.035)
P- value	0.001	0.001	0.001	0.001
DIC(-2log likelihood)	7926.056	7749.25	7720.74	7613.56
ICC (%)	21.25	16.1	18.3	15.86
Explained variation –PCV (%)	Reference	40.95	21.0	43.1
MOR	2.44	2.13	2.3	2.1

Note: Model 1= empty model (without the predictors); Model 2= adjusted for individual factors; Model 3 = adjusted for community level factors; Model 4 = adjusted for both community and individual level factors; DIC = Deviance Information Criterion; ICC= Intra-cluster Correlation Coefficient; MOR= Median Odds Ratio; PCV = Percentage Change in Variance; SE= Standard Error; SNNPR=Southern Nations, Nationalities and Peoples' Region

Spatial data analysis

Figure 3 displays the empirical Bayes smoothed proportion estimate of anemia among women across regions in Ethiopia. A severe anemia prevalence rate (≥40%) among women of reproductive age was observed in Afar and Somali Regional States. Likewise, a moderate anemia prevalence rate (20-40%) occurred in Oromia, Gambella, SNNPR, Harari and Dire Dawa Regional States. Whereas, and a mild anemia prevalence rate (<20%) was observed in Tigray and Amhara Regional Sates and Addis Ababa.

Similarly, the standardized prevalence ratio by regions (standardized to the national average prevalence of 23.6%), ranging from 0.63 to 2.39, was displayed on the map (Figure 3). A higher prevalence ratio of anemia was observed in Somali (2.39), Afar (1.8) Oromia (1.17), Dire Dawa 1.15, Gambella (1.12) regional states (Figure 4); whereas, a lower prevalence ratio of anemia occurred in other regional states - Addis Ababa (0.64), Amhara (0.76), Benishangul-Gumuz (0.79), SNNPR (0.96), Tigray (0.85)

Figure 5 displays the smoothed anemia prevalence rates at zonal level where higher anemia rates were observed in all zones in Afar and Somali regions, as well as in some zones in Oromia. Likewise, the higher standardized ratio of anemia was observed in all zones in Afar and Somali regions as well as in some zones in Oromia (Figure 6).

The spatial distributions of anemia among women at the lower level (cluster level) is displayed in figure 6. The spatial investigation at the cluster level indicated that statistically high hotspots of anemia were observed in the eastern (Somali, Dire Dawa and Harari regions) and in north-eastern (Afar) parts of the country, while cold spots of anemia were observed in the northern (Tigray, Amhara), central (Addis Ababa, Oromia) and western (Benishangul-Gumuz and Gambella) parts of the country (Figure 7).

Discussion

Approximately a quarter of women of reproductive age were anemic in the current study, indicating that anemia is a moderate public health problem at the national level in Ethiopia [1]. However, geographic differences demonstrated that anemia is a serious public health problem in five of the 11 Ethiopian states. A higher proportion of anemia cases was observed in the eastern and north-eastern parts of the country, which are less developed compared to other Ethiopian states in terms of economy, gender, health care facility and food availability [38]. The geographical difference of anaemia across the regional states might be attributable to the regional variation of food consumption preferences [39, 40], the occurrence of communicable diseases [41], and differences in availability of health care facilities [42]. In addition, lack of clean water and unimproved latrine facilities would increase the occurrence of soil transmitted infection [43] which in turn could lead to anemia [44]; which might explain some of the observed geographical differences.

According to the final model, both individual and community level factors were responsible for about 43% of the disparity of anemia prevalence rates among women of reproductive age in Ethiopia. After adjusting for all factors in the model, the likelihood of having anemia was higher among those of younger age, with lower levels of education, living in rural areas, in the lowest wealth quantile, who were currently pregnant or breastfeeding, with high gravidity, who had given birth in the year prior to the survey and who were without access to an improved latrine facility.

Women aged 40-49 years had a lower likelihood of being anemic compared to women aged between 15-19 years. This finding is in line with other study findings from Ethiopia [16, 19] and Benin [45]. This could be due to the fact that low fertility rates occurred in this age group (40-49) [11]. However, in Iran [46] it has been reported that women aged 20-24 were less likely to be anemic compared to those aged 45-49; this might be a result of Iran having a targeted intervention for younger women or women of reproductive age [46].

In this study, it was found that there is variation of the anemia rate in terms of education status of the women. A higher proportion of anemic cases were observed among women with no education. It was found that women who did not have formal education had higher odds of anemia than those with higher education. This is consistent with other studies conducted in developing countries [24] including Ethiopia [16], Timor-Leste [47], Benin [45] and India [48, 49] in which it was reported that a low level of education was associated with higher odds of anemia among women of reproductive age. Formal education might assist women to obtain knowledge that in turn helps them to follow better lifestyle behaviours like good nutrition, and to form better health-seeking habits and hygiene practices that can prevent anemia among women.

