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# **BMJ Open**

# Spatio-temporal distribution and associated factors of anemia among children aged 6–59 months in Ethiopia: Based on the EDHS 2005- 2016: A spatial and multilevel analysis

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1 2	1	Spatio-temporal distribution and associated factors of anemia among children aged 6-59
3 4	2	months in Ethiopia: Based on the EDHS 2005- 2016: A spatial and multilevel analysis
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1 2 2	21	Abstract
3 4 5	22	Objectives: Anemia is a global public health problem with major health and socio-economic
6 7	23	consequences. Though childhood anemia is a major public health problem in Ethiopia, there
8 9	24	is limited evidence on the spatio-temporal variability of childhood anemia overtime. Therefore,
10 11 12	25	this study aimed to assess the spatio-temporal distribution and associated factors of childhood
13 14 15	26	anemia using the Ethiopian Demographic and health survey (EDHS) data from 2005-2016.
16 17 18	27	<b>Design:</b> Survey-based cross-sectional study design was employed for the EDHS.
19 20	28	Setting: Data were collected in all nine regions and two city administrations of Ethiopia in
21 22 23	29	2005, 2011 and 2016.
24 25	30	<b>Participants:</b> The source population for this study was all 6–59 months of children in Ethiopia.
26 27 28	31	A total weighted sample of 21,302 children aged 6-59 months were included in this study.
29 30 31	32	Outcome measure: The outcome variable was child anemia status.
32 33	33	<b>Results</b> : The prevalence of anemia has been declined from 53.9% in 2005 to 44.6% in 2011,
34 35 36	34	but it showed increment 2016 to 57.6%. The Spatial analysis revealed that the spatial
37 38	35	distribution of anemia varied across the country. In spatial scan statistics analysis, a total of 22
39 40	36	clusters (RR= 1.54, P-value < 0.001) in 2005, 180 clusters (RR = 1.14, P-value < 0.001) in
41 42 43	37	2011, and 219 clusters (RR = 1.44, P-value < 0. 0.001) in 2016 significant primary clusters
44 45	38	were identified. Child age, women age, maternal anemia status, wealth index, birth order,
46 47 48	39	fever, stunting, wasting status, and region were significant predictors of childhood anemia.
49 50	40	Conclusions: In this study, childhood anemia remains a public health problem. The spatial
51 52	41	distribution of childhood anemia was significantly varied across the country. Identifying the risk
53 54 55 56 57	42	areas and determinants would help to design strategies in the area. Therefore, regions with a

1 2	43	high risk of childhood anemia, individual and community level factors should be intensified by						
3 4	44	allocating additional resources and providing appropriate and tailored strategies.						
5 6 7 8	45	Keywords: Anemia, children, EDHS, Spatial analysis, Ethiopia						
9 10	46							
11 12	47	Strengths and limitations of this study						
13 14	48	This study applied different methods of spatial pattern, trend and a multilevel regression						
15 16 17	49	models accounting the nested nature of EDHS data						
18 19	50	• The study was based on three consecutive EDHS dataset's representing the whole						
20 21	51	country of Ethiopia						
22 23 24	52	The cross-sectional nature of the data prevents causality from being inferred between						
24 25 26	53	the independent and dependent variables						
27 28	54	Respondents' data that didn't have files (longitude and latitude) were excluded from the						
29 30 31	spatial analysis which could affect the generalizability of the findings							
32 33	56							
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Anemia is a condition characterized by a low level of hemoglobin in the blood(1). Over 273 million under-five children suffer from anemia worldwide(2). Sub-Saharan Africa is one of the most affected regions which accounts for about 53.8%(2). World health organization had developed a classification system to facilitate international comparisons of anemia as public health crises. The problem was considered severe if anemia prevalence is  $\geq 40\%$ , moderate from 20% to 39.9%, and mild from 5% to 19.9%(3). The high prevalence of anemia and its consequences on children's health, especially on their growth and development, have made it an important public health problem and it also increases the risk of mortality and morbidity which come from other diseases(4,5). 

Anemia is a public health problem that affects populations in both industrialized and non-industrialized countries. It affects all segments of the population. It is frequently observed among children and pregnant women who are the most vulnerable group because their requirements for iron are higher than any other group. Childhood anemia is mostly caused by dietary Iron deficiency. Foliate, vitamin B12 and vitamin A deficiencies, chronic inflammation, parasitic infections, and inherited disorders can also contribute to childhood anemia (6). For children, age 6-59month Anemia is defined as a hemoglobin level below 11.0 g/dl(6). Childhood anemia is mostly coexisting with malaria, parasitic infection, nutritional deficiencies, and hemoglobinopathies(7). 

The prevalence of anemia in Africa, South East Asia, America, and European regions was,62.3%,53.8%,23.3%, and,22.9%, respectively(3). Pregnant women and children in low-income countries were at risk for anemia because they were believed to be those with the greatest problems with inadequate nutrition, high infectious disease burden, and poor access to routine health care(8). In sub-Saharan Africa, Anemia is a major public health problem associated with an increased risk of death and impaired cognitive development(9). In Ethiopia,

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the three crude summaries of the country reported between,2005 and 2016, indicated the prevalence of anemia among Ethiopian children declined from,54% to,44% from, 2005 to,2011 but increased to,57% in 2016(10–12).

Different studies across different countries showed that the prevalence of anemia among 6-59-month children is high and a severe public health problem. Evidence from different studies indicated that women age, residence, family income, maternal education(13), an introduction of complementary foods, poor breastfeeding practice, poor utilization of folic acid by mothers(14), maternal anemia(15), unemployment of the parent, malaria, and presence of sickle hemoglobin(13), household wealth index, sex of the child(16), and nutritional status were factors for childhood anemia. There are few studies done in Ethiopia on factors associated with anemia. But at the national level, there was no yet study done on the spatio-temporal patterns of childhood anemia and associated factors using multilevel analysis. Therefore, this study attempts to fill the gap by investigating the spatial distribution of anemia and its associated factors using multilevel model analysis in Ethiopia using the EDHS survey between 2005-20016 data.

# 103 Methods

# 104 Study design and setting

The survey-based cross-sectional study design was employed using the Ethiopian Demography and Health Surveys (EDHS) in 2005, 2011, and 2016. Data access, extraction, and analysis were conducted from January to June 2020. The study was conducted in Ethiopia located at the horn of Africa (3°-14°N and 33° – 48°E). Administratively, the country is divided into nine regional states and two city administrations. Each region is sub-divided into zones, districts, towns, and kebeles (the smallest administrative units).

# 111 Source and study population

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The source population for this study was all 6–59 months of children in Ethiopia. The study population was all children aged from 6-59 months in the selected enumeration areas within five years before the survey. 

Sampling size and sampling technique 

A total of 21,302 children (3,868 children in 2005, 8,958 children in 2011, and 8476 Children 11 116 <sup>13</sup> 117 in 2016) were included in this study. Weighted values were used to restore the representativeness of the sample data. Sample weights were calculated in each children's Record (KR) EDHS dataset. The survey covered all nine regions and the two city 18 119 20 120 administrations of Ethiopia. Participants were selected based on a stratified two-stage cluster sampling technique in each survey year (2005, 2011, and 2016). After excluding clusters with <sub>25</sub> 122 zero coordinates and missing information, a total of 503 clusters in 2005, 569 clusters in 2011, 27 123 and 615 clusters in 2016 were included. The detailed sampling procedure was available in each EDHS report(10-12) 

Data collection tools and procedures 

The three EDHS datasets were downloaded from the measure DHS program (Demographic 34 126 <sup>36</sup> 127 and Health Survey) website (www.measuredhsprogram.com) after obtaining the necessary permissions for the download and further analyses. Data extraction was performed using STATA version 14.1 similarly, location data (latitude and longitudinal) were extracted from the 41 129 43 130 downloaded excel file. Then after extraction, the missing values for the significant independent variables were excluded and the analysis was undertaken using a complete set of data. 

Key variables and Measurements 

**Dependent variable**: The study variables were grouped into dependent and independent 51 133 <sup>53</sup> 134 variables. The dependent variable is child anemia status, categorized as "anemic/not-anemic"

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variable. Children whose hemoglobin level was less than 11Hb were taken as anemic and not anemic otherwise. 

#### Independent variables:

From the EDHS dataset all sociodemographic variables, Maternal and Child-related factors (individual and community level) were taken as independent variables in the three-consecutive survey. 

#### Data management and analysis 15 141

The data were cleaned using STATA 14.1 software and Microsoft excel. The data were weighted using sampling weight, primary sampling unit, and strata before any statistical analysis to restore the representativeness of the survey to take into account the sampling 22 144 design when calculating standard errors to get reliable statistical estimates.

#### Spatial analysis

The weighted frequency of outcome variable with cluster number was cross-tabulated in STATA software and exported to excel to get the case to the total proportion. Geographic 32 148 coordinate data were merged in STATA 14.1. Observations within clusters having longitude and latitude 0 were dropped from the spatial analysis section. Then CSV file imported to ArcGIS 10.7 for spatial analysis. 

#### 41 152 Spatial autocorrelation analysis

The spatial autocorrelation (Global Moran's I) statistic measures whether childhood anemia patterns were dispersed, clustered or randomly distributed in the study area. Moran's, I output 48 155 value ranges from (-1 to +1). Values close to -1 indicate disease dispersed, whereas moran's I close to +1 indicate childhood anemia clustered and distributed randomly if I value is zero. 

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Anselin Local Moran's I was used to investigating the local level cluster locations of anemia in terms of positively correlated (high-high and low-low) clusters or negatively correlated (high-low and low-high). 

#### Hot spot analysis (Getis-Ord Gi\* statistic)

Getis-OrdGi\* statistics were computed to measure how spatial autocorrelation varies over the 11 161 study location by calculating GI\* statistic for each area. Z-score is computed to determine the statistical significance of clustering, and the p-value computed for the significance. Statistical output with high GI\* indicates "hotspot" whereas low GI\* means a "cold spot". hot spot areas 18 164 20 165 indicated that there was a high proportion of anemia and the cold spot indicated that there was a low proportion of anemia.

#### Spatial interpolation

Spatial interpolation technique is used to predict anemia in the un-sampled areas in the country 27 168 based on sampled EAs. There are various deterministic and geostatistical interpolation methods. Ordinary Kriging spatial interpolation method was used for this study for predictions 34 171 of childhood anemia in unobserved areas of Ethiopia since it had low mean square error and <sup>36</sup> 172 residual as compared to the other interpolation techniques.

Spatial scan statistical analysis 

Spatial scan statistical analysis Bernoulli based model was employed to test for the presence 44 175 of statistically significant spatial clusters of anemia using Kulldorff's Sat Scan version 9.6 software. The spatial scan statistic uses a circular scanning window that moves across the study area. Children with anemia were taken as cases and those who were not-anemic as controls to fit the Bernoulli model. The default maximum spatial cluster size of <50% of the 53 179 population was used, as an upper limit, which allowed both small and large clusters to be detected and ignored clusters that contained more than the maximum limit. The scanning 

window with maximum likelihood was the most likely performing cluster, and the p-value was assigned to each cluster using Monte Carlo hypothesis testing by comparing the rank of the maximum likelihood from the real data with the maximum likelihood from the random datasets. The primary and secondary clusters were identified and assigned p-values and ranked based on their likelihood ratio test, based on 999 Monte Carlo replications(17). 

#### Model building

Four models were fitted using **melogit**, a STATA command, the null model without predictors. 19 188 the model I with only individual-level variables, model II with only community-level variables, and model III both individual-level and community-level variables. Model comparison was conducted by using deviance and likelihood ratio. 

ICC (Intra-class correlation), MOR (median odds ratio), and PCV (proportional change in variance) were computed to measure the variation between clusters. The intra-class 31 193 correlation coefficient (ICC) quantifies the degree of heterogeneity of childhood anemia between clusters (the proportion of the total observed individual variation in anemia that is attributable between cluster variations) calculated as ICC=  $62/(62+\pi 2/3)(18)$  but MOR is quantifying the variation or heterogeneity in outcomes between clusters and is defined as the 38 196 median value of the odds ratio between the cluster at high risk of anemia and cluster at lower risk when randomly picking out two clusters (EAs) MOR:  $exp(sqrt(2*Va)*0,6745) \sim MOR = exp$ (0.95\* sqrt(Va)(19). PCV measures the total variation attributed by individual-level factors and community-level factors in the multilevel model as compared to the null model PCV. In the multivariable multilevel logistic regression analysis variables with a p-value of <0.05 were considered as statistically significant. Adjusted Odds Ratio (AOR) with their corresponding 54 203 95% confidence interval was determined to identify factors associated with anemia. After comparing all models, a model with low deviance was considered as a better model. 

**BMJ** Open Page 11 of 39 Multicollinearity was checked using the Variance Inflation Factor (VIF). VIF less than 10% was taken as no multicollinearity. Ethics and confidentiality Ethical clearance was obtained from the ethical review board of the University Of Gondar Institute Of Public Health, CMHS. Permission for data access was obtained from the measure demographic and health survey through an online request by a written letter of objective and 13 210 significance of the study from http://www.dhsprogram.com Patient and public involvement This study did not involve patients and the public 21 213 **Results** 24 214 Descriptive characteristics of the study population A total of 21,302 children with known hemoglobin levels (3,868 in 2005, 8,958 in 2011, and 8467 in 2016) were included in this study. The prevalence of anemia for the three consecutive 32 217 34 218 surveys was 53.9%, 44.6%, and 57.6% in 2005, 2011, and 2016 EDHS data respectively. The majority of the participants were in the age group of 36-47 (23%), 36-47 (24%), and, 12-23 (22%) in EDHS 2005, 2011, and 2016 survey respectively. The mean age of children was 32.57 ±15.6-SD, 32.6±15.4-SD, and 31.7±15.6-SD in 2005, 2011, and 2016 respectively. 41 221 Among the eligible children, male participants were high proportion in 2011 and 2016 EDHS as compared to 2005 survey periods. The majority of children were from rural residency in five years preceding the survey in three surveys. About 78.6%, 70%, and 67% of women were 48 224 

middle economic class families were more anemic than children from rich families across the

unable to read and write in 2005, 2011, and 2016 survey respectively. Children from poor and

<sup>50</sup> 225

- <sup>1</sup> 227 three EDHS survey (Table 1). During the study period the trends in the prevalence of childhood
- $\frac{3}{4}$  228 anemia in Ethiopia, were ups and down across regions (Fig.1).

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Table 1: Descriptive characteristics of study participants included in the analysis for childhood anemia five years preceding the survey from EDHS 2005 - 2016 in Ethiopia

Characteristics	2005 (N, 3868) Frequency (%)	2011(N, 8958) Frequency (%)	2016(N, 8476) Frequency (%
Sex of child			
Male	1,931(49.93)	4,500(51.35)	4,395(51.85)
Female	1,937(50.07)	4,358(48.65)	4,081(48.15)
Age of child			
6-11	418 (10.81)	1,029(11.48)	1,000(11.80)
12-23	842 (21.76)	1,804(20.14)	1,902(22.43)
24-35	825 (21.33)	1,895(21.16)	1,803(21.27)
36-47	919 (23.76)	2,184(24.37)	1,832(21.62)
48-59 Moon + SD	864 (22.34) 32.57 ±15.6	2,047(22.85) <b>32.6±15.4</b>	1,939(22.87) <b>31.7±15.6</b>
Mean ± SD Residence	32.37 ±13.0	JZ.0±13.4	31.7113.0
Urban	244 (6.31)	1,047(11.69)	857(10.12)
Rural	3,624 (93.69)	7,911(88.31)	7,619(89.88)
Religion			.,()
Orthodox	1,624 (41.97)	3,416(38.13)	2,913(34.37)
Muslim	1,276 (32.99)	3,108(34.70)	3,432(40.48)
Protestant	836 (21.61)	2,151(24.01)	1,874(22.11)
Others	133 (3.43)	283(3.16)	258(3.05)
Women age			
15-29	1,930(49.90)	4,908(54.78)	4,356(51.40)
30-39	1,474(38.10)	3,223(35.98)	3,335(39.34)
40-49	464(12.00)	828(9.24)	785(9.26)
Women educatio	n		
No education	3,042 (78.63)	6,285(70.16)	5,685(67.07)
Primary	684 (17.68)	2,389(26.67)	2,275(26.84)
Secondary	136 (3.51)	168(1.88)	346(4.08)
Higher	7 (0.18)	117(1.30)	170(2.01)
Marital status			

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2 Married	ł	3,704(95.74)	8,425(94.04)	8,129(95.9)			
3 Widowe	ed	80(2.06)	178(1.99)	93(1.10)			
1 Divorce	ed	78(2.03)	306 (3.41)	210(2.48)			
5 Husba	nd educatio	on					
5 No-edu	cation	2,235 (58)	4,532(50.87)	4, 33(51.10)			
Primary	/	1,233(32)	3,710(41.65)	3,273(38.62)			
3 Second	lary	362(9)	412(4.63)	572(6.75)			
Higher	education	31(0.81)	255 (2.86)	300(3.53)			
<b>Wealth</b>	index						
L Poor		1,697(43.86)	4,048(45.19)	3,977(46.92)			
2 Middle		854(22.07)	1,873(20.91)	1,821(21.48)			
Rich		1,318(34.07)	3,038 (33.91)	2,678(31.60)			
Wome	Women working status						
5 Not wo	rking	2,841(73.45)	5,793(64.67)	6,140(72.44)			
5 Working	9	1,027(26.55)	3,165(35.33)	2,336(27.56)			
7 Total		3,868(100)	8,958(100)	8,476(100)			
3							
Comm	unity-level	characteristics of	of the study population				
Finding	s from this	study revealed th	nat there is a regional varia	ation of childhood anemia,			
000/	0						

42 282 Benishangul with 43% which was relatively low compared to other regions.