A higher proportion of anemic cases were observed among women in the poorest wealth quantile. The lowest wealth quantile compared to highest quantile was associated with a higher risk of anemia. Results of this study show that women who were in the poorest wealth quintile were 30% more likely to be anemic than women who belong to the richest quintile; this is in line with the results of other studies conducted in other developing countries [24] like Benin

[45] and India [49, 50]. This might be due to the fact that having a low income would mean having less money to buy nutritious foods or have a balanced diet [51, 52], which in turn leads to inadequate nutrient intake and nutritional status [53]. More than 38% of the Ethiopian population belongs to the poor and poorest wealth quintile, which indicates a large percentage of women are at risk for anemia because of low socioeconomic position [11].

Lactating mothers were 9% more likely to have anemia than non-lactating mothers. Lactating may predispose women to low haemoglobin, which results in anemia. In a study conducted in India [54], a similar finding was reported, that lactating mothers were more likely to be anemic than non-lactating women.

The findings of our study clearly show the role of women's fertility in anemia. Increased odds of anemia was associated with high gravidity, births in the past five years of the survey and having a birth in the last year. Similar studies in Ethiopia [16], Iran [46] and Timor-Leste [47] also document this association between parity and risk of anemia. The study results from Pakistan [55, 56] and Iran [46] indicate that women with a parity of four or more were found to be at increased risk of anaemia than women with lower parity. This might be explained by that fact that the more the women give birth, the more they are exposed to blood loss which in turn results in low hemoglobin levels in the blood [57]. Similarly, prior births may deplete maternal iron stores due to the increased nutritional demands of pregnancy and puerperal blood loss [58]. Consequently, emphasis needs to be placed on family planning services. Increased odds of anemia were observed in women who were HIV positive. In this study, women who were HIV positive had twofold increased odds for anemia. This could be due to the direct effects of the HIV infection on the bone marrow and depletion of hemoglobin levels in the blood [59]. Many of the opportunistic infections to which HIV patients are susceptible might also lead to anemia [59].

This study revealed there to be a significant difference in the proportion of anemic cases according to place of residence (urban/rural). The likelihood of having anemia was higher for rural residents compared to urban residents. This is in agreement with a study conducted in low income countries in which it was revealed that living in a rural area was a determinant factor for anemia [24]. A recent report illustrated that more than half of the Ethiopian population had access to unimproved toilet facilities [60]. Our study findings revealed that women from households with unimproved latrine facilities were more likely to be anemic than women from households with improved latrine facilities, which is in agreement with other research findings

[45, 61]. The possible justification might be that an unimproved latrine facility would expose women to helminthic infections [43], which in turn resulted them developing anemia [44].

Strength and Limitations

This study used large population-based data with a large sample size, which is representative of all regions of Ethiopia. Furthermore, a combination of statistical methods (spatial analysis and multilevel logistics analysis) were applied for this study which allows for the understanding of the role of contextual and geographical factors in the occurrence of anemia among women of reproductive age. Due to the cross sectional nature of the EDHS data, the cause/effect and temporal relationship could not be established based on these study findings. Similarly, essential factors such as dietary intake and behavioural factors were not available in the EDHS survey so that it was not possible to incorporate these variables in the analysis. Furthermore, EDHS was a questionnaire based survey and relied on the memory of the respondents, and as such, recall bias in the results might be a weakness for this study.

Conclusion

This study indicates that considerable geographic disparities in anemia prevalence rate occur within Ethiopia. The results of this study revealed that anemia among women varied across the country; significant anemia hotspots were observed in the eastern and north eastern part of the country while anemia cold spots were observed in the northern and western parts of the country. About 43% of the disparity in anemia occurrence across communities was attributable to both individual and community level factors. The increased occurrence of anemia among women was associated with individual and community level factors. For women, being of rural residence, having no formal education, being in the poorest wealth index, either currently pregnant or breastfeeding, and higher gravidity were factors that increased the odds of anemia at the individual level, whereas lack of a clean water source, and access to an unimproved toilet facility were factors significantly associated with anemia among women.

Accordingly, the prevention of anemia among women requires multifaceted intervention approaches, for instance, improving the economic and educational status of women, and improving the availability of clean water and toilet facilities. Anemia prevention strategies must be targeted on these identified factors. Priority should be given for those states or areas which have anemia hotspots. Particularly, any intervention programs need to be prioritized for pregnant women, women recently giving birth, those with lower levels of education, and women living in rural areas. The regions with the greatest numbers of anemic women (Afar and Somali) should be prioritized, as the burden of anemia is higher in these areas, with more than 50% of women being anemic.

Acknowledgments

We would like to thank the DHS program for allowing the use of EDHS data for this study. We are also very grateful to Dr Ryan O'Neill for his help in language editing.

Authors' contributions

Formulating the research question(s): KTK CC DL EG; designing the study: KTK CC DL EG; analysing the data: KTK Interpreting the results: KTK CC DL EG; drafting, writing, reviewing and approving the final manuscript: KTK CC DL EG.

Financial support

This research received no specific grant from any funding agency, or the commercial or not-for-profit sectors.

Conflicts of interest

The authors declare that they have no conflicting interests.

Data sharing statement

This study was an in-depth analysis of a publicly available dataset from the Demographic and Health Surveys Program (DHS Program). The dataset is available at the DHS program website (http://www.measuredhs.com)

Figure 1: Selection of the Sample in the 2016 EDH Survey

Figure 2: Average hemoglobin value with 95% CI for women of reproductive age at different age groups, Ethiopia, 2016

Figure 3. Spatial Empirical Bayesian smoothed (SEBS) percentage of anemia among women of reproductive age across regions, EDHS, 2016

Figure 4. Standardized prevalence ratio for anemia among women of reproductive age across the regions in Ethiopia (standardized to national prevalence of 23.6%), EDHS, 2016

Figure 5. Spatial Empirical Bayesian smoothed (SEBS) percentage of anemia among women of reproductive age across Zones, EDHS, 2016

Figure 6. Standardized prevalence ratio for anemia among women of reproductive age across Zones in Ethiopia (standardized to national prevalence of 23.6%), EDHS, 2016

Figure 7. Spatial pattern of hotspots and cold spots of anemia rate among women of reproductive age at cluster level in Ethiopia, EDHS, 2016

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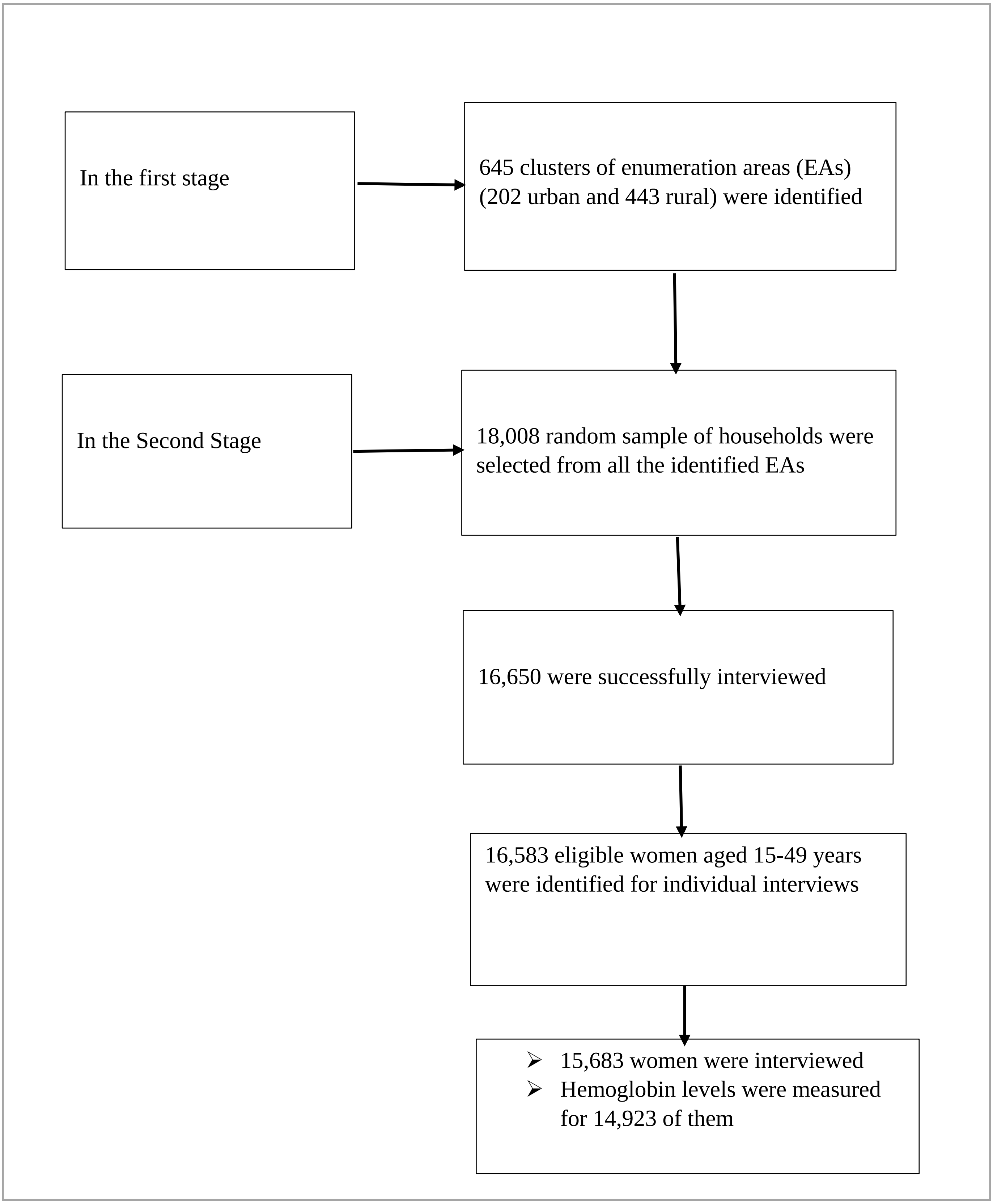