Childhood Anemia varies by urban-rural of residence. Children residing in communities with low poverty level had a lower percent of anemia (51.2%) as compared to with high community poverty level (62.5%%). Children from low community women education level (59.5%) were more anemic than children resided with high community women (53%) educational level (Table 54 287 2). 

83% in Somalia, 75%, in Afar, 72% in Dire Dawa, and 67% in Harari. However, Amhara, and

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- Table 2: Community Level Factors of under five children participated on EDHS (2016),
- Ethiopia. (N, 8476) З

community level factors	Not-anemic (%)	Anemic (%)	Total (%)
asiaonco			
	435(50.6)	424(49.4)	857(100)
	( )	( )	7619(100)
mhara	950(57.5)	703(42.5)	1653(100
Dromia	1273(34.2)	2446(65.8)	3719(100
SNNP	875(49.1)	906(50.9)	1781(100
Somali	58(16.7)	290(83.3)	348(100)
ïgray	263(46)	309(54)	572(100)
ddis Ababa	82(50.9)	79(49.1)	161(100)
.far	21(25.3)	62(74.7)	83(100)
Benishangul	51(56.6)	39(43.4)	90(100)
Sambelia	8(42.1)	11(57.9)	19(100)
larari	5(31.2)	11(68.8)	16(100)
Dire Dawa	9(28.1)	23(71.9)	32(100)
community women education			
ow	2281(40.5)	3358(59.5)	5639(100)
ligh	1315(46.4)	1520(53.6)	2837(100)
community women poverty			
ow	1815(48.8)	1905(51.2)	3719(100)
ligh	1782(37.5)	2974(62.5)	4756(100)
otal			8476(100
	oromia NNP omali igray ddis Ababa far enishangul ambelia arari ire Dawa <b>community women education</b> ow igh <b>community women poverty</b> ow	aural       3164(41.5)         region       mhara       950(57.5)         promia       1273(34.2)         NNP       875(49.1)         omali       58(16.7)         igray       263(46)         ddis Ababa       82(50.9)         far       21(25.3)         enishangul       51(56.6)         ambelia       8(42.1)         arari       5(31.2)         ire Dawa       9(28.1)         community women education       0w         ow       2281(40.5)         igh       1315(46.4)         ow       1815(48.8)         igh       1782(37.5)	tural3164(41.5)4455(58.5)region

The spatial distribution of childhood anemia in Ethiopia was non-random in all three 46 317 consecutive surveys. A global spatial autocorrelation statistic was estimated using Moran's I statistic. The global Moran's I test value was 0.176 (P-value < 0.001) in 2005, 0.18 (P-value < 0.001) in 2011, and 0.09(P-value < 0.005) in 2016 Ethiopian Demographic and health surveys. Hot spot analysis of the three surveys

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The spatial distribution of childhood anemia in Ethiopia was different in the three survey periods. In EDHS 2005, a high proportion of childhood anemia was detected in Dire Dawa, Harari, Eastern Oromia, Benishangul in Metekel zone, Gambela, Southern and Eastern Tigray, and Somali region mainly Liben, Afdar, and Fafna zone which was hotspot area within 95% confidence level. On the counterpart, GamoGofa, Wolayita, Hadiya, Southern Omo, and Segen zone of SNNPR, Addis Ababa, central Oromia, Jima, North Shewa zone were cold spot area. In EDHS 2011, highly significant clustering of childhood anemia was detected in Somalia, 15 328 Dire Dawa, Harari, Afar, Gambela, Benishangul, Eastern Oromia, Bale, and Arsi zone were the hotspot areas within 95% level of confidence. The low hotspot area of childhood anemia was detected in central Tigray, East and West Gojam, North Gondar, a central part of Oromia, 24 332 Addis Ababa and SNNPR were areas identified as the low percentage of childhood anemia in the 2011 EDHS survey. 

In EDHS-2016 sampled data, hot spot (high risk) regions for childhood anemia were observed in Somalia, Dire Dawa, Harari, Gambela, Eastern, and Southern part of Oromia, However, Amhara, Benishangul, and Southern Nations Nationalities and Peoples (SNNP) were identified 34 336 <sup>36</sup> 337 as cold spot (low risk) regions for childhood anemia within a 95% confidence interval (Fig.2)

Spatial interpolation 

Based on EDHS-2005 sampled data, the geostatistical analysis predicts that the highest prevalence of childhood anemia (65.75%-88.89%) was detected in East Oromia, Ilubabur, Arsi, 46 341 some parts of Benishangul, Agnuak zone in Gambela, North Shewa Amhara region, South and central Tigray Afar in zone2, some parts of Dire Dawa city and Somalia. In EDHS-2011 Geostatistical analysis, a high percent of anemia was detected in Afar, most parts of Somalia, 53 344 Oromia in East Harerge and Borena, some part of Dire Dawa, and the Meketel zone in Benishangul. In 2016 EDHS most of Somalia, some parts of Gambela, Guji and some parts of 

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Borena, East Shewa, East Harerge and Arsi in Oromia and part of Dire Dawa were highly prevalent areas in childhood anemia (Fig.3) 

#### **Spatial scan statistics**

In 2005 EDHS most likely (primary clusters) and secondary clusters of anemia were identified. A total of 3 significant clusters were identified. One was most likely (primary) clusters and 2 11 350 were secondary clusters of spatial sat scan analysis. The primary cluster's spatial window was located in Somalia, which was centered at (9.018373 N, 43.110635 E) of geographic location with a 97.93 km radius, and Log-Likelihood ratio (LLR) of 20.03, at p < 0.001 which was 18 353 20 354 detected as the most likely cluster with Maximum Likelihood. It showed that children within the spatial window had 1.54 times more likely a higher risk of anemia than the children outside areas of the spatial window. The secondary clusters scanning window was located in the 27 357 southern part of Somali region. Which was centered at (3.998656 N, 41.240691 E) with a 92.08 km radius and LLR of 1.73 at p-value 0.0010. It showed that children within the spatial window had a 1.73 times higher risk of anemia than children outside the window. 

In 2011 EDHS, a total of 10 clusters were identified and five of them were significant clusters with p-value <0.05. A total of 180 locations/spots with a total sampled population of 2478 were 37 361 found as primary cluster areas were identified using sat scan analysis with a p-value < 0.001. The primary cluster spatial window was located mainly in Somali, Afar, Eastern Oromia, Dire Dawa, and Harari. The primary cluster spatial window was centered at (8.975207 N, 43.790264 E) / 540.29 km, with a relative risk (RR) of 1.43 and a log-likelihood ratio (LLR) of 127.79. It showed that children within the spatial window had 1.4 times more likely a higher risk of anemia than the children outside areas of the spatial window. The secondary cluster spatial window 53 368 was located mainly in Afar regional state and 72 cases were found among the total population.

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The secondary cluster spatial window was centered at (12.758587 N, 40.175990 E) / 39.58 km, with a relative risk (RR) of 1.68 and a log-likelihood ratio (LLR) of 21.5 P-value=0.001. In 2016 EDHS, a total of 7 clusters (1 most likely cluster) which were located in Somalia, Afar, Eastern Oromia, Dire Dawa, and Harari. The cluster window was centered with a radius at (7.650693 N, 47.007920 E) / 912.19 km with a Relative Risk (RR) of 1.44. The Log-Likelihood 11 373 Ratio (LLR) for the most likely cluster was 182.86, p < 0.001. Secondary clusters were located in Gambela which was centered at (8.195862 N, 34.289837 E) with a radius of 29.01 km, and LLR of 18.8 at p-value 0.001. It showed that children within the spatial window had a 1.5 times 18 376 20 377 higher risk of anemia than outside the window (Fig.4). 23 378 **Multilevel Analysis** The intra-cluster correlation coefficient (ICC) in the empty model indicated that 18.8% of the 26 379 total variability for children anemia was due to differences between clusters and the remaining unexplained 81.2% attributable to individual differences. The median odds ratio for anemia 33 382 was 2.3 in the null model which indicates that there was variation between clusters. If we randomly select children from two different clusters children at the cluster with a higher risk of anemia had 2.3 times higher odds of experiencing anemia as compared with children at cluster 40 385 with a lower risk of anemia. 

Bi-variable multilevel logistic regression analysis was done to identify variables for 43 386 multivariable multilevel logistic analysis and Variable with a p-value less than 0.2 were considered for multivariable analysis. 

Individual-level predictors for anemia

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In multivariable multilevel mixed-effect logistic regression analysis individual-level factors such as the age of the child, wealth index, mother age, maternal anemic status, birth order, fever, stunting, and wasting status were a significant predictor of childhood anemia. Children age between 12-23 months (AOR = 0.66, 95%CI = 0.53-0.81), between 24-35 months (AOR= 0.35, 95% CI = 0.28-0.43), between 36-47 months (AOR = 0.23-95%CI = 0.19-0.29), and between 48–59 months (AOR = 0.15, 95%CI = 0.12-0.19) were less likely to develop anemia when compared with children age between 6-11 months. The likelihood of developing anemia for those children residing with the family wealth index of middle and rich was lower by 21% (AOR=0.79, 95%CI = 0.67-0.94), and 23% (AOR=0.77, 23 399 95%CI = 0.65-0.91), respectively as compared with children with poor wealth index. Children 

anemia as compared to age 15-29, (AOR=0.75, 95%CI = 0.59-0.95). 

Community-level predictors for anemia

The odds of experiencing anemia for those birth orders 4-5, 6, and above six were 1.22 times (AOR=1.22, 95%CI = 1.01-1.47) and 1.35 times (AOR=1.35, 95%CI = 1.08-1.67) higher as 33 403 compared with first-order respectively. The odds of developing anemia of children born from who had anemia history mother was 1.39 higher than that of children born from not anemic 40 406 history before. Children who had fever were 39% (AOR =1.39, 95% CI: 1.24-1.58) more likely 42 407 to develop anemia as compared with their counterparts. Children with moderate and severe stunting status were 35% (AOR=1.35, 95% CI: 1.17-1.54) and, 96% (AOR=1.95, 95% CI: 1.68-2.28), more likely to develop anemia respectively as compared to no stunting status. Similarly, 49 410 children who had to sever wasting status were 51% more (AOR =1.51, 95% CI: 1.07-2.12) likely to develop anemia as compared with those children who had no wasting. 

whose mother's age were between 40-49 had 25% decreased odds of developing childhood

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1 2	413	In the multivariable multilevel logistic regression model region of residence was significantly
$     \begin{array}{c}       2 \\       3 \\       4 \\       4     \end{array}     $ 414     5     6     415	associated with community-level factors for childhood anemia.	
	Odds of children live in Somalia were 5.65 times (AOR=5.65, 95% CI: 3.92-8.16), Dire Dawa	
7 8 9	416	3.45 times (AOR=3.45, 95% CI: 2.27-5.26), Afar 3.01 times (AOR=3.01, 95% CI: 2.09-4.34),
9 10 11	417	and Oromia 2.34 times (AOR=2.34, 95% CI: 1.73-3.18) had more likely to develop childhood
12 13		anemia as compared to Amhara regional state. Similarly, the odds of developing anemia in
	419	Addis Ababa was 2.10 times (AOR=2.10, 95% CI: 1.40-3.16), Gambella 1.94 times
16 17 18	420	(AOR=1.94, 95% CI: 1.32-2.84), and Tigray 1.46 times (AOR=1.46, 95% CI: 1.08-1.98), more
19 20	101	likely as compared to Amhara region. Benishangul and SNNPR had not significantly different
21 22	422	in the prevalence of anemia as compared to the reference region Amhara (Table 3).

Table 3: Multilevel logistic regression analysis result of both individual and community level
 factors associated with anemia in Ethiopia, EDHS 2016

Religion         1         1           Orthodox         1         1           Muslim         2.07[1.77-2.47] **         1.21 [0.97-1.46]           Protestant         1.20 [1.002-1.48] *         1.09[0.86-1.37]           Others          1.55[1.07-2.32] *            Wealth index         Poor         1         1           Middle         0.71[0.61-0.84] **         0.79 [0.67-0.94] *						
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Individual Level	Null Model				
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Age in month					
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			1		1	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			0.66[0.54-0.82] **		0.66 [0.53-0.81] **	
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	24 – 35		0.35[0.28-0.44] **		0.35 [0.28-0.43] **	
Religion         1         1           Orthodox         1         1           Muslim         2.07[1.77-2.47] **         1.21 [0.97-1.46]           Protestant         1.20 [1.002-1.48] *         1.09[0.86-1.37]           Others          1.55[1.07-2.32] *            Wealth index         Poor         1         1           Poor         1         1         1           Middle         0.71[0.61-0.84] **         0.79 [0.67-0.94] *           Rich          0.72[0.63-0.85] **            Child size at birth         Small         1         1           Small         1         1         1           Average         0.96[0.84-1.09]         0.93 [0.80-1.07]           Large          0.94[0.81-1.08]            Stationarian         1         1           2-3         1.09[0.94-1.28]         1.13[0.97-1.32]	36 – 47					
Orthodox11Muslim $2.07[1.77-2.47]^{**}$ $1.21 [0.97-1.46]$ Protestant $1.20 [1.002-1.48]^{*}$ $1.09[0.86-1.37]$ Others $1.55[1.07-2.32]^{*}$ <b>Wealth index</b> $$ $1.44[0.96-2.13]$ Poor11Middle $0.71[0.61-0.84]^{**}$ $0.79 [0.67-0.94]^{*}$ Rich $0.72[0.63-0.85]^{**}$ Othild size at birth $1$ 1Small11Average $0.96[0.84-1.09]$ $0.93 [0.80-1.07]$ Large $0.94[0.81-1.08]^{*}$ $0.96 [0.84-1.10]^{*}$ <b>Birth order</b> 1112-3 $1.09[0.94-1.28]^{*}$ $1.13[0.97-1.32]^{*}$	48 – 59		0. 15[0.12-0.19] **		0.15 [0.12-0.19] **	
Orthodox11Muslim $2.07[1.77-2.47]$ ** $1.21 [0.97-1.46]$ Protestant $1.20 [1.002-1.48]$ * $1.09[0.86-1.37]$ Others $1.55[1.07-2.32]$ * <b>Wealth index</b> $$ $1.55[1.07-2.32]$ *Poor11 $1.44[0.96-2.13]$ Wealth index $0.71[0.61-0.84]$ ** $0.79 [0.67-0.94]$ *Poor11 $0.77 [0.65-0.91]$ *Rich $0.72[0.63-0.85]$ **Oritid size at birth $1$ $1$ Small1 $1$ Average $0.96[0.84-1.09]$ $0.93 [0.80-1.07]$ Large $0.94[0.81-1.08]$ $1st$ 1 $1$ $2-3$ $1.09[0.94-1.28]$ $1.13[0.97-1.32]$	Religion					
Protestant $1.20 [1.002-1.48] *$ $1.09[0.86-1.37]$ Others $1.55[1.07-2.32] *$ Wealth indexPoor11Middle $0.71[0.61-0.84] **$ $0.79 [0.67-0.94] *$ Rich $0.72[0.63-0.85] **$ Othild size at birth $1$ 1Small11Average $0.96[0.84-1.09]$ $0.93 [0.80-1.07]$ Large $0.94[0.81-1.08]$ Birth order111st112-3 $1.09[0.94-1.28]$ $1.13[0.97-1.32]$			1		1	
Others $1.55[1.07-2.32]^*$ $1.44[0.96-2.13]$ Wealth indexPoor11Middle $0.71[0.61-0.84]^{**}$ $0.79[0.67-0.94]^*$ Rich $0.72[0.63-0.85]^{**}$ O.77 [0.65-0.91] *0.77 [0.65-0.91] *Child size at birth1Small11Average $0.96[0.84-1.09]$ $0.93[0.80-1.07]$ Large $0.94[0.81-1.08]$ Birth order111st112-3 $1.09[0.94-1.28]$ $1.13[0.97-1.32]$	Muslim		2.07[1.77-2.47] **		1.21 [0.97-1.46]	
Wealth index         1         1           Poor         1         1           Middle         0.71[0.61-0.84] **         0.79 [0.67-0.94] *           Rich          0.72[0.63-0.85] **          0.77 [0.65-0.91] *           Child size at birth         1         1         1           Small         1         1         1           Average         0.96[0.84-1.09]         0.93 [0.80-1.07]         Large           Large          0.94[0.81-1.08]          0.96 [0.84-1.10]           Birth order         1         1         1         1           2-3         1.09[0.94-1.28]         1.13[0.97-1.32]         1.13[0.97-1.32]	Protestant		1.20 [1.002-1.48]	*	1.09[0.86-1.37]	
Poor11Middle $0.71[0.61-0.84]$ ** $0.79[0.67-0.94]$ *Rich $0.72[0.63-0.85]$ **Child size at birth11Small11Average $0.96[0.84-1.09]$ $0.93[0.80-1.07]$ Large $0.94[0.81-1.08]$ Birth order111st112-3 $1.09[0.94-1.28]$ $1.13[0.97-1.32]$	Others		1.55[1.07-2.32] *	🛁	1.44[0.96-2.13]	
Middle $0.71[0.61-0.84]$ ** $0.79[0.67-0.94]$ *Rich $0.72[0.63-0.85]$ ** $0.77[0.65-0.91]$ *Child size at birth11Small11Average $0.96[0.84-1.09]$ $0.93[0.80-1.07]$ Large $0.94[0.81-1.08]$ Birth order111st112-3 $1.09[0.94-1.28]$ $1.13[0.97-1.32]$	Wealth index					
Rich        0.72[0.63-0.85] **        0.77 [0.65-0.91] *         Child size at birth       1       1       1         Small       1       1       1         Average       0.96[0.84-1.09]       0.93 [0.80-1.07]         Large        0.94[0.81-1.08]          Birth order       1       1         1st       1       1         2-3       1.09[0.94-1.28]       1.13[0.97-1.32]	Poor		1		1	
Child size at birth         1         1           Small         1         1           Average         0.96[0.84-1.09]         0.93 [0.80-1.07]           Large          0.94[0.81-1.08]          0.96 [0.84-1.10]           Birth order         1         1         1         1           2-3         1.09[0.94-1.28]         1.13[0.97-1.32]         1	Middle		0.71[0.61-0.84] **		0.79 [0.67-0.94] *	
Small       1       1         Average       0.96[0.84-1.09]       0.93 [0.80-1.07]         Large        0.94[0.81-1.08]          Birth order       1       1         1st       1       1         2-3       1.09[0.94-1.28]       1.13[0.97-1.32]	Rich		0.72[0.63-0.85] **		0.77 [0.65-0.91] *	
Average       0.96[0.84-1.09]       0.93 [0.80-1.07]         Large        0.94[0.81-1.08]        0.96 [0.84-1.10]         Birth order       1       1       1         2-3       1.09[0.94-1.28]       1.13[0.97-1.32]	Child size at birth					
Large          0.94[0.81-1.08]          0.96 [0.84-1.10]           Birth order         1         1         1           1st         1         1         1           2-3         1.09[0.94-1.28]         1.13[0.97-1.32]         1	Small		1		1	
Birth order         1         1           1st         1         1           2-3         1.09[0.94-1.28]         1.13[0.97-1.32]	Average				0.93 [0.80-1.07]	
1st112-31.09[0.94-1.28]1.13[0.97-1.32]	Large		0.94[0.81-1.08]		0.96 [0.84-1.10]	
2-3 1.09[0.94-1.28] 1.13[0.97-1.32]	Birth order					
	1st		1		1	
4-5       1.17[0.97-1.40]       1.22 [1.01-1.47] *	2-3		1.09[0.94-1.28]			
	4-5		1.17[0.97-1.40]		1.22 [1.01-1.47] *	