Figure 1: Selection of sample in the 2016 EDH Survey

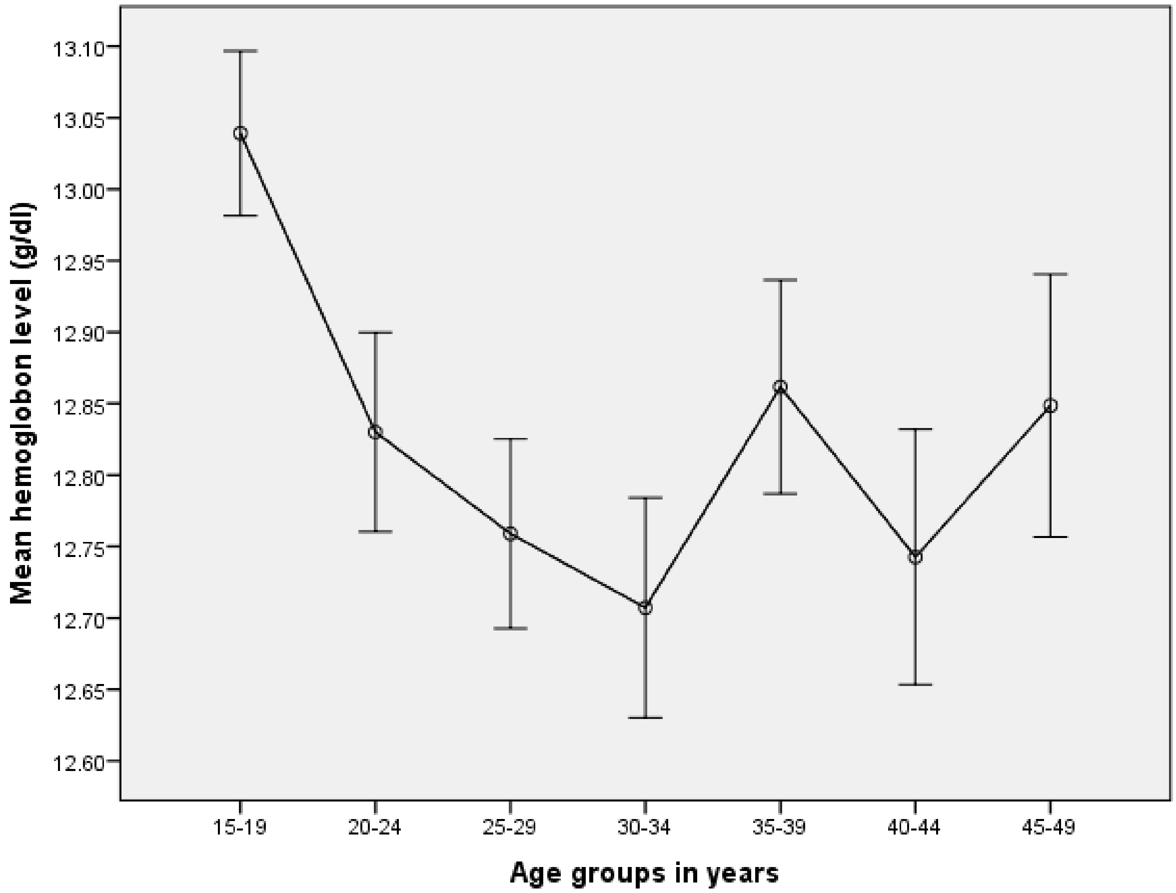

Figure 2: Average hemoglobin value with 95% CI for women of reproductive age at different age groups, Ethiopia, 2016

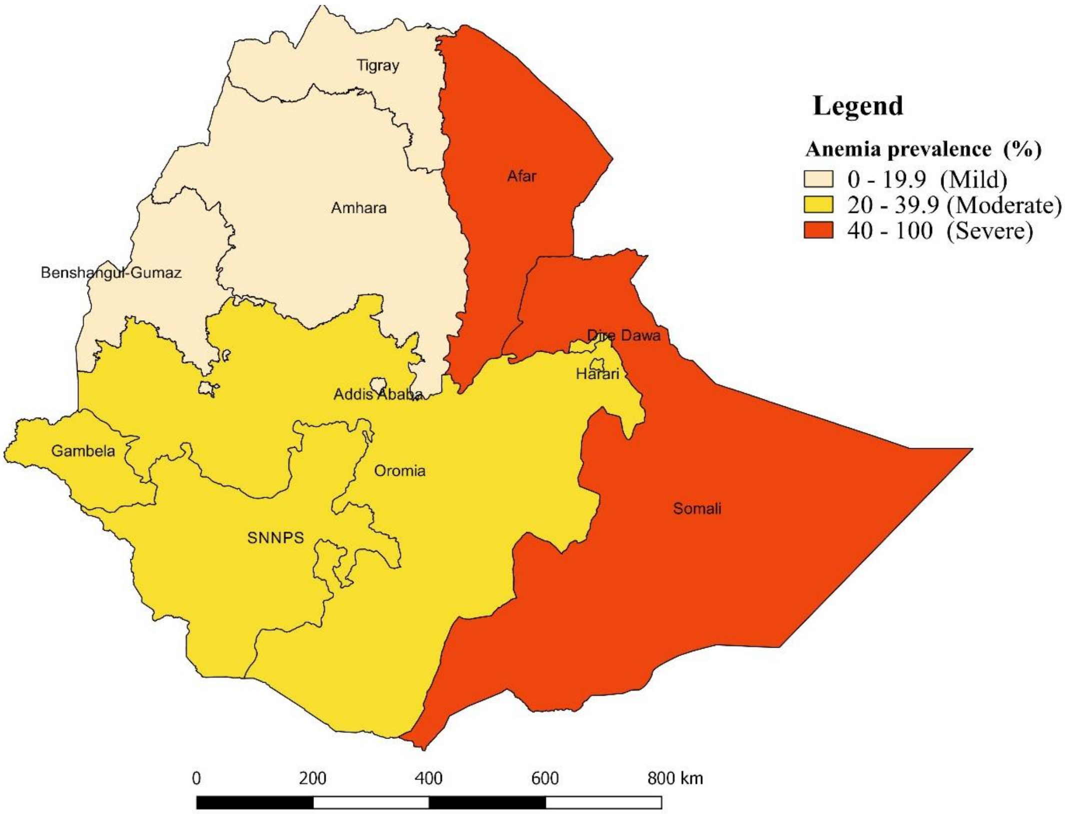

Figure 3. Spatial Empirical Bayesian smoothed (SEBS) percentage of anemia among women of reproductive age across regions, EDHS 2016