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1 450	6 and above	1.30[1.05-1.62]	1.35 [1.08-1.67] **
<sup>2</sup> 451	No of children under 5		
3 452	1-2 children	1	1
4 <sup>132</sup> 5 453	≥ 3 children	1.22[1.1-1.4] *	1.09 [0.94-1.27]
5 6 454	Maternal anemia		
7 455	Not-anemic	1	1
<sup>8</sup> 456	Anemic	1.51[1.34, 1.72] **	1.39 [1.24-1.58] **
9 10 457	Maternal BMI		1.00 [1.24 1.00]
10 450	≥18.5 kg/m2	1	1
11 458			
12 459	<18.5 kg/m2	1.12[0.97-1.26]	1.05 [0.92-1.19]
13 460	Mather's working status		4
$^{14}$ 461 $^{15}$ 462	Not-working		1
15 462 16	Working	0.88[0.77-0.99] *	0.92 [0.81-1.04]
17 463	Women age		
18 464	15-29	1	1
19 465	30-39	0.91[0.71-1.06]	0.90 [0.78-1.04]
20 466	40-49 <	0.75[0.59-1.12] *	0.75 [0.59-0.95] *
<sup>21</sup> 467	Breastfeeding		
22	No	1	1
23 <sup>468</sup> 24 469	Yes	0.92[0.81-1.04]	0.98 [0.87-1.12]
25 470	Vitamins in last 6 month		
26 471	No		1
<sup>27</sup> 472	Yes	0.90[0.81-1.09]	0.93 [0.84-1.05]
28 12		0.90[0.81-1.09]	0.93 [0.84-1.05]
29 473	Diarrhea last 2 week		4
30 474	No		1
31 475	Yes	0.88[0.73, 1.04]	0.90 [0.76-1.07]
<sup>32</sup> 476	Fever in last 2 weeks		
<sup>33</sup> 477 34	No	1	1
34 35 478	Yes	1.35[1.15-1.59] ** 🔍	1.32 [1.13-1.56] *
<sub>36</sub> 479	Stunting status		
37 480	No-stunting	1	
38 481	Moderate stunting	1.27[1.10-1.46] **	1.35 [1.17-1.54] **
<sup>39</sup> 482	Severely stunting	1.81[1.55-2.11] **	1.96 [1.68-2.28] **
40 183	Wasting status		
41	No-wasting	1	
42 484 43 485	Moderate wasting	1.27[1.11-1.45]	0.98 [0.80-1.19]
43 485 44 486	Severe wasting	1.68[1.55-2.10] *	1.51 [1.07-2.12] *
<sup>44</sup> 480 <sup>45</sup> 487		1.00[1.00-2.10]	1.01 [1.07-2.12]
46	Place of residence		,
47 488	Urban	1	1
48 489	Rural -	1.40[1.12-1.78]	1.28 [0.99-1.64]
<sup>49</sup> 490	Region	-	
50 401	Amhara	1	1
51		1.46 [1.09-1.97]	
52 492	Tigray		
53 493 54 404	Afar	3.90 [2.84-5.35]	
54 55 494	Oromia	2.48 [1.89-3.25]	** 2.34 [1.73-3.18] **
56 495	Somali	6.34[4.65-8.63]	5.65 [3.92-8.16] **
57			
58			19
59			
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96	Benishangul			0.86 [0.62-1.17]	0.81 [0.58-1.15]			
97	SNNPR			1.33 [1.00-1.76]	1.30 [0.94-1.80]			
98	Gambela			1.93 [1.38-2.69] **	1.94 [1.32-2.84] **			
99	Hareri			3.08 [2.15-4.43] **	2.98 [1.99-4.46] **			
00	Addis Ababa			1.91[1.29-2.83] **	2.10 [1.40-3.16] **			
1	Dire Dawa			3.92 [2.67-5.77] **	3.45 [2.27-5.26] **			
2	Community educa	tion				-		
}	Low education			1	1			
	High education			1.07[0.90-1.26]	1.13[0.94-1.34]	_		
5	Community pove	erty		<u>,</u>				
, ,	Low poverty			1				
	High poverty Model comparise			1.41[1.17-1.68] *	1.15[0.94-1.40]	-		
	Random effect	on and						
)	ICC	0.187				-		
	Log-likelihood	-4981.63	-4513.17	-4836.83	-4436.60			
	Deviance	9963.26	9026.34	9673.66	8873.2			
	PVC (%)	Ref	41.22	60.11	62.59			
	MOR	2.30	1.72	1.42	1.38	_		
	*Key: 1: referenc Multicollinearity	e group; p-v	value 0.05-0	.01 *: p-value < 0.01 *	*			
)	Multicollinearity y	vas chackad	for those y	variables included in	the final model using VIE			
	Walloonnoarty V	Multicollinearity was checked for those variables included in the final model using VIF.						
	Accordingly, the	Accordingly, the VIF for all predictor variables included in the final model was below 10						
	indicating the abs	ence of multi	collinearity a	mong the predictor var	riables.			
}	Comparison of n	nodels						
24	Deviance was use	ed to compare	e the models	s. The model with the lo	owest value of deviance was	i		
	considered to be	the better mo	de					

525 considered to be the better mode.

# 47 526 **Discussion**

This study tried to identify spatio-temporal distribution and predictors of childhood anemia across the regions in Ethiopia. 2005, 2011, and, 2016 Ethiopian Demographic and Health 54 529 Survey data were used. In this study, the trend of anemia was decreased from 2005 to 2011, while the rate significantly increased from 2011 to 2016. The study revealed that 57.56% [CL: 

0.56-0.59] of children were anemic in 2016 preceding the survey. This finding was in line with a study done in Gondar, Northwest Ethiopia 58.6% (20), whereas higher than the study done in cape Verde, west Africa 51.8%(21), and southern Ethiopia(22). Among children of 6-59 months, anemia is still considered to be a major public health problem in Ethiopia. Though the levels of anemia among children vary by background factors like region and lowest household wealth index and maternal related factors, more of the children in Ethiopia were suffering anemia. 15 537 

The spatial pattern figures out that the geographical inequality of anemia by using sat scan 18 538 20 539 and GIS spatial techniques like cluster mapping tools and interpolation techniques. The spatial analysis indicates that the distribution of childhood anemia was non- random across the country with global Moran's I index of 0.176 in 2005, 0.18 in 2011, and 0.09 in 2016 with 27 542 significant p-value which indicates significant clustering areas. Findings from this study were in line with a study done in Nigeria, Malawi, Tanzania, and Uganda (23,24). 

The spatial pattern of sat scan analysis showed that Eastern Somalia regions were primary (most likely) cluster and secondary cluster also located in the southern part of Somalia in 2005 sat scan analysis. In 2011 Somali, Afar, Eastern Oromia, Dire Dawa, and Harari were located 37 546 <sup>39</sup> 547 in the primary window and centered at (8.975207 N, 43.790264 E/ 540.29 km with a significant p-value. Similarly, spatial sat scan analysis showed that Somalia, Afar, Eastern Oromia, Dire Dawa, Harari were hotspot areas in the 2016 EDHS spatial analysis. 

47 550 This study indicated that children age 12-59 months were less affected by childhood anemia. This finding was consistent with studies conducted in Ethiopia and Togo (25–27). This could 49 551 be explained by the fact that children who are getting older receive a diet that is richer and complete, with a sufficient intake of iron which could prevent the occurrence of iron deficiency 

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anemia. The deficiency may result from inadequate dietary intake of iron, malabsorption of iron an increased iron demand during rapid growth might it be the possible reason (28). 

The finding of this study indicated that children whose mother's age was between 40-49 were less anemic as compared to age 15-29. This finding is a study done in line with other studies conducted in sub-Saharan Africa and Ghana (15,29). This group consists of more at-risk population segments (Adolescent) for anemia. They are vulnerable to malnutrition because they are growing faster than at any time after their first year of life which contributes to the intergenerational cycle of malnutrition and he most common forms of malnutrition among 18 561 20 562 Ethiopian adolescent girls is iron deficiency anaemia. Aside from, the bodies of the growing adolescent mother and her baby may compete for nutrients, raising the infant's risk of low birth weight, however, the lack of such nutrients might lead to anemia. 

Children from households of middle and rich wealth indexes were less affected by childhood anemia as compared to children from a poor household. This finding has also been 30 566 demonstrated in similar studies in Nigeria and northern Ethiopia (23,30). This is due to the reason that children from poor households are less likely to get iron-rich foods like animal foods and vitamin-rich foods especially vitamins A and C which are very important for iron absorption. 37 569

Maternal anemia was highly associated with the occurrence of childhood anemia. This finding 40 570 <sup>42</sup> 571 was in line with a study done in South Africa, Haiti, and India(31–33). Reasons may be mothers and children share a common home environment, socioeconomic, and dietary conditions, and maternal and child anemia may reflect the common nutritional status of the household and poor maternal iron intake during pregnancy, reduce breast milk might be the possible reason. 49 574 

52 575 EDHS data set indicated that the incidence of fever had an impact on childhood anemia. This is in line with studies done in Ghana and South Ethiopia Wolaita (22,34) Results showed that children who had a fever in the last two weeks before the survey had had a higher likelihood 

of anemia than children who had not to fever. This could be attributed to the infectious cause of childhood fever mainly malaria, tuberculosis, and Leishmaniasis which cause anemia by destructing red blood cells or other related mechanisms. 

The nutritional status of children had a significant association with childhood anemia. The stunting status of children was an independent predictor in the multilevel mixed effect model of this study. The result of this study indicated that it was in line with previous studies conducted in South Africa(33), Bangladesh(35,36), and Ethiopia(37,38). This study revealed that there was a greater prevalence of anemia among stunted children compared to non-stunted children. 18 585 20 586 Children suffering from nutritional deficiency were more likely to have weak immune systems which makes them vulnerable to various illnesses and healthiness such as parasitic infections or chronic inflammation. Many of these conditions reduce the hemoglobin level in the blood 27 589 leading to increased anemia prevalence. The statement is supported by the evidence given in other studies(39)that nutritional deficiency causes several health hazards. 

Besides, severely wasting children were 1.51 times more likely to be anemic than their counterpart. Since stunting and wasting are long-term and short-term indicators of malnutrition, the results implied that under-nourished children experience a higher risk of developing anemia 37 593 as compared to nourished children. Odds of experiencing anemia for those birth order four up to five and six and greater than six were higher than that of with first order. This finding was similar to a study done in Indian(15,40). This could be due to the distribution of scarce resources within the family and interrelated to maternal exhaustion of micronutrients feeding practice. 

In a multivariable multilevel analysis, the odds of developing childhood anemia were higher among children who lived in Somalia, Dire Dawa, Afar, and Gambela as compared to the Amhara region. This might be due to the unavailability and inaccessibility of health facilities as 56 601

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compared to the regions. Regional variation in the nutrient intake can cause significant health disparity, and this variability may be mediated by factors such as food availability, food customs, and culture. 

This study was used different methods of spatial pattern, trend and a multilevel regression model used because of nested or cluster samples to show the effect of individual predictors 11 606 and community-level variables on the dependent variable. The study was based on a large dataset representing the whole country of Ethiopia and which was weighted to make it nationally representative and adjusted for the design to get a reliable estimate. However, there 18 609 20 610 were some limitations to this study. The cross-sectional nature of the data prevents causality from being inferred between the independent and dependent variables. Also, respondents' data that didn't have files (longitude and latitude) were excluded from the spatial analysis which 27 613 could affect the overall result and the generalizability of the findings. 

#### Conclusion 30 614

<sub>33</sub> 615 Findings from this study indicated that the prevalence of childhood anemia decreased between the 2005-2011 survey while the prevalence increased from 2011-2016 EDHS. The spatial 35 616 pattern of child anemia in Ethiopia was non-random among the three consecutive surveys with the global Moran's I value of 0.176, 0.18, and 0.09 in EDHS 2005, 2011, and 2016 respectively. 42 619 In this study, Sat Scan analysis identified the primary and secondary clusters for the three survey periods. In 2005 EDHS the hotspot area was identified in eastern and southern parts of Somalia, in 2011 Somali, Afar, Eastern Oromia, Dire Dawa, and Harari were among the 49 622 hotspot regions. Spatial sat scan analysis revealed that spatial clustering of childhood anemia 51 623 was identified in Somalia, Afar, Eastern Oromia, Dire Dawa, Harari hotspot area in the 2016 EDHS period.

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Child age, women age, wealth index, maternal anemia, had a fever, birth order, stunting, wasting and region were significant predictors among 6-59 months. Therefore, these results provide further insight into identifying the true picture of childhood anemia spatio-temporal clusters in the country and enable timely spatial targeting factors to alleviate home delivery. Therefore, policymakers and health planners should design effective intervention strategies for the identified hot spot areas and individual and community-level factors. 

#### Abbreviations 15 631

AOR-Adjusted Odds Ratio, CSA-Central Statics Agency, CI-Confidence Interval, COR-Crude 18 632 20 633 Odds Ratio, EDHS-Ethiopia Demographic and Health Survey, GPS-Global Positioning System, ICC-Intra Class Correlation Coefficient, LLR-Log-Likelihood Ratio, MOR-Median odds ratio, OR-Odds Ratio, RR-Relative Risk, PVC-Proportional Change in Variance, SNNPR-27 636 Southern Nations, Nationalities, and Peoples' Region. . C.I.C.