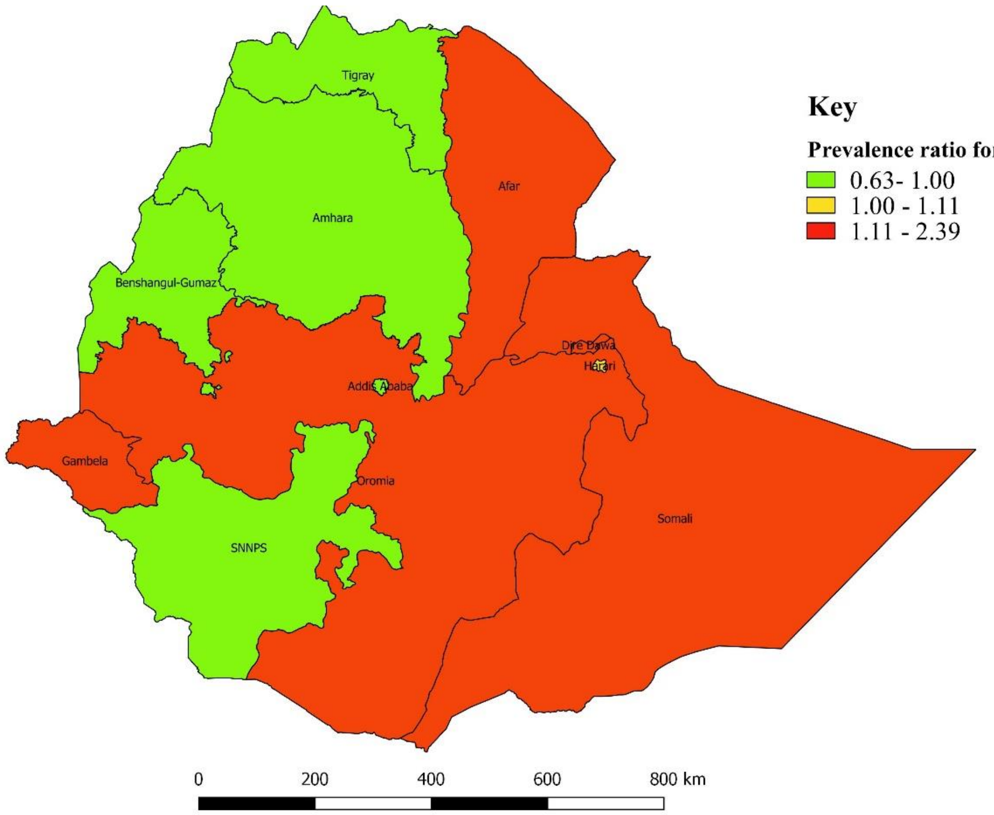

Figure 4. Standardized prevalence ratio for anemia among women of reproductive age across the regions in Ethiopia (standardized to national prevalence of 23.6%), EDHS 2016

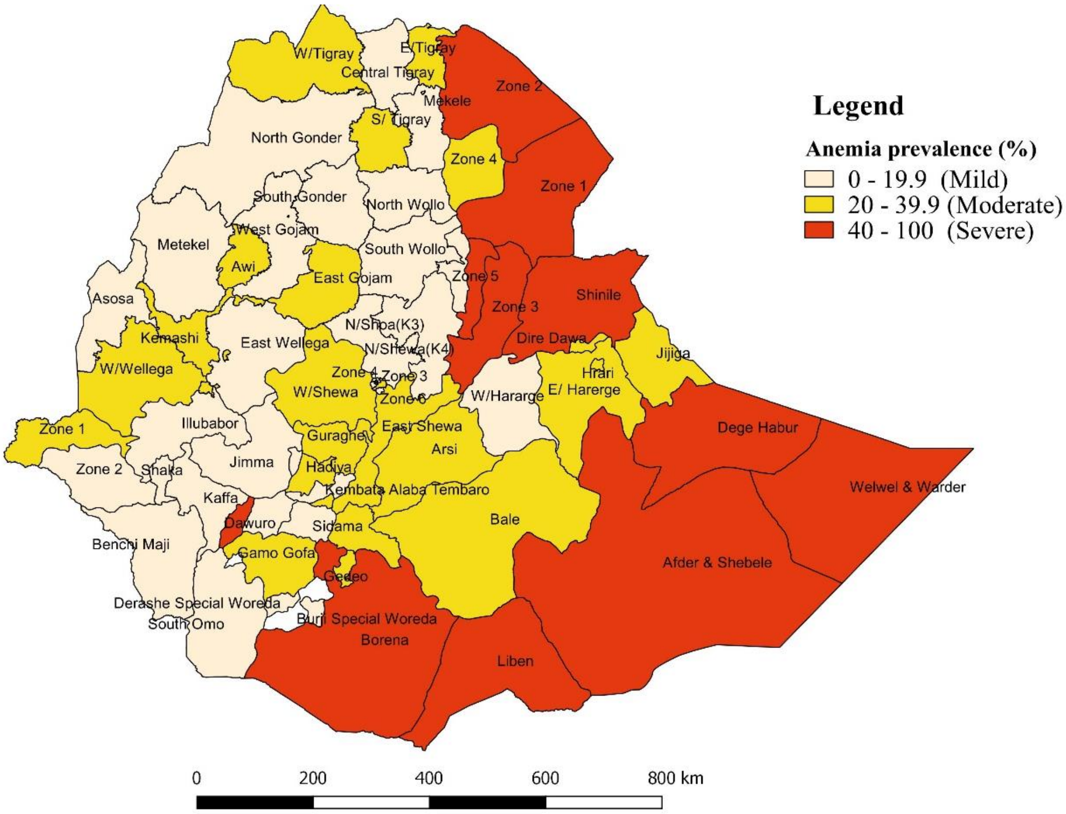

Figure 5. Spatial Empirical Bayesian smoothed (SEBS) percentage of anemia among women of reproductive age across Zones, EDHS 2016

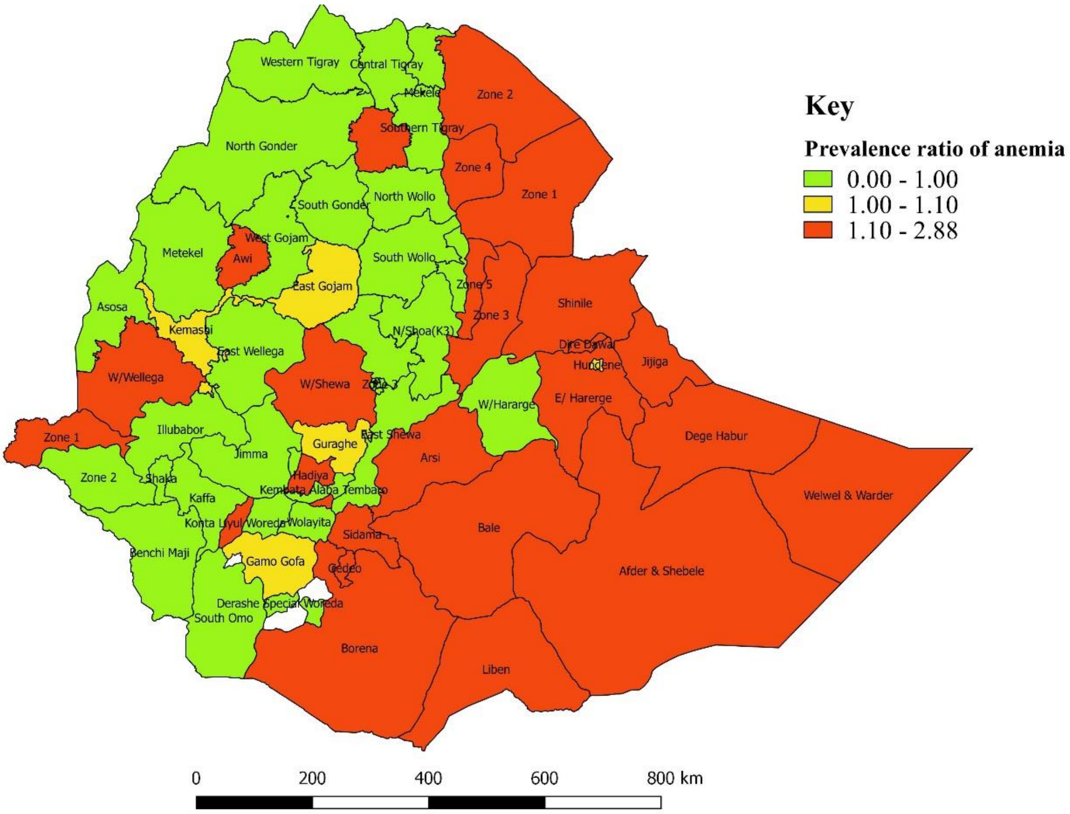

Figure 6. Standardized prevalence ratio for anemia among women of reproductive age across Zones in Ethiopia (standardized to national prevalence of 23.6%), EDHS 2016