#### **Declarations**

#### onsent to participate

The study was approved by the institutional ethical review committee board of the University of Gondar and ethical clearance was obtained from the board. Upon this clearance, the study 42 641 was conducted. The congeniality of the data was maintained by using the extracted data only for the study purpose and keeping the data from a third party. 

#### **Consent for publication**

Not-applicable 

#### Data sharing statement

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5 6 783	Figure 1: Trends in anemia overtime across the regions in Ethiopia, EDHS 2005 to 2016
7 8 784	Figure 2: Hot spot and cold spot analysis of anemia in Ethiopian, EDHS 2005 to 20016
9 785 10 785	Figure 3: Ordinary Kriging interpolation of anemia in Ethiopia, EDHS 2005 to 2016
<sup>11</sup> 786 12	Figure 4: SaTScan scan statistics analysis of anemia in Ethiopia, EDHS, 2005-2016
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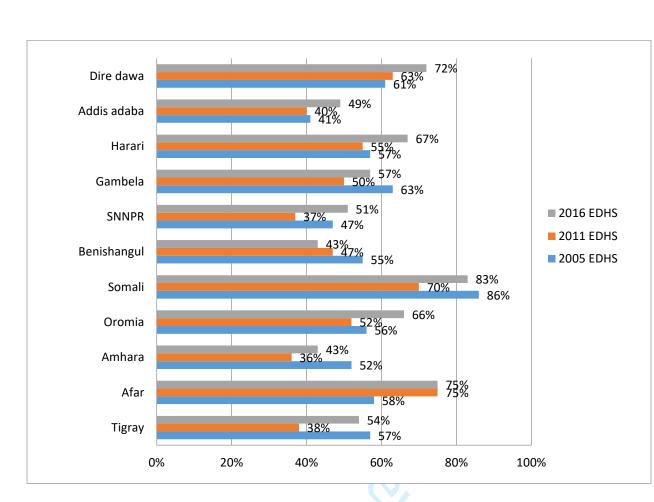
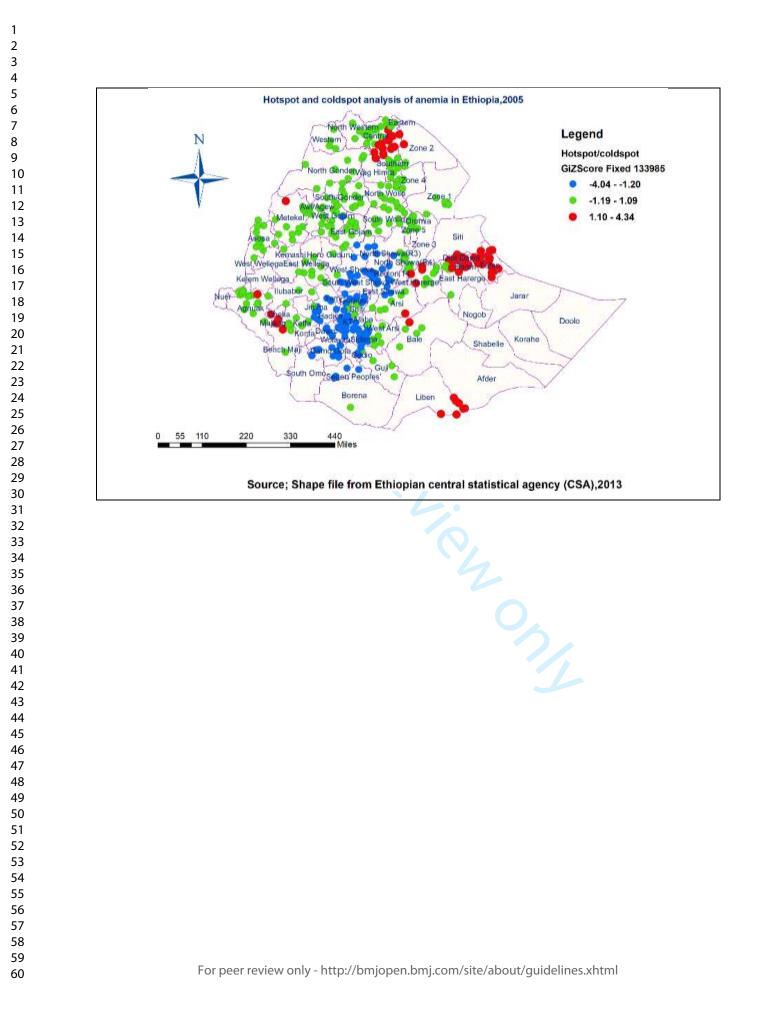
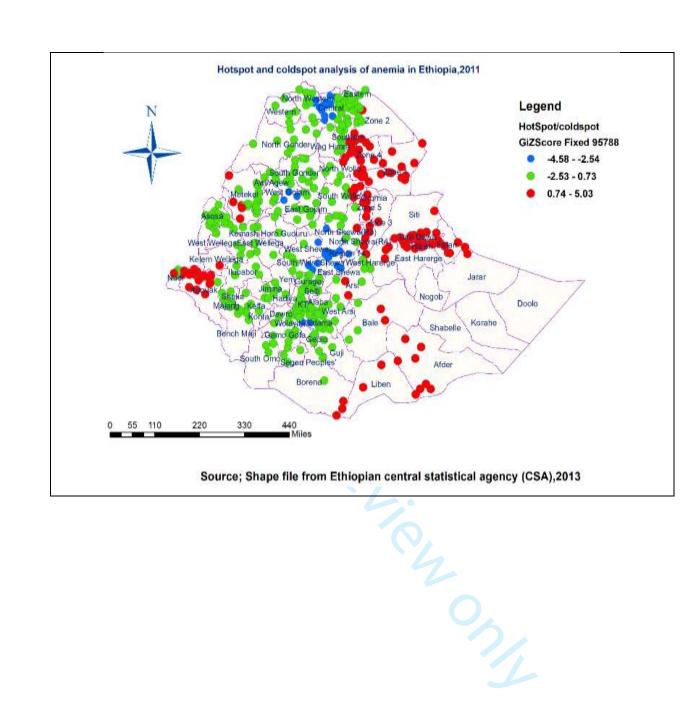


Figure 1: Trends in anemia overtime across the regions in Ethiopia, EDHS 2005 to 2016

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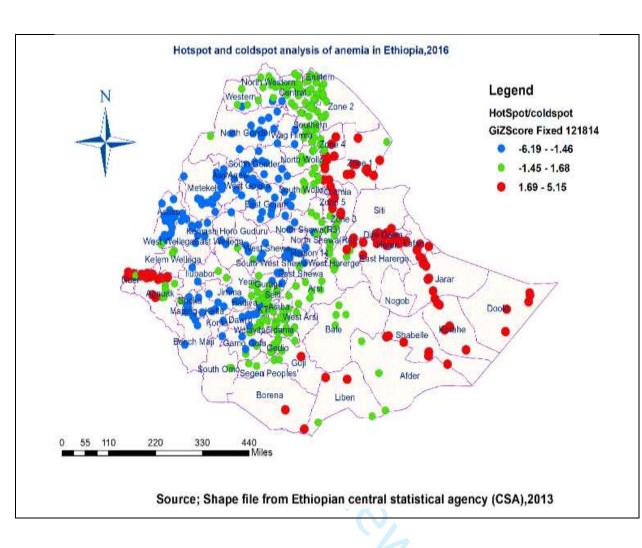
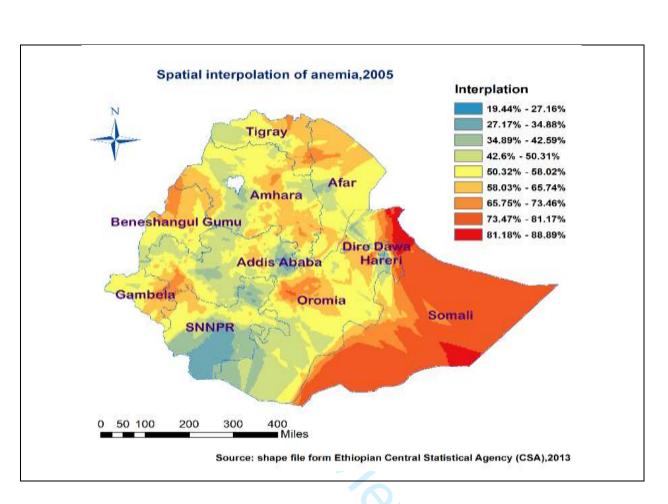
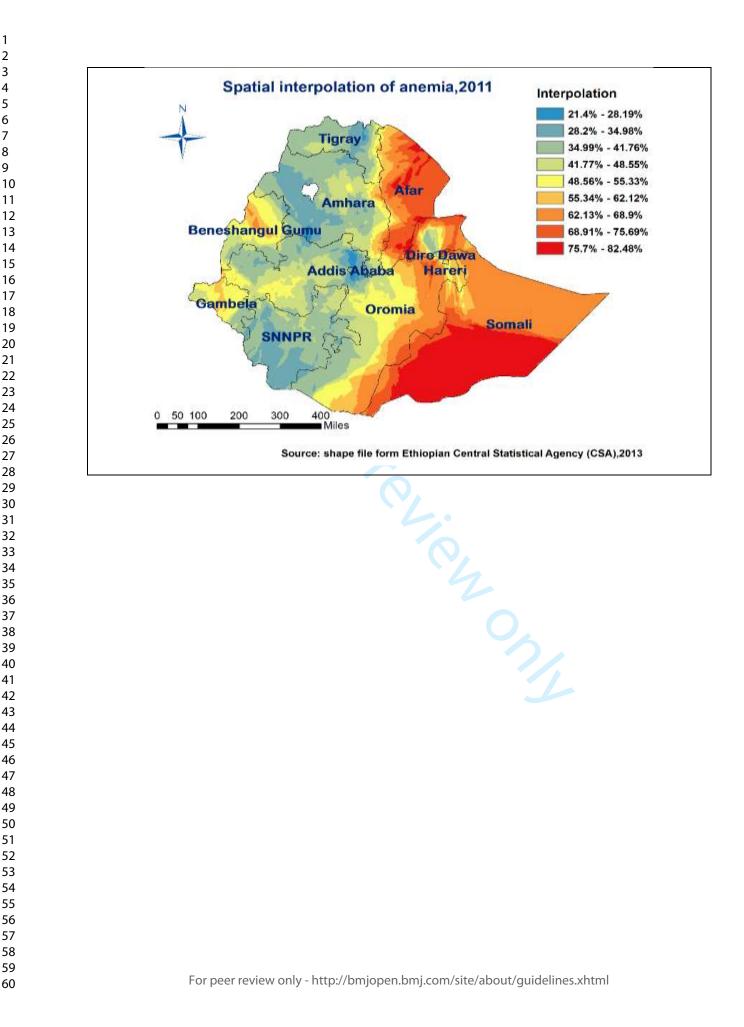


Figure 2: Hot spot and cold spot analysis of anemia in Ethiopian, EDHS 2005 to 20016



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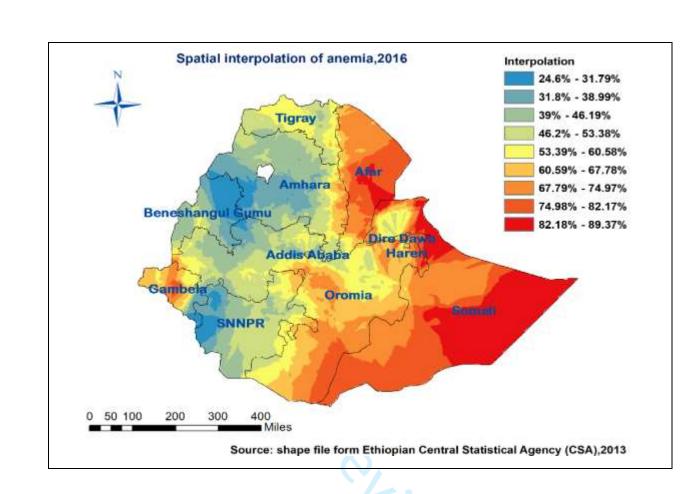
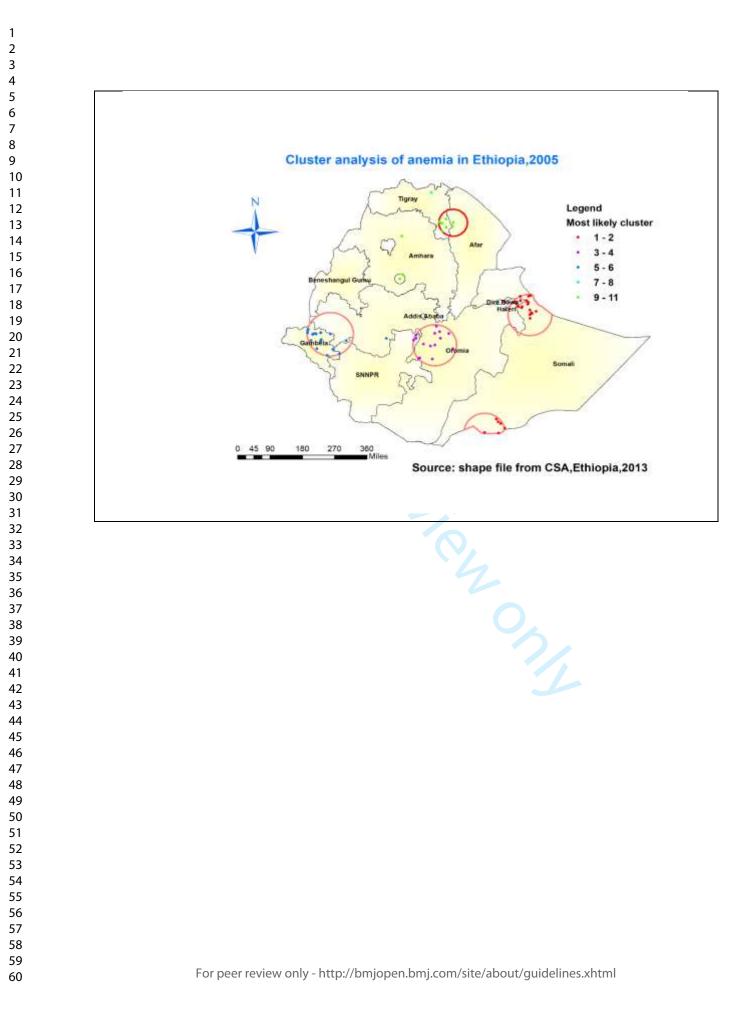
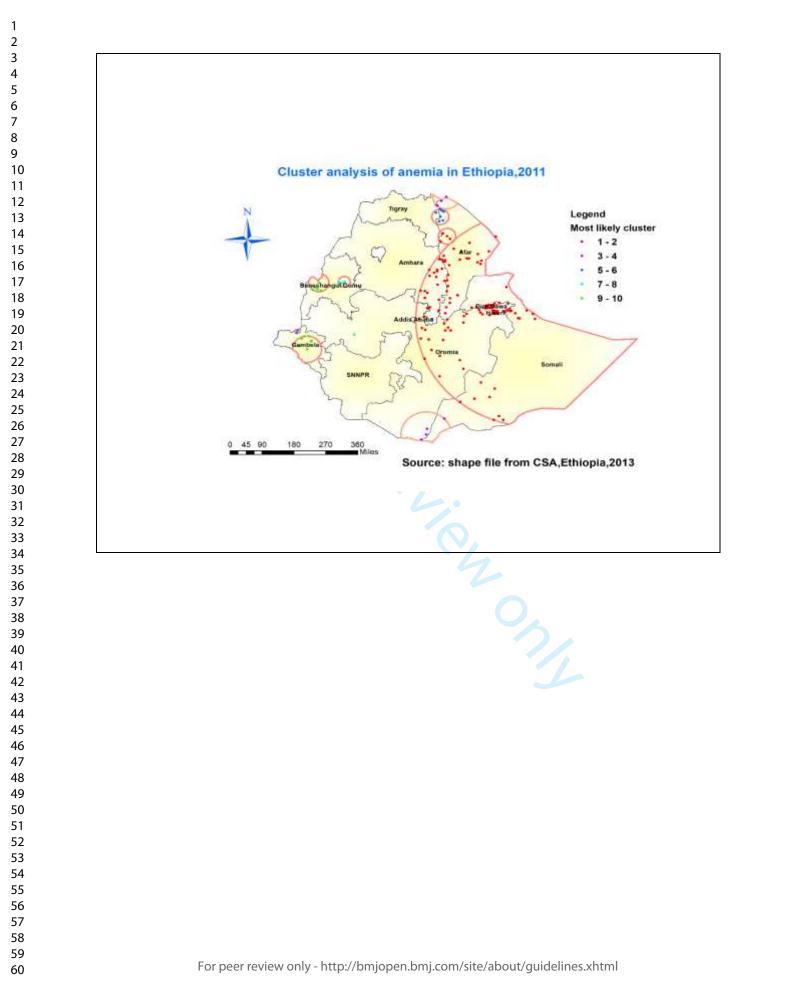
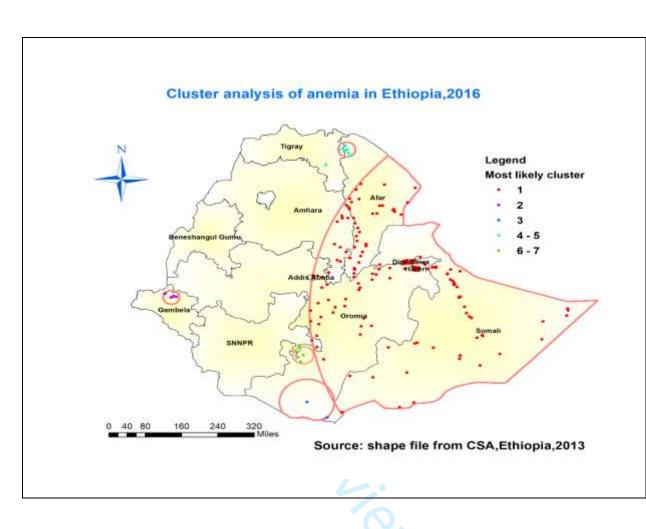


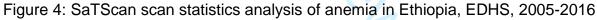
Figure 3: Ordinary Kriging interpolation of anemia in Ethiopia, EDHS 2005 to 2016





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# Spatio-temporal distribution and associated factors of anaemia among children aged 6–59 months in Ethiopia: Based on the EDHS 2005- 2016: A spatial and multilevel analysis

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1 2	1	Spatio-temporal distribution and associated factors of anaemia among children aged 6-59
2 3 4 5	months in Ethiopia: Based on the EDHS 2005- 2016: A spatial and multilevel analysis	
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1 2	22	Abstract						
3 4 5	23	Objectives: Anaemia is a global public health problem with major health and socio-economic						
6 7 8 9 10 11 12 13 14	24	consequences. Though childhood anaemia is a major public health problem in Ethiopia, there						
	25	is limited evidence on the spatio-temporal variability of childhood anaemia overtime.						
	26	Therefore, this study aimed to assess the spatio-temporal distribution and associated factors						
	27	of childhood anaemia using the Ethiopian Demographic and health survey (EDHS) data from						
15 16 17	28	2005-2016.						
18 19 20	29	Design: Survey-based cross-sectional study design was employed for the EDHS.						
21 22	30	Setting: Data were collected in all nine regions and two city administrations of Ethiopia in						
23 24 25	31	2005, 2011 and 2016.						
26 27	32	Participants: The source population for this study was all 6-59 months of children in						
28 29 30	33	Ethiopia. A total of 21,302 children aged 6-59 months were included in this study.						
31 32 33	34	Outcome measure: The outcome variable was child anaemia status.						
34 35 36	35	Results: The prevalence of anaemia declined from 53.9% in 2005 to 44.6% in 2011, but it						
37 38	36	showed an increment in 2016 to 57.6%. The Spatial analysis revealed that the spatial						
39 40	37	distribution of anaemia varied across the country. In spatial scan statistics analysis, a total of						
41 42 43	38	22 clusters (RR= 1.54, P-value < 0.001) in 2005, 180 clusters (RR = 1.14, P-value < 0.001) in						
44 45	39	2011, and 219 clusters (RR = 1.44, P-value < 0. 0.001) in 2016 significant primary clusters						
46 47	40	were identified. Child age, women age, maternal anaemia status, wealth index, birth order,						
48 49 50	41	fever, stunting, wasting status, and region were significant predictors of childhood anaemia.						
51 52 53	42	Conclusions: In this study, childhood anaemia remains a public health problem. The spatial						
55 55	43	distribution of childhood anaemia was significantly varied across the country. Identifying the						
56 57 58	44	risk areas and determinants would help to design strategies in the area. Therefore, in regions 2						
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml						

1 2	45	with a high risk of childhood anaemia, individual and community level factors should be									
3 4	46	intensified by allocating additional resources and providing appropriate and tailored									
5 6 7	47	strategies.									
8 9 10	48	Keywords: Anemia, children, EDHS, Spatial analysis, Ethiopia									
11 12 13	49										
14	50	Strengths and limitations of this study									
15 16 17	51	• This study applied different methods of spatial pattern, trend and a multilevel									
18 19	52	regression models accounting for the nested nature of EDHS data									
20 21 22	53	• The study was based on three consecutive EDHS dataset's representing the whole									
22 23 24	54	country of Ethiopia									
25 26	55	• The cross-sectional nature of the data prevents causality from being inferred between									
27 28	56	the independent and dependent variables									
29 30 31	57	• Respondents' without coordinate (longitude and latitude) were excluded from the									
32 33	58	spatial analysis, which could affect the generalizability of the findings									
34 35 36	59										
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# 67 Background

Anaemia is a condition characterized by a low level of haemoglobin in the blood(1). Over 273 million under-five children suffer from anaemia worldwide(2). Sub-Saharan Africa is one of the most affected regions, accounting for about 53.8%(2). World health organization had developed a classification system to facilitate international comparisons of anaemia as public health crises. The problem was considered severe if anaemia prevalence is  $\geq$ 40%, moderate from 20% to 39.9%, and mild from 5% to 19.9%(3). The high prevalence of anaemia and its consequences on children's health, especially on their growth and development, have made it important public health problem, It also increases the risk of mortality and morbidity that come from other diseases(4,5).

Anaemia is a public health problem that affects populations in both industrialized and nonindustrialized countries. It affects all segments of the population. It is frequently observed among children and pregnant women who are the most vulnerable group because their iron requirements are higher than any other group. Childhood anaemia is mainly caused by dietary Iron deficiency. Foliate, vitamin B12 and vitamin A deficiencies, chronic inflammation, parasitic infections, and inherited disorders can also contribute to childhood anaemia (6). For children age 6-59month Anaemia is defined as a haemoglobin level below 11.0 g/dl(6). Childhood anaemia is mostly coexisting with malaria, parasitic infection, nutritional deficiencies, and hemoglobinopathies(7).

The 2015 WHO report, from the global anaemia prevalence in 2011 showed that Africa, South East Asia, America, and European regions was,62.3%,53.8%,23.3%, and,22.9%, respectively(3). Pregnant women and children in low-income countries were at risk for anaemia because they were believed to be those with the most significant problems with inadequate nutrition, high infectious disease burden, and poor access to routine health 91 care(8). In sub-Saharan Africa, anaemia is a significant public health problem associated with 92 an increased risk of death and impaired cognitive development(9). In Ethiopia, the three 93 crude summaries of the country reported between 2005 and 2016 indicated the prevalence of 94 anaemia among Ethiopian children declined from 54% to 44% from 2005 to 2011 but 95 increased to 57% in 2016(10–12).

Various-studies showed that the prevalence of anaemia among 6-59-month children is high and a severe public health problem. Evidence from various studies indicated that women age, residence, family income, maternal education(13), an introduction of complementary foods, poor breastfeeding practice, poor utilization of folic acid by mothers(14), maternal anaemia(15), unemployment of the parent, malaria, and presence of sickle haemoglobin(13), household wealth index, sex of the child(16), and nutritional status were factors for childhood 27 102 anaemia. Few studies have been done on factors associated with anemia in Ethiopia, to date; the risk areas (hot spot) of anaemia among children are not identified. Thus, this study aimed to explore the spatiotemporal patterns of anaemia among children in Ethiopia over the last one and half-decades to point out whether there was either the shift or improvement in 34 105 anaemia risk areas following intervention programs in between the survey periods in Ethiopia. Geographical differences in the causes of anemia can be partially explained by large-scale variability in environmental drivers, particularly nutritional and infectious 41 108 43 109 causes(17). The risk of malaria is known to be associated with elevation and land surface temperature(18). Environmental drivers of anemia tend to show a high degree of spatial 48 111 dependence. Therefore, detecting the geographic variation of anemia during childhood is important to prioritize and design targeted intervention programs to reduce anemia especially 50 112 in those areas with a consistently higher risk of anemia over time. Therefore, this study attempts to fill the gap by investigating the spatio-temporal distribution of anaemia and its 

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#### Methods and materials

#### Study design, setting and period

The survey-based cross-sectional study design was employed using the Ethiopian 13 120 Demography and Health Surveys (EDHS) in 2005, 2011, and 2016. Data access, extraction, and analysis were conducted from January to June 2020. The study was conducted in Ethiopia located at the horn of Africa (3°-14°N and 33° – 48°E). Administratively, the country 18 122 is divided into nine regional states and two city administrations. Each region is sub-divided 20 123 into zones, districts, towns, and kebeles (the smallest administrative units).

#### Source and study population

All 6–59 months children in Ethiopia were the source population for this study whereas all children aged from 6-59 months in the selected enumeration areas within five years before the survey were the study population. 33 128

#### Sample size and sampling technique 36 129

A total of 21,302 children (3,868 in 2005, 8,958 - in 2011, and 8476 in 2016) were included in this study. children's Record (KR) EDHS dataset was used for analysis. The survey covered all nine regions and the two city administrations of Ethiopia. Participants were selected based on a stratified two-stage cluster sampling technique in each survey year. After excluding clusters with zero coordinates and missing information, a total of 503 clusters in 2005, 569 clusters in 2011, and 615 clusters in 2016 were used for analysis. The detailed sampling procedure was available in each EDHS report(10–12) 52 136 

#### Data collection tools and procedures

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The three EDHS datasets were downloaded from the measure DHS program (Demographic and Health Survey) website (www.measuredhsprogram.com) after obtaining the necessary permissions for the download and further analyses. Similarly, location data (latitude and longitudinal) were extracted from the downloaded excel file. After extraction, the missing values for the significant independent variables were excluded and the analysis was undertaken using a complete set of data. In all survey years for all children age 6-59 month from whom consent was obtained from their parents. Blood samples were drawn from the 15 144 drop of blood taken from a finger prick or a heel prick in the case of 6-11 month, and collected in a microcuvette. Haemoglobin analysis was carried out on-site using a battery-operated portable HemoCue analyzer. 22 147

Key variables and Measurements 25 148

**Dependent variable:** The study variables were grouped into dependent and independent variables. The dependent variable is child anaemia status, categorized as "anaemic/not-anaemic" variable. Children whose haemoglobin level was less than 11g/dl were considered 32 151 34 152 anaemic and not anaemic otherwise.

#### Independent variables:

sociodemographic (religion, mother age, marital status, educational status, husband 39 154 education, wealth index, mothers working status, numbers of under five children) Maternal and Child- related (child sex, age, birth size, birth order, maternal BMI, maternal anaemia, breastfeeding, fever, diarrhoea, vitamin supplement, stunting and wasting). Community-level 46 157 48 158 (residence, region, community women education and community women poverty). 

We created community education and community poverty variables by aggregating the individual characteristics within their clusters. The aggregates were computed using the 55 161 median values of the proportions of women in each category of a given variable. We

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Community women's education: was defined as the proportion of women who attended primary, secondary and higher education within the cluster. The aggregate of individual primary, secondary and higher educational attainment can show the overall educational and 11 166 academic status of women within the cluster. They were categorized into two categories a higher proportion of women's education within the cluster and a lower proportion of women education based on the national median value. 18 169

20 170 **Community poverty status:** defined as the proportion of poor and poorest mothers within the cluster. For each cluster, the proportion of poor and poorest as-was aggregated and show overall poverty status within the cluster. It was categorized into two categories based 27 173 on national median value as higher proportion of poor/poorest mother's and lower proportion of mothers within a cluster. 

### <sup>31</sup> 32 175 Data management and analysis

The data were cleaned using STATA 14.1 software and Microsoft excel. The data were weighted using sampling weight, primary sampling unit, and strata before any statistical analysis to restore the representativeness of the survey to take into account the sampling design when calculating standard errors to get reliable statistical estimates.

### 44 180 **Spatial analysis**

For the spatial analysis, ArcGIS V.10.7 software was used to evaluate whether the pattern was clustered, dispersed or random across the study area, and SaTScan V.9.6 software was used for the local cluster detection analysis. It uses a circular window that moves 53 184 systematically throughout the study area to identify a significant SaTScan clustering of childhood anaemia. 

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Spatial autocorrelation analysis

The spatial autocorrelation (Global Moran's I) statistic measures whether childhood anaemia patterns were dispersed, clustered or randomly distributed in the study area. Moran's I output value ranges from (-1 to +1). Values close to -1 indicate disease dispersed, whereas Moran's I close to +1 indicate childhood anaemia clustered and distributed randomly if I value zero. Anselin Local Moran's I was used to indicate the local level cluster locations of anaemia positively correlated (high-high and low-low) clusters or negatively correlated (high-low and 15 192 low-high). 

#### Hot spot analysis (Getis-Ord Gi\* statistic)

Local Moran's I, Gettis-OrdGi\* statistics was computed to measure how spatial autocorrelation of anemia among under-five children varies across different locations in 27 197 Ethiopia. Hotspot analysis computes Z-score and p-value to determine the statistical significance of the clustering of anaemia over the study area at different significance levels simultaneously. Statistical output with high GI\* indicates "hotspot" whereas low GI\* means a "cold spot". hot spot areas showed that there was a high proportion of anaemia and the cold 34 200 spot indicated a low proportion of anaemia. 

#### Spatial interpolation

There are various deterministic and geostatistical interpolation methods. Among all of the methods, ordinary Kriging and empirical Bayesian Kriging are considered the best methods since they incorporate spatial autocorrelation and statistically optimize the weight. Ordinary Kriging spatial interpolation method was used for this study for predictions of childhood anaemia in unobserved areas of Ethiopia since it had low mean square error and residual as 53 208 compared to the other interpolation techniques.

#### Spatial scan statistical analysis 56 209

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Spatial scan statistical analysis used to Identifying most likely clusters was done using the spatial Scan statistical method. This method is widely recommended as it is very important in detecting local clusters and has higher power than other available spatial statistical methods. Bernoulli based model was employed to test for statistically significant spatial clusters of anaemia using Kulldorff's Sat Scan version 9.6 software. Children with anaemia were taken as cases, and were not-anaemic as controls to fit the Bernoulli model. The default maximum spatial cluster size of <50% of the population was used. The scanning window with maximum 15 216 likelihood was the most likely cluster, and the p-value was assigned to each cluster using Monte Carlo hypothesis testing. The primary and secondary clusters were identified and assigned p-values and ranked based on their likelihood ratio test, based on 999 Monte Carlo 24 220 replications(19). 

#### Associated factors of anaemia

Four models were fitted using melogit, a STATA command, the null model without predictors, model I with only individual-level variables, model II with only community-level Model III both individual-level and community-level variables. Model variables, and 35 224 comparison was conducted by using deviance and likelihood ratio. 

Intra-class correlation (ICC), median odds ratio (MOR), and proportional change in variance (PCV) were computed to measure the variation between clusters. The intra-class correlation coefficient (ICC) quantifies the degree of heterogeneity of childhood anaemia between clusters (the proportion of the total observed individual variation in anaemia that is attributable between cluster variations) calculated as

 $ICC = \frac{62}{(62 + \pi^2/3)}$  (20) 

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but MOR is guantifies the variation or heterogeneity in outcomes between clusters and is defined as the median value of the odds ratio between the cluster at high risk of anaemia and cluster at lower risk when randomly picking out two clusters (EAs). 

 $MOR = e^{(0.95 * \text{ sqrt}(\text{Va})(21))}$ 

PCV measures the total variation attributed by individual-level factors and community-level factors in the multilevel model compared to the null model PCV. In the multivariable multilevel 15 238 logistic regression analysis variables with a p-value of <0.05 were considered as statistically significant. Adjusted Odds Ratio (AOR) with their corresponding 95% confidence interval was determined to identify factors associated with anaemia. After comparing all models, a model with low deviance was considered a better model. Multicollinearity was checked using the 22 241 Variance Inflation Factor (VIF). VIF less than 10% was taken as no multicollinearity.

Ethics and confidentiality 

Ethical clearance was obtained from the ethical review board of the University of Gondar Institute of Public Health, CMHS. Permission for data access was obtained from the measure demographic and health survey through an online request by a written letter of objective and 34 246 36 247 significance of the study from http://www.dhsprogram.com

- Patient and public involvement
- 42 249 This study did not involve patients and the public
- **Results** 45 250
- Descriptive characteristics of the study population

A total of 21,302 children with known haemoglobin levels (3,868 in 2005, 8,958 in 2011, and 8467 in 2016) were included in this study. The prevalence of anaemia for the three consecutive surveys was 53.9%, 44.6%, and 57.6% in 2005, 2011, and 2016 EDHS data 55 254

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1 2	255	respectively. The majority of the participants were in the age group of 36-47 (23%), 36-47
3 4	256	(24%), and, 12-23 (22%) in EDHS 2005, 2011, and 2016 survey respectively. The mean age
5 6	257	of children was 32.57 ±15.6-SD, 32.6±15.4-SD, and 31.7±15.6-SD in 2005, 2011, and 2016
7 8 9	258	respectively. Among children involved in the analysis, male participants were high proportion
9 10 11	259	in 2011 and 2016 EDHS compared to 2005 survey periods. The majority of children were
12 13		from rural residency in five years preceding the survey in three surveys. About 78.6%, 70%,
14 15 16	261	and 67% of women were unable to read and write in 2005, 2011, and 2016 survey
17 18	262	respectively. Children from poor and middle-class families were more anaemic than children
19 20		from rich families across the three EDHS survey (Table 1). During the study period, the
21 22		trends in the prevalence of childhood anaemia in Ethiopia, were fluctuates across regions
23 24 25	265	(Fig.1).

Table 1: Descriptive characteristics of study participants included in the analysis for 27 266 childhood anaemia in EDHS 2005,2011, and2016 in Ethiopia 

Characteristics	2005 (N, 3868)	2011(N, 8958)	2016(N, 8476)
	Frequency (%)	Frequency (%)	Frequency (%
Sex of child			
Male	1,931(49.93)	4,500(51.35)	4,395(51.85)
Female	1,937(50.07)	4,358(48.65)	4,081(48.15)
Children age (6-5	9) month		
6-11	418 (10.81)	1,029(11.48)	1,000(11.80)
12-23	842 (21.76)	1,804(20.14)	1,902(22.43)
24-35	825 (21.33)	1,895(21.16)	1,803(21.27)
36-47	919 (23.76)	2,184(24.37)	1,832(21.62)
48-59	864 (22.34)	2,047(22.85)	1,939(22.87)
Mean ± SD	32.57 ±15.6	32.6±15.4	31.7±15.6
Residence			
Urban	244 (6.31)	1,047(11.69)	857(10.12)
Rural	3,624 (93.69)	7,911(88.31)	7,619(89.88)
Religion			
Orthodox	1,624 (41.97)	3,416(38.13)	2,913(34.37)
Muslim	1,276 (32.99)	3,108(34.70)	3,432(40.48)
Protestant	836 (21.61)	2,151(24.01)	1,874(22.11)
Others	133 (3.43)	283(3.16)	258(3.05)

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15-2 30-3 40-4 Wo No Prin Sec Higl Mar Sing Mar Wid Dive	39 49 <b>men educatior</b> education nary condary her <b>rital status</b>	1,930(49.90) 1,474(38.10) 464(12.00) 3,042 (78.63) 684 (17.68) 136 (3.51) 7 (0.18) 7(0.17)	4,908(54.78) 3,223(35.98) 828(9.24) 6,285(70.16) 2,389(26.67) 168(1.88) 117(1.30)	4,356(51.40) 3,335(39.34) 785(9.26) 5,685(67.07) 2,275(26.84) 346(4.08) 170(2.01)
30-3 40-4 Wo No Prin Sec Higl Mar Sing Mar Wid	39 49 men education education nary condary her rital status gle rried	1,474(38.10) 464(12.00) 3,042 (78.63) 684 (17.68) 136 (3.51) 7 (0.18)	3,223(35.98) 828(9.24) 6,285(70.16) 2,389(26.67) 168(1.88)	3,335(39.34) 785(9.26) 5,685(67.07) 2,275(26.84) 346(4.08)
40-4 Wo Prin Sec Higl Mar Sing Mar Wid	49 men education education mary condary her rital status gle rried	464(12.00) 3,042 (78.63) 684 (17.68) 136 (3.51) 7 (0.18)	828(9.24) 6,285(70.16) 2,389(26.67) 168(1.88)	785(9.26) 5,685(67.07) 2,275(26.84) 346(4.08)
Wo No Prin Sec Higl Mar Sing Mar Wid	men education education nary condary her rital status gle rried	3,042 (78.63) 684 (17.68) 136 (3.51) 7 (0.18)	6,285(70.16) 2,389(26.67) 168(1.88)	5,685(67.07) 2,275(26.84) 346(4.08)
No Prin Sec <u>Higl</u> Mar Sing Mar Wid	education nary condary her <b>rital status</b> gle rried	3,042 (78.63) 684 (17.68) 136 (3.51) 7 (0.18)	2,389(26.67) 168(1.88)	2,275(26.84) 346(4.08)
Prin Sec <u>Hig</u> l <b>Mar</b> Sing Mar Wid	nary condary <u>her</u> <b>rital status</b> gle rried	684 (17.68) 136 (3.51) 7 (0.18)	2,389(26.67) 168(1.88)	2,275(26.84) 346(4.08)
Sec <u>Hig</u> Mar Sine Mar Wid Dive	condary her rital status gle rried	136 (3.51) 7 (0.18)	168(1.88)	346(4.08)
Higl Mar Sing Mar Wid Dive	her <b>rital status</b> gle rried	7 (0.18)		
<b>Mar</b> Sing Mar Wid Dive	<b>rital status</b> gle rried	0,	117(1.30)	170(2.01)
Sinę Mar Wid <u>Dive</u>	gle rried	7(0.17)		
Mar Wid Dive	rried	7(0.17)		
Wid Dive			50(0.56)	45(0.53)
Dive	lowed	3,704(95.74)	8,425(94.04)	8,129(95.9)
	lowed	80(2.06)	178(1.99)	93(1.10)
Hus	orced	78(2.03)	306 (3.41)	210(2.48)
	sband educatio	on		
No-	education	2,235 (58)	4,532(50.87)	4, 33(51.10)
Prin	mary	1,233(32)	3,710(41.65)	3,273(38.62)
Sec	condary	362(9)	412(4.63)	572(6.75)
Hig	her education	31(0.81)	255 (2.86)	300(3.53)
Wea	alth index			
Poc	or	1,697(43.86)	4,048(45.19)	3,977(46.92)
Mid	dle	854(22.07)	1,873(20.91)	1,821(21.48)
Rick	h	1,318(34.07)	3,038 (33.91)	2,678(31.60)
Wo	men working s	status		
Not	working	2,841(73.45)	5,793(64.67)	6,140(72.44)
Wo	rking	1,027(26.55)	3,165(35.33)	2,336(27.56)
Tota	al	3,868(100)	8,958(100)	8,476(100)

59

C	-							
F	Findings from this study revealed a regional variation of childhood anaemia, with 83% in							
Somali, 75%, in Afar, 72% in Dire Dawa, and 67% in Harari. However, Amhara, and								
E	Benishangul with 43%, which wa	as relatively low comp	ared to other region	ons.				
C	Childhood anaemia varies by urban-rural of residence. Children residing in communities with							
lo	low poverty level had a lower percent of anaemia (51.2%) than high community poverty level							
(	62.5%%). Children from low co	mmunity women educ	ation level (59.5%	6) were more anaemi				
tl	han children resided with high c	community women (53	8%) educational le	vel (Table 2).				
	Table 2: Community Level Facto Ethiopia. (N, 8476)	ors of under five childr	en participated on	EDHS (2016),				
E	Background characteristics	Child anaemia	status					
C	Community level factors	Not-anaemic (%)	Anaemic (%)	Total (%)				
F	Residence							
	<b>Residence</b> Jrban	435(50.6)	424(49.4)	857(100)				
ι		435(50.6) 3164(41.5)	424(49.4) 4455(58.5)	857(100) 7619(100)				
L F	Jrban	· · · ·	· · · ·	( )				
ן ד <b>ד</b>	Jrban Rural	· · · ·	· · · ·	· · ·				
L F F	Jrban Rural <b>Region</b>	3164(41.5)	4455(58.5)	7619(100)				
L F F C	Jrban Rural <b>Region</b> Amhara	3164(41.5) 950(57.5)	4455(58.5) 703(42.5) 2446(65.8)	7619(100) 1653(100)				
	Jrban Rural <b>Region</b> Amhara Dromia SNNP	3164(41.5) 950(57.5) 1273(34.2) 875(49.1)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9)	7619(100) 1653(100) 3719(100) 1781(100)				
	Jrban Rural <b>Region</b> Amhara Dromia SNNP Somali	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3)	7619(100) 1653(100) 3719(100) 1781(100) 348(100)				
	Jrban Rural <b>Region</b> Amhara Dromia SNNP	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100)				
	Jrban Rural <b>Region</b> Amhara Dromia SNNP Somali Tigray	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100)				
	Jrban Rural <b>Region</b> Amhara Dromia SNNP Somali Tigray Addis Ababa	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9) 21(25.3)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1) 62(74.7)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100) 83(100)				
	Jrban Rural Region Amhara Dromia SNNP Somali Figray Addis Ababa	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9) 21(25.3) 51(56.6)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1) 62(74.7) 39(43.4)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100)				
	Jrban Rural <b>Region</b> Amhara Dromia SNNP Somali Figray Addis Ababa Afar Benishangul	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9) 21(25.3)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1) 62(74.7) 39(43.4) 11(57.9)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100) 83(100) 90(100) 19(100)				
	Jrban Rural Region Amhara Dromia SNNP Somali Tigray Addis Ababa Afar Benishangul Gambelia Harari	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9) 21(25.3) 51(56.6) 8(42.1) 5(31.2)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1) 62(74.7) 39(43.4) 11(57.9) 11(68.8)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100) 83(100) 90(100) 19(100) 16(100)				
	Jrban Rural Region Amhara Dromia SNNP Somali Tigray Addis Ababa Afar Benishangul Gambelia Harari Dire Dawa	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9) 21(25.3) 51(56.6) 8(42.1) 5(31.2) 9(28.1)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1) 62(74.7) 39(43.4) 11(57.9)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100) 83(100) 90(100) 19(100)				
	Jrban Rural Region Amhara Dromia SNNP Somali Figray Addis Ababa Afar Benishangul Gambelia Harari Dire Dawa Community women education	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9) 21(25.3) 51(56.6) 8(42.1) 5(31.2) 9(28.1)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1) 62(74.7) 39(43.4) 11(57.9) 11(68.8) 23(71.9)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100) 83(100) 90(100) 19(100) 16(100) 32(100)				
	Jrban Rural Region Amhara Dromia Dromia SNNP Somali Tigray Addis Ababa Afar Benishangul Gambelia Harari Dire Dawa Community women education	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9) 21(25.3) 51(56.6) 8(42.1) 5(31.2) 9(28.1) 2281(40.5)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1) 62(74.7) 39(43.4) 11(57.9) 11(68.8) 23(71.9) 3358(59.5)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100) 83(100) 90(100) 19(100) 16(100) 32(100) 5639(100)				
	Jrban Rural Region Amhara Dromia Dromia SNNP Somali Tigray Addis Ababa Afar Benishangul Gambelia Harari Dire Dawa Community women education Low High	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9) 21(25.3) 51(56.6) 8(42.1) 5(31.2) 9(28.1)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1) 62(74.7) 39(43.4) 11(57.9) 11(68.8) 23(71.9)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100) 83(100) 90(100) 19(100) 16(100) 32(100)				
	Jrban Rural Region Amhara Dromia Dromia SNNP Somali Tigray Addis Ababa Afar Benishangul Gambelia Harari Dire Dawa Community women education	3164(41.5) 950(57.5) 1273(34.2) 875(49.1) 58(16.7) 263(46) 82(50.9) 21(25.3) 51(56.6) 8(42.1) 5(31.2) 9(28.1) 2281(40.5)	4455(58.5) 703(42.5) 2446(65.8) 906(50.9) 290(83.3) 309(54) 79(49.1) 62(74.7) 39(43.4) 11(57.9) 11(68.8) 23(71.9) 3358(59.5)	7619(100) 1653(100) 3719(100) 1781(100) 348(100) 572(100) 161(100) 83(100) 90(100) 19(100) 16(100) 32(100) 5639(100)				

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1	351	Total 8476(100)
2 3 4	352	
5 6 7	353	Spatio-temporal distribution of anaemia among children age 6-59 months in Ethiopia
8 9 10	354	The spatial distribution of childhood anaemia in Ethiopia was non-random in all three
11 12	355	consecutive surveys The global Moran's I test value was 0.176 (P-value <0.001) in 2005,
	356	0.18 (P-value < 0.001) in 2011, and 0.09(P-value < 0.005) in 2016 Ethiopian Demographic
15 16 17	357	and health surveys.
18 19 20	358	Hot spot analysis of the three surveys
21 22	359	The spatial distribution of childhood anaemia in Ethiopia was different in the three survey
23 24	360	periods. In EDHS 2005, a high proportion of childhood anaemia was detected in Dire Dawa,
	361	Harari, Eastern Oromia, Benishangul in Metekel zone, Gambela, Southern and Eastern
27 28 29	362	Tigray, and Somali region mainly Liben, Afdar, and Fafna zone which was hotspot area
30 31		within 95% confidence level. On the counterpart, GamoGofa, Wolayita, Hadiya, Southern
	364	Omo, and Segen zone of SNNPR, Addis Ababa, central Oromia, Jima, North Shewa zone
34 35 36	365	were cold spot area. In EDHS 2011, a highly significant clustering of childhood anaemia was
37 38	366	detected in Somalia, Dire Dawa, Harari, Afar, Gambela, Benishangul, Eastern Oromia, Bale,
39 40	367	Arsi zone were the hotspot areas within 95% level of confidence. The low hotspot area of
	368	childhood anaemia was detected in central Tigray, East and West Gojam, North Gondar, a
43 44 45	369	central part of Oromia, Addis Ababa and SNNPR were areas identified as the low percentage
46 47 48	370	of childhood anaemia in the 2011 EDHS survey.
49 50	271	In EDHS-2016 sampled data, hot spot (high risk) regions for childhood anaemia were
	372	observed in Somali, Dire Dawa, Harari, Gambela, Eastern, and Southern part of Oromia.
53 54	373	However, Amhara, Benishangul, and Southern Nations Nationalities and Peoples (SNNP)

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were identified as cold spot (low risk) regions for childhood anaemia within a 95% confidence interval (Fig.2) 

#### **Spatial interpolation**

Based on EDHS-2005 sampled data, the geostatistical analysis predicts that the highest prevalence of childhood anaemia (65.75%-88.89%) was detected in East Oromia, Ilubabur, 11 378 Arsi, some parts of Benishangul, Agnuak zone in Gambela, North Shewa Amhara region, South and central Tigray Afar in zone2, some parts of Dire Dawa city and Somali. In EDHS-2011 Geostatistical analysis, a high percentage of anaemia was detected in Afar, most parts 18 381 20 382 of Somalia, Oromia in East Harerge and Borena, some part of Dire Dawa, and the Meketel zone in Benishangul. In 2016 EDHS most of Somali, some parts of Gambela, Guji and some parts of Borena, East Shewa, East Harerge and Arsi in Oromia and part of Dire Dawa were highly prevalent areas in childhood anaemia (Fig.3) 

#### Spatial scan statistics

In 2005 EDHS, a total of 3 significant clusters were identified, one most likely (primary) cluster and 2 were secondary clusters of spatial sat scan analysis. The primary cluster's spatial window was located in Somali, which was centered at (9.018373 N, 43.110635 E) of 37 389 geographic location with a 97.93 km radius, and Log-Likelihood ratio (LLR) of 20.03, at p < 0.001 which was detected as the most likely cluster with Maximum Likelihood. It showed that children within the spatial window had 1.54 times more likely a higher risk of anaemia than the children outside the spatial window areas. The secondary clusters scanning window was located in the southern part of Somali region, which was centered at (3.998656 N, 41.240691 E) with a 92.08 km radius and LLR of 1.73 at p-value 0.0010. It showed that children within 53 396 the spatial window had a 1.73 times higher risk of anaemia than children outside the window.

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In 2011 EDHS, 10 clusters were identified and five of them were significant clusters with a p-value <0.05. A total of 180 locations/spots with a total sampled population of 2478 were found as primary cluster areas were identified using sat scan analysis with a p-value < 0.001. The primary cluster spatial window was located mainly in Somali, Afar, Eastern Oromia, Dire Dawa, and Harari. The primary cluster spatial window was centered at (8.975207 N, 43.790264 E) / 540.29 km, with a relative risk (RR) of 1.43 and a log-likelihood ratio (LLR) of 127.79. It showed that children within the spatial window had 1.4 times more likely a higher risk of anaemia than the children outside the spatial window areas. The secondary cluster spatial window was located mainly in Afar regional state. The secondary cluster spatial window was centered at (12.758587 N, 40.175990 E) / 39.58 km, with a relative risk (RR) of 24 407 1.68 and a log-likelihood ratio (LLR) of 21.5 P-value=0.001. 

27 408 In 2016 EDHS, 7 clusters (1 most likely cluster) were located in Somali, Afar, Eastern Oromia, Dire Dawa, and Harari. The cluster window was centered with a radius at (7.650693 N. 47.007920 E) / 912.19 km with a Relative Risk (RR) of 1.44. The Log-Likelihood Ratio (LLR) for the most likely cluster was 182.86, p < 0.001. Secondary clusters were located in 34 411 Gambela which was centered at (8.195862 N. 34.289837 E) with a radius of 29.01 km, and LLR of 18.8 at p-value 0.001. It showed that children within the spatial window had a 1.5 41 414 times higher risk of anaemia than outside the window (Fig.4).

# 44 415 Multilevel Analysis

The intra-cluster correlation coefficient (ICC) in the empty model indicated that 18.8% of the 49 417 total variability for children anaemia was due to differences between clusters. The remaining unexplained 81.2% were attributable to individual differences. The median odds ratio for anaemia was 2.3 in the null model, indicating variation between clusters. If we randomly select children from two different clusters children at the cluster with a higher risk of anaemia 56 420 

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had 2.3 times higher odds of experiencing anaemia than children at the cluster with a lower risk of anaemia.

Bi-variable multilevel logistic regression analysis was done to identify variables for multivariable multilevel logistic analysis, and variable with a p-value less than 0.2 were considered for multivariable analysis. 11 425

#### 14 426 Individual-level predictors for anaemia

In multivariable multilevel mixed-effect logistic regression analysis, individual-level factors 17 427 19 428 such as the age of the child, wealth index, mother age, maternal anaemic status, birth order, fever, stunting, and wasting status were significant predictor of childhood anaemia.

Children age between 12-23 months (AOR = 0.66, 95%CI = 0.53-0.81), between 24-35 months (AOR= 0.35, 95% CI = 0.28-0.43), between 36-47 months (AOR = 0.23-95%CI = 29 432 0.19-0.29), and between 48–59 months (AOR = 0.15, 95%CI = 0.12-0.19) were less likely to develop anaemia when compared with children age between 6–11 months. 

The likelihood of developing anaemia for those children residing with the family wealth index of middle and rich was lower by 21% (AOR=0.79, 95%CI = 0.67-0.94), and 23% (AOR=0.77, 95%CI = 0.65-0.91), respectively as compared with children with low wealth index. Children 39 436 <sup>41</sup> 437 whose mother's age were between 40-49 had 25% decreased odds of developing childhood anaemia compared to age 15-29, (AOR=0.75, 95%CI = 0.59-0.95). 

The odds of experiencing anaemia for those birth orders 4-5, 6, and above six were 1.22 49 440 times (AOR=1.22, 95%CI = 1.01-1.47) and, 1.35 times (AOR=1.35, 95%CI = 1.08-1.67) 51 441 higher as compared with first-order respectively. The odds of developing anaemia of children born from anaemia history mother were 1.39 higher more elevated than those born from not anaemic history before. Children who had fever were 39% (AOR =1.39, 95% CI: 1.24-1.58) 

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1 2	444	more likely to deve	elop anaemia	than their counte	rparts. Children v	vith moderate and severe		
2 3 4	445	stunting status we	re 35% (AOF	R=1.35, 95% CI: <sup>2</sup>	1.17-1.54) and, 9	6% (AOR=1.95, 95% CI:		
5 6	446	1.68-2.28), more li	kely to develo	op anaemia respe	ctively as compa	red to no stunting status.		
7 8	447	Similarly, children	who had to s	sever wasting stat	us were 51% ma	ore (AOR =1.51, 95% CI:		
9 10 11	448	1.07-2.12) likely to	develop anae	emia compared wit	h those children v	who had no wasting.		
12	449	Community-level	predictors fo	or anaemia				
	450	The multivariable r	multilevel logi	istic regression ar	nalysis region wa	s significantly associated		
18 19	451	with community-lev	el factors for	childhood anaemi	a.			
	452	Odds of children liv	ve in Somali	were 5.65 times ( <i>i</i>	AOR=5.65, 95% (	CI: 3.92-8.16), Dire Dawa		
22 23 24	453	3.45 times (AOR=3.45, 95% CI: 2.27-5.26), Afar 3.01 times (AOR=3.01, 95% CI: 2.09-4.34),						
25 25 26	454	and Oromia 2.34 times (AOR=2.34, 95% CI: 1.73-3.18) had more likely to develop childhood						
	455	anaemia as compa	naemia as compared to Amhara regional state. Similarly, the odds of developing anaemia in					
	456	Addis Ababa were 2.10 times (AOR=2.10, 95% CI: 1.40-3.16), Gambella 1.94 times						
31 32 33	457	(AOR=1.94, 95% CI: 1.32-2.84), and Tigray 1.46 times (AOR=1.46, 95% CI: 1.08-1.98), more						
34 35		likely as compared	to Amhara re	gion. Benishangu	I and SNNPR had	d not significantly different		
	459	in the prevalence o	f anaemia tha	an the reference re	egion Amhara (Ta	ble 3).		
	460	Table 3: Multilevel	• •			al and community level		
41	401				52010			
42 43	462 463	Individual Level	Null Model	Model I AOR (95% CI)	Model II AOR (95% CI)	Model III AOR (95% CI)		
15		Children age (6-59) month						
46	464							
	465 466	6 – 11 12 – 23		1 0.66[0.54-0.82] **		0.66 [0.53-0.81] **		
	466 467	12 – 23 24 – 35		0.35[0.28-0.44] **		0.35 [0.28-0.43] **		
	467 468	24 – 35 36 – 47		0.23[0.18-0.28] **		0.23 [0.19-0.29] **		
51	468 469	48 – 59		0. 15[0.12-0.19] **		0.15 [0.12-0.19] **		
52				0. 10[0.12-0.18]		0.10[0.12-0.19]		
53	470	Religion Orthodox		1		1		
	471	Orthodox		1 2.07[1.77-2.47] **	e	1 21 [0 07 1 46]		
	472 473	Muslim Protestant				1.21 [0.97-1.46]		
57		Protestant		1.20 [1.002-1.48]		1.09[0.86-1.37]		
50						10		

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474 475	Others		1.55[1.07-2.32] *		1.44[0.96-2.13]	
475	Wealth index					_
76	Poor		1		1	
7	Middle		0.71[0.61-0.84] **		0.79 [0.67-0.94] *	
3	Rich		0.72[0.63-0.85] **		0.77 [0.65-0.91] *	
	Child size at birth					
	Small		1		1	
	Average		0.96[0.84-1.09]		0.93 [0.80-1.07]	
	Large		0.94[0.81-1.08]		0.96 0.84-1.10	
	Birth order					
	1st		1		1	
	2-3		1.09[0.94-1.28]		1.13[0.97-1.32]	
	4-5		1.17[0.97-1.40]		1.22 [1.01-1.47] *	
	6 and above	_	1.30[1.05-1.62]		1.35 [1.08-1.67] **	
	No of children und	der 5				
	1-2 children		1		1	
	≥ 3 children		1.22[1.1-1.4] *		1.09 [0.94-1.27]	
	Maternal anemia					
	Not-anemic				1	
	Anemic		1.51[1.34, 1.72] **		, 1.39 [1.24-1.58] **	
	Maternal BMI				1.00 [1.27 1.00]	
	≥18.5 kg/m2				1	
	<18.5 kg/m2		1.12[0.97-1.26]		1.05 [0.92-1.19]	
	Mother's working	etatue	1.12[0.07 1.20]			
	Not-working	ວເລເບວ			1	
	Working		0.88[0.77-0.99] *		0.92 [0.81-1.04]	
			0.00[0.77-0.00]		0.02 [0.01-1.04]	
	<b>Women age</b> 15-29		1		1	
	30-39		0.91[0.71-1.06]		0.90 [0.78-1.04]	
	40-49		0.75[0.59-1.12] *	5	0.75 [0.59-0.95] *	
			0.10[0.08-1.12]		0.70 [0.09-0.80]	
	Breastfeeding		1		1	
	No Yes		ا [0.92[0.81-1.04]		0.98 [0.87-1.12]	
		 manik	0.92[0.01-1.04]		0.30 [0.07-1.12]	
	Vitamins in last 6	ΠΟΠΤΠ	4		1	
	No					
	Yes -	 	0.90[0.81-1.09]		0.93 [0.84-1.05]	
	Diarrhea last 2 we	ек	A		A	
	No					
	Yes -		0.88[0.73, 1.04]		0.90 [0.76-1.07]	
	Fever in last 2 wee	eks			<i>.</i>	
	No		1		1	
	Yes		1.35[1.15-1.59] **		1.32 [1.13-1.56] *	
	Stunting status					
	No-stunting		1			
	Moderate stunting		1.27[1.10-1.46] **		1.35 [1.17-1.54] **	
	Severely stunting		1.81[1.55-2.11] **		1.96 [1.68-2.28] **	
	Wasting status					_
						20
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1 521	No-wasting				
<sup>2</sup> 522 <sup>3</sup> 522	Moderate wasting		1.27[1.11-1		0.98 [0.80-1.19]
4 523	Severe wasting Place of residence		1.68[1.55-2	.10]	1.51 [1.07-2.12] *
5 524 6 525	Urban			1	1
<sup>7</sup> 526	Rural			, 1.40[1.12-1.78]	1.28 [0.99-1.64]
8					1.20 [0.00 1.04]
9 527 10 528	<b>Region</b> Amhara			1	1
<sup>10</sup> 520	Tigray			1.46 [1.09-1.97] **	1.46 [1.08-1.98] **
<sup>12</sup> 520	Afar			3.90 [2.84-5.35] **	3.01 [2.09-4.34] **
13 <sup>550</sup> 14 531	Oromia			2.48 [1.89-3.25] **	2.34 [1.73-3.18] **
<sup>15</sup> 532	Somali			6.34[4.65-8.63]	5.65 [3.92-8.16] **
16 533	Benishangul			0.86 [0.62-1.17]	0.81 [0.58-1.15]
17 <sup>533</sup> 18 534	SNNPR			1.33 [1.00-1.76]	1.30 [0.94-1.80]
19 535	Gambela			1.93 [1.38-2.69] **	1.94 [1.32-2.84] **
20 526	Hareri			3.08 [2.15-4.43] **	2.98 [1.99-4.46] **
21 530 22 537	Addis Ababa			1.91[1.29-2.83] **	2.10 [1.40-3.16] **
22 537 23 538	Dire Dawa			3.92 [2.67-5.77] **	3.45 [2.27-5.26] **
<sup>24</sup> 520	Community education			5.92 [2.07-5.77]	5.45 [2.27-5.20]
25 539 26 540	Low education	lion		1	1
26 540 27 541	High education			1.07[0.90-1.26]	1.13[0.94-1.34]
28 542	Community pove	rty			
<sup>29</sup> 543	Low poverty	5		1	1
<sup>30</sup> 544 31	High poverty			1.41[1.17-1.68] *	1.15[0.94-1.40]
<sub>32</sub> 545	Model compariso	on and		10	
33 546 <sup>34</sup> 547	Random effect	0.187			
<sup>35</sup> 548	Log-likelihood	-4981.63	 -4513.17	-4836.83	-4436.60
<sup>36</sup> 549	Deviance	9963.26	9026.34	9673.66	8873.2
37 545 38 550	PVC (%)	Ref	41.22	60.11	62.59
39 551	MORÙ	2.30	1.72	1.42	1.38
40 552 41 553 42 554 43	*Key: 1: reference	e group; p-v	alue 0.05-0/	.01 *: p-value < 0.01 **	1
$44 \\ 45$ 555	Multicollinearity				
46 47 556 48	Multicollinearity w	as checked	for those	variables included in	the final model using VIF.
49 557 50	Accordingly, the	√IF for all p	redictor var	iables included in the	final model was below 10
<sup>51</sup> 558 52	indicating the abse	ence of multi	collinearity a	among the predictor var	iables.
53 54 559	Comparison of m	odels			
55 56					
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58 50					21
59 60	F	or peer review o	nly - http://bmj	open.bmj.com/site/about/gu	idelines.xhtml

Deviance was used to compare the models, and the lowest value of deviance (Model III) was considered the better mode. 

#### Discussion

This study tried to identify spatio-temporal distribution and predictors of childhood anaemia across the regions in Ethiopia. 2005, 2011, and, 2016 Ethiopian Demographic and Health Survey data were used. In this study, anaemia's trend was decreased from 2005 to 2011, while the rate significantly increased from 2011 to 2016. The study revealed that 57.56% [CL: 0.56-0.59] of children were anaemic in 2016, preceding the survey. This finding was in line 20 568 with a study done in Gondar, Northwest Ethiopia 58.6% (22), whereas higher than the study 22 569 done in cape Verde, west Africa 51.8%(23), and southern Ethiopia(24). Among children of 6-59 months, anaemia is still considered a significant public health problem in Ethiopia. Though the levels of anaemia among children vary by background factors like region and lowest household wealth index and maternal related factors, more of the children in Ethiopia were 29 572 suffering anaemia. 

The spatial pattern shows the geographical inequality of anaemia by using sat scan and GIS spatial techniques like cluster mapping tools and interpolation techniques. The spatial analysis indicates that the distribution of childhood anaemia was non-random across the 39 576 country with a global Moran's I index of 0.176 in 2005, 0.18 in 2011, and 0.09 in 2016 with a significant p-value, which indicates substantial-considerable clustering areas. This study's 46 579 findings were in line with a study done in Nigeria, Malawi, Tanzania, and Uganda (25,26).

The spatial pattern of sat scan analysis showed that Eastern Somali regions were primary 49 580 51 581 (most likely) cluster and secondary cluster also located in the southern part of Somali in 2005 sat scan analysis. In 2011 Somali, Afar, Eastern Oromia, Dire Dawa, and Harari were located in the primary window and centered at (8.975207 N, 43.790264 E/ 540.29 km with a 

significant p-value. Similarly, spatial sat scan analysis showed that Somali, Afar, Eastern Oromia, Dire Dawa, Harari were hotspot areas in the 2016 EDHS spatial analysis. In addition, this study revealed that eastern parts of the country had similar spatiotemporal trend over the study periods. It might be, which are less developed compared with other Ethiopian states in terms of economy, gender, healthcare facility and food availability(27). 

This study indicated that children age 12-59 months were less affected by childhood anaemia. This finding was consistent with studies conducted in Ethiopia and Togo (28-30). This could be explained by the fact that children who are getting older receive a richer and 18 591 20 592 complete diet, with a sufficient intake of iron which could prevent the occurrence of iron deficiency anaemia. The deficiency may result from inadequate dietary intake of iron, malabsorption of iron an increased iron demand during rapid growth might it be the possible 27 595 reason (31).

The finding of this study indicated that children whose mother's age was between 40-49 were 30 596 less anaemic as compared to age 15-29. This finding is a study done in line with other studies conducted in sub-Saharan Africa and Ghana (15,32). This group consists of more at-risk population segments (Adolescent) for anaemia. They are vulnerable to malnutrition because they are growing faster than at any time after their first year of life which contributes to the intergenerational cycle of malnutrition and he most common forms of malnutrition among Ethiopian adolescent girls is iron deficiency anaemia. Aside from, growing adolescent mother and her baby's bodies may compete for nutrients, raising the infant's risk of low birth weight; however, the lack of such nutrients might lead to anaemia. 

Children from households of middle and rich wealth indexes were less affected by childhood anaemia as compared to children from a poor household. This finding has also been demonstrated in similar studies in Nigeria and northern Ethiopia (25.33). This is due to the 56 607

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reason that children from poor households are less likely to get iron-rich foods like animal foods and vitamin-rich foods especially vitamins A and C which are very important for iron absorption. 

Maternal anaemia was highly associated with the occurrence of childhood anaemia. This finding was in line with a study done in South Africa, Haiti, and India(34–36). Reasons may 11 612 be mothers and children share a common home environment, socioeconomic, and dietary conditions, and maternal and child anaemia may reflect the household's common nutritional status, and poor maternal iron intake during pregnancy, reduce breast milk might be the 18 615 20 616 possible reason. 

23 617 EDHS data set indicated that the incidence of fever had an impact on childhood anaemia. This is in line with studies done in Ghana and South Ethiopia Wolaita (24,37) Results showed that children who had a fever in the last two weeks before the survey had had a higher likelihood of anaemia than children who had not to fever. This could be attributed to the 30 620 infectious cause of childhood fever mainly malaria, tuberculosis, and Leishmaniasis which cause anaemia by destructing red blood cells or other related mechanisms. 

The nutritional status of children had a significant association with childhood anaemia. The stunting status of children was an independent predictor in the multilevel mixed effect model 40 624 42 625 of this study. The result of this study indicated that it was in line with previous studies conducted in South Africa(36), Bangladesh(38,39), and Ethiopia(40,41). This study revealed that there was a greater prevalence of anaemia among stunted children compared to non-49 628 stunted children. Children suffering from nutritional deficiency were more likely to have weak immune systems, making them vulnerable to various illnesses and healthiness such as parasitic infections or chronic inflammation. Many of these conditions reduce the haemoglobin level in the blood leading to increased anaemia prevalence. The statement is 56 631 

supported by the evidence given in other studies(42)that nutritional deficiency causes several health hazards. 

Besides, severely wasting children were more likely to be anaemic than their counterpart. Since stunting and wasting are long-term and short-term indicators of malnutrition, the results implied that under-nourished children experience a higher risk of developing anaemia than nourished children. Odds of experiencing anaemia for those birth order four up to five and six and greater than six were higher than those of the first order. This finding was similar to a study done in Indian(15,43). This could be due to the distribution of scarce resources within 18 639 20 640 the family and related to the maternal exhaustion of micronutrient feeding practices.

In a multivariable multilevel analysis, the odds of developing childhood anaemia were higher among children who lived in Somali, Dire Dawa, Afar, and Gambela compared to the Amhara region. This might be due to the unavailability and inaccessibility of health facilities as compared to the regions. Regional variation in the nutrient intake can cause significant health 30 644 disparity, and this variability may be mediated by factors such as food availability, food customs, and culture. 

This study, used different spatial pattern, trends, and a multilevel regression model because 40 648 of nested or cluster samples to show the effect of individual predictors and community-level 42 649 variables on the dependent variable. The study was based on a large dataset representing the whole country of Ethiopia and which was weighted to make it nationally representative and adjusted for the design to get a reliable estimate. However, there were some limitations to this study. The cross-sectional nature of the data prevents causality from being inferred between the independent and dependent variables. Also, respondents' data that didn't have files (longitude and latitude) were excluded from the spatial analysis which could affect the overall result and the generalizability of the findings. 56 655 

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This study indicated that the prevalence of childhood anaemia decreased between the 2005-2011 survey while the prevalence increased from 2011-2016 EDHS. The spatial pattern of child anaemia in Ethiopia was non-random among the three consecutive surveys with the global Moran's I value of 0.176, 0.18, and 0.09 in EDHS 2005, 2011, and 2016. In this study, Sat Scan analysis identified the primary and secondary clusters for the three survey periods. In 2005 EDHS, the hotspot area was identified in eastern and southern parts of Somalia, in 2011, Somali, Afar, Eastern Oromia, Dire Dawa, and Harari were among the hotspot regions. 20 664 Spatial sat scan analysis revealed that spatial clustering of childhood anaemia was identified 22 665 in Somali, Afar, Eastern Oromia, Dire Dawa, Harari hotspot area in the 2016 EDHS period.

25 666 Child age, women age, wealth index, maternal anaemia, fever, birth order, stunting, wasting and region were significant predictors among 6-59 months. Therefore, these results provide further insight into identifying the true picture of childhood anaemia spatio-temporal clusters and enable timely spatial targeting factors to alleviate childhood anaemia. Therefore, 32 669 policymakers and health planners should design effective intervention strategies for the identified hot spot areas and individual and community-level factors. 

#### Abbreviations 39 672

AOR-Adjusted Odds Ratio, CSA-Central Statics Agency, CI-Confidence Interval, COR-Crude 42 673 Odds Ratio, EDHS-Ethiopia Demographic and Health Survey, GPS-Global Positioning System, ICC-Intra Class Correlation Coefficient, LLR-Log-Likelihood Ratio, MOR-Median 49 676 odds ratio, OR-Odds Ratio, RR-Relative Risk, PVC-Proportional Change in Variance, 51 677 SNNPR- Southern Nations, Nationalities, and Peoples' Region. 

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# 12 683

**Declarations** 

Onset to participate

The institutional ethical review committee board approved the study. Ethical clearance was obtained from ethical review board of the University of Gondar. Upon this clearance, the study was conducted. The congeniality of the data was maintained by using the extracted data only for the study purpose and keeping the data from a third party.

# **Consent for publication**

686 Not-applicable

# 687 Data sharing statement

 $\frac{1}{5}$  688 The data in which the authors used to produce this manuscript are available upon reasonable  $\frac{1}{5}$  689 request

# <sup>8</sup> 690 **Competing interests**

<sup>30</sup> 691 The authors declare that they have no competing interests.

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# 36 694 Contributors

Proposal preparation, acquisition of data, analysis, and interpretation of data was done by
 696 SH, AM, ZM and BF guided the study design data collection and analysis. SH drafted the
 697 manuscript and all authors have a substantial contribution in revising and finalizing the
 698 manuscript. All authors read and approved the final manuscript.

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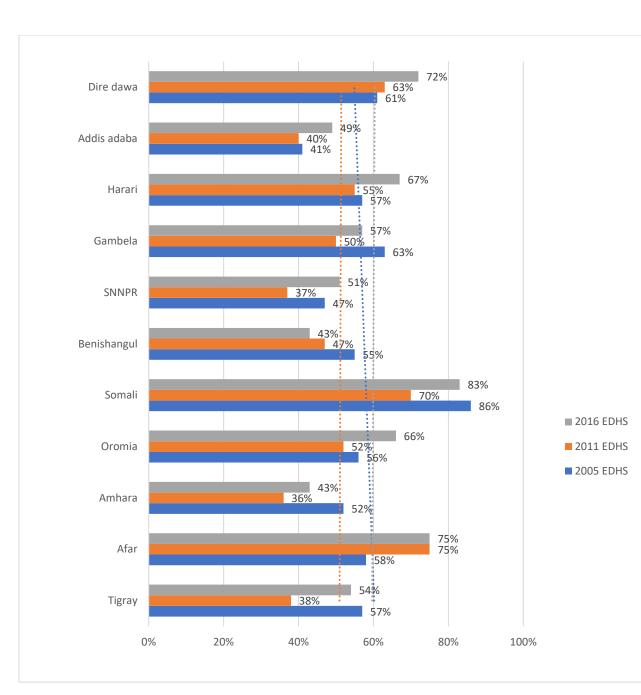
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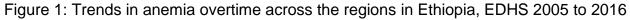
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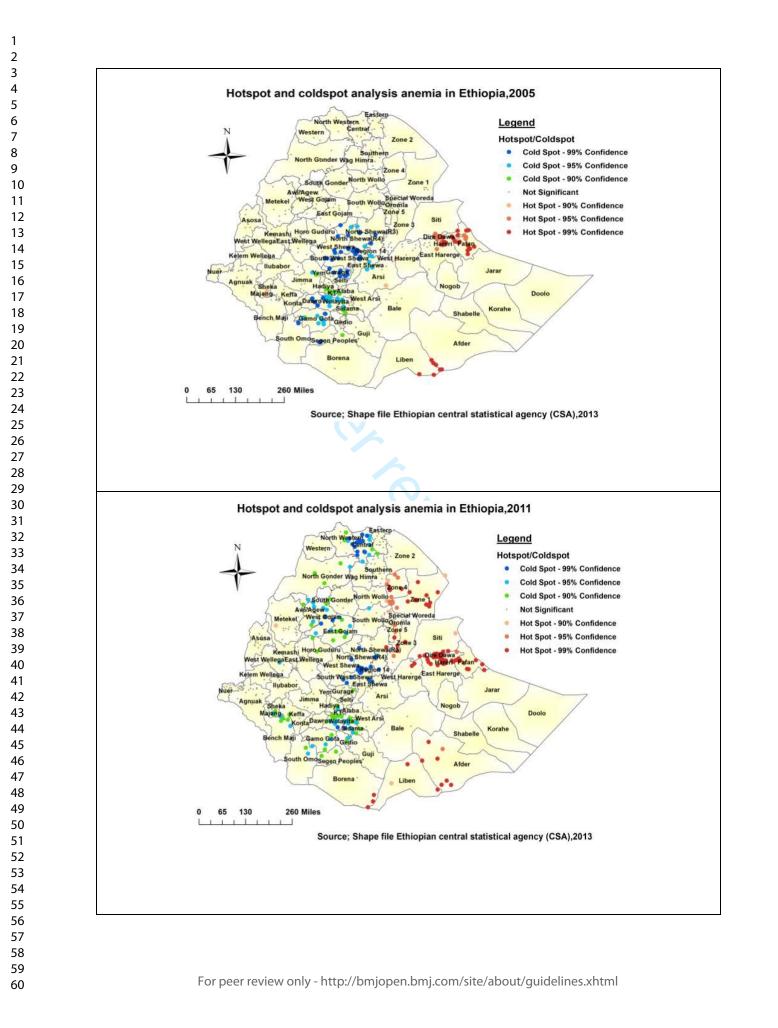
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Figure	e 1: Trends in anemia overtime across the regions in Ethiopia, EDHS 2005 to 2016	v on A
Figure	e 2: Hot spot and cold spot analysis of anemia in Ethiopian, EDHS 2005 to 20016	April 1
Figure	e 3: Ordinary Kriging interpolation of anemia in Ethiopia, EDHS 2005 to 2016	7, 20
Figure	e 4: SaTScan scan statistics analysis of anemia in Ethiopia, EDHS, 2005-2016	24 by g
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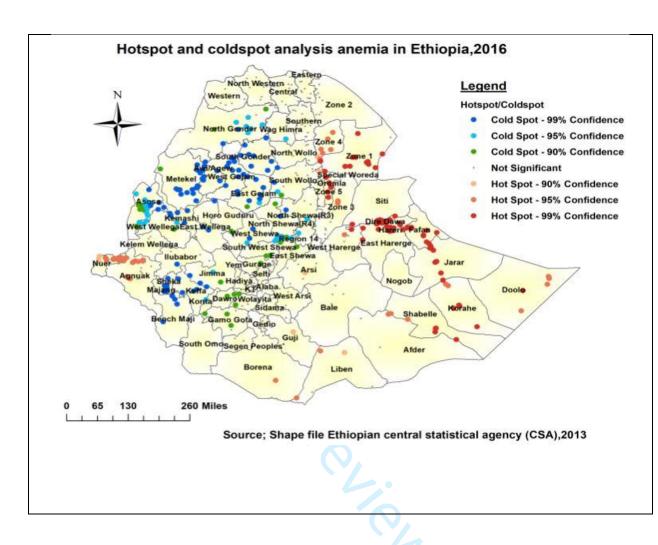
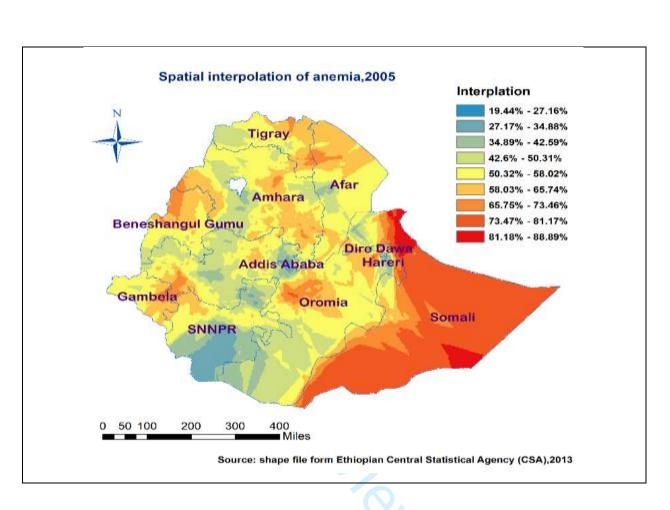
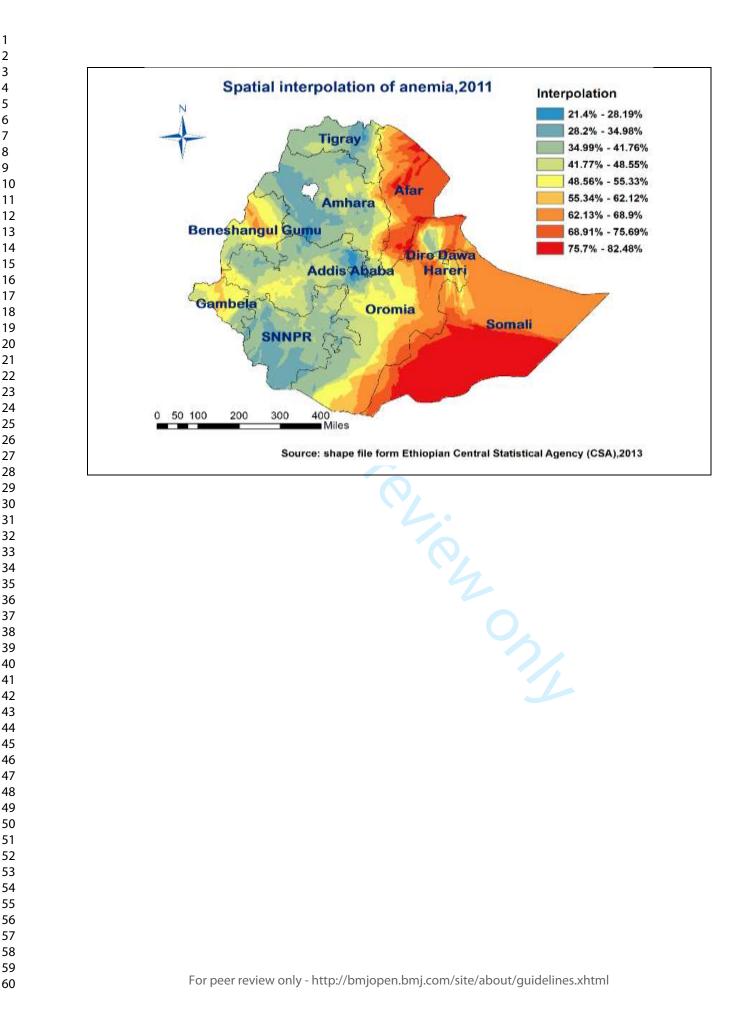


Figure 2: Hot spot and cold spot analysis of anemia in Ethiopian, EDHS 2005 to 20016





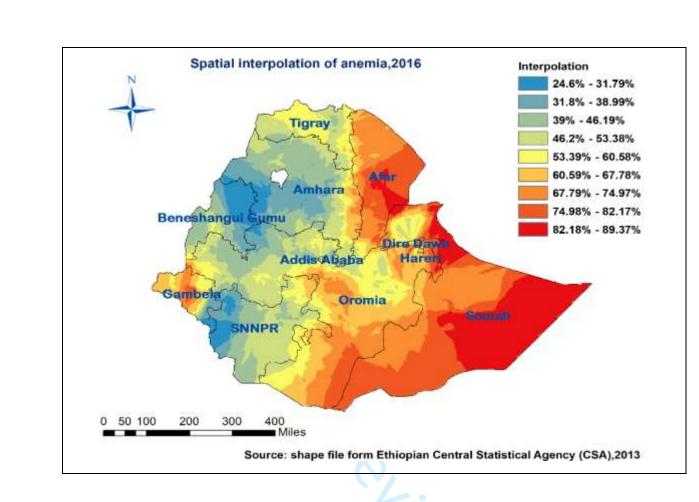
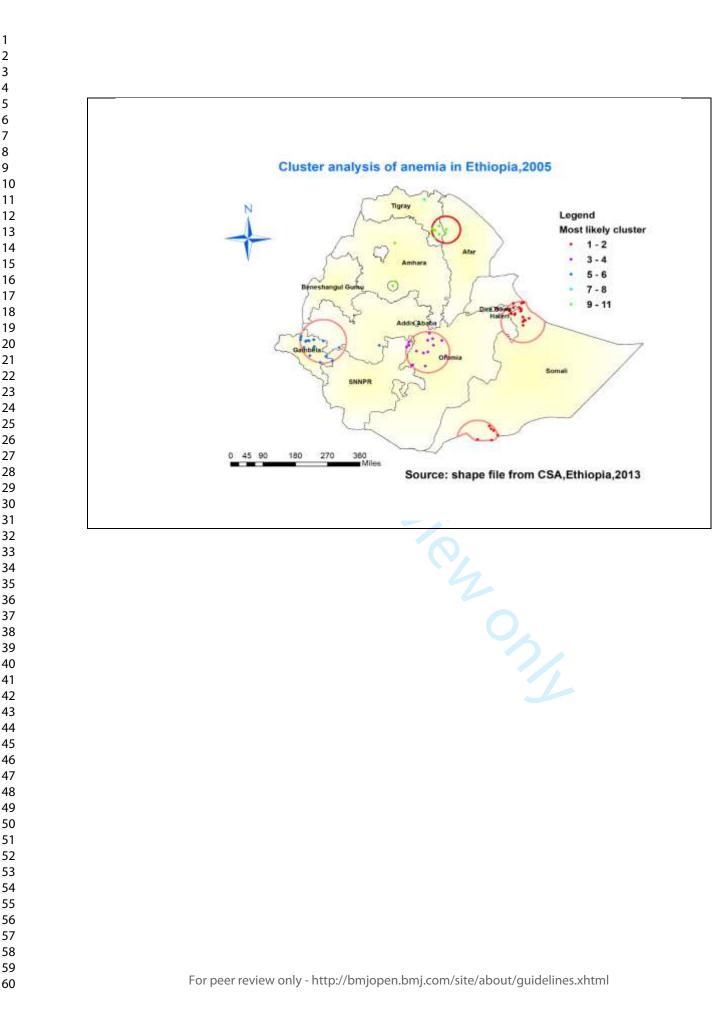