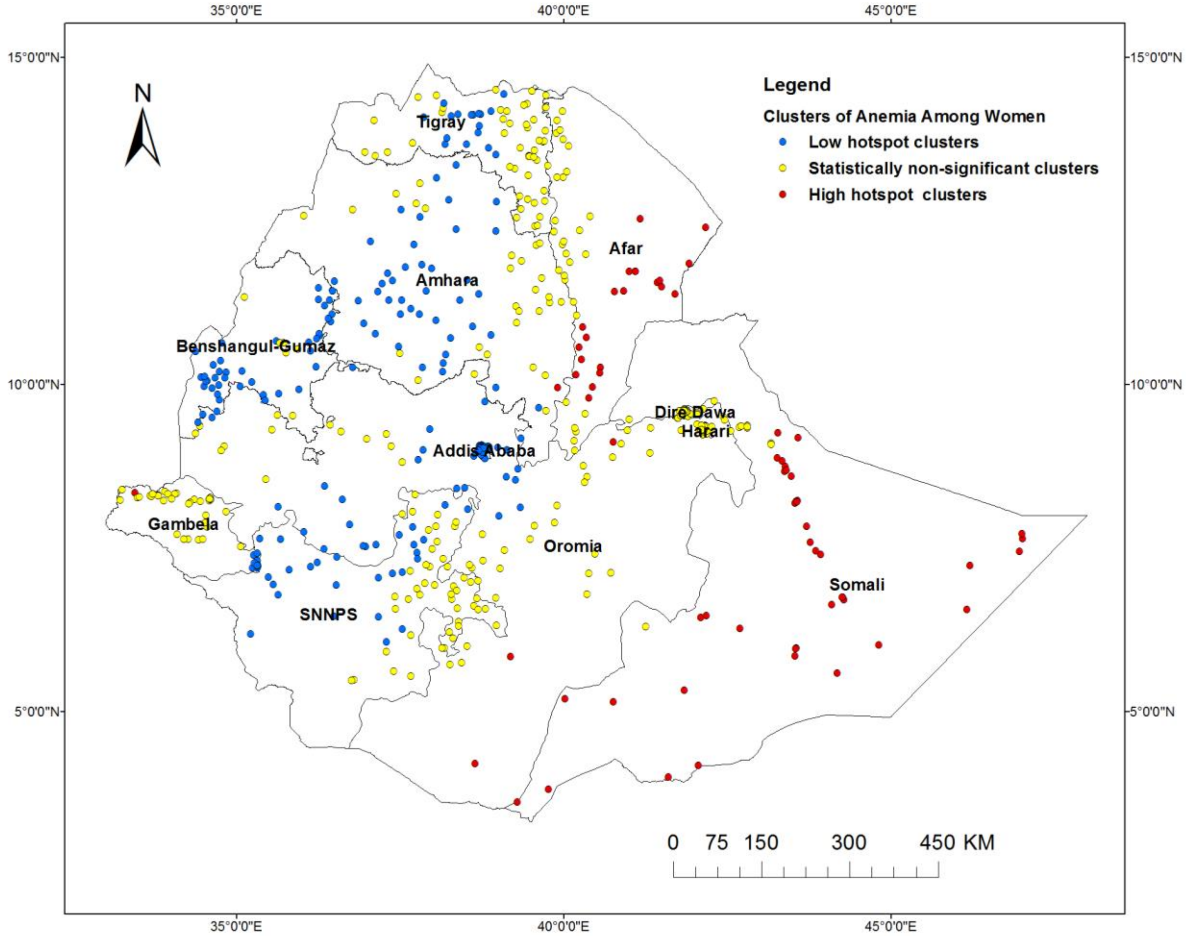

Figure 7. Spatial pattern of hotspots and cold spots of anemia rate among women of reproductive age at cluster level in Ethiopia, EDHS, 2016

Table 1 Variables identified for this study with coding

Variable	Categories
Age (Age in 5-year groups)	1=15-19; 2=20-29; 3=30-39; 4=40-49
Region	1=Tigray; 2=Afar; 3=Amhara; 4= Oromia; 5=Somali; 6=Benishangul-Gumuz; 7=SNNNP; 8=Gambella; 9=Harari; 10=Addis Ababa; 11=Dire Dawa
Area of residence	1=Urban; 2=Rural
Education level	1=No Education; 2= Primary; 3=Secondary; 4=Higher
Source of drinking water	1=piped water; 2=other improved (public taps, standpipes, tube wells, boreholes, protected dug wells and springs, and rainwater, bottled water); 3=unimproved (river, pond, unprotected spring and well)
Type of toilet facility	1= Improved (flush/pour flush toilets to piped sewer systems, septic tanks, and pit latrines; ventilated improved pit (VIP) latrines; pit latrines with slabs; and composting toilets); 2=Unimproved; 3=Open defecation; 4= Others
Religion	1=Orthodox; 2=Protestant; 3=Muslim; 4= Others (Catholic, traditional, other)
Ethnicity	1=Amhara; 2= Oromo; 3= Tigray; 4= Somali; 5= Sidama; 6=Gurage; 7=Welayta; 8=Hadya; 9=Other
Wealth index	1=Poorest; 2=Poorer; 3=Middle; 4=Richer; 5=Richest
Preceding birth interval (months) (for index child- for youngest child) except the first birth, no interval for 1st birth	1= <24 Months; 2= ≥24 Months
Total children ever born	1=0; 2= 1-3; 3= 4+
Births in past year (number of births in the 12 months (not 0 to 11) prior to the month of interview)	1= 0; 2= 1-2
Currently pregnant	0=No or unsure; 1=Yes

Variable	Categories
Age (Age in 5-year groups)	1=15-19; 2=20-29; 3=30-39; 4=40-49
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Currently pregnant	0=No or unsure; 1=Yes

Births in the last three years (0 to 35 prior to the month of interview)	1= Yes; 2= No
Current contraceptive use	1= Yes; 2 = No
Hemoglobin level adjusted for altitude and smoking (g/dl - 1 decimal)	(g/dl - 1 decimal)
Anemia	1=Anemic (Severe (<7 g/dl), Moderate (7-9.9 g/dl), Mild 10-10.9/11.9 g/dl); 2=Non-Anemic
BMI	1=<18.5; 2=18.5-24.9;3=>=25
Smoking	1=Yes; 2=No
Current marital status	1=Single; 2=Married/Living with partner; 3=Divorced/Widowed/Separated
During pregnancy, given or bought iron tablets/syrup for most recent pregnancy	0=No; 1=Yes; 3= I Don't Know
Currently breastfeeding	0=No; 1=Yes
HIV test	1= Positive 2 = Negative

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

Title: The Spatial Distribution and Determinant Factors of Anemia among Women of Reproductive Age in Ethiopia: A Multilevel and Spatial Analysis

	Item No	Recommendation	Page numbers
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4,5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7,8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	9

Outcome data	15*	Report numbers of outcome events or summary measures	9,10,11,12
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15,16,1718
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	21
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	24
Generalisability	21	Discuss the generalisability (external validity) of the study results	22,23
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.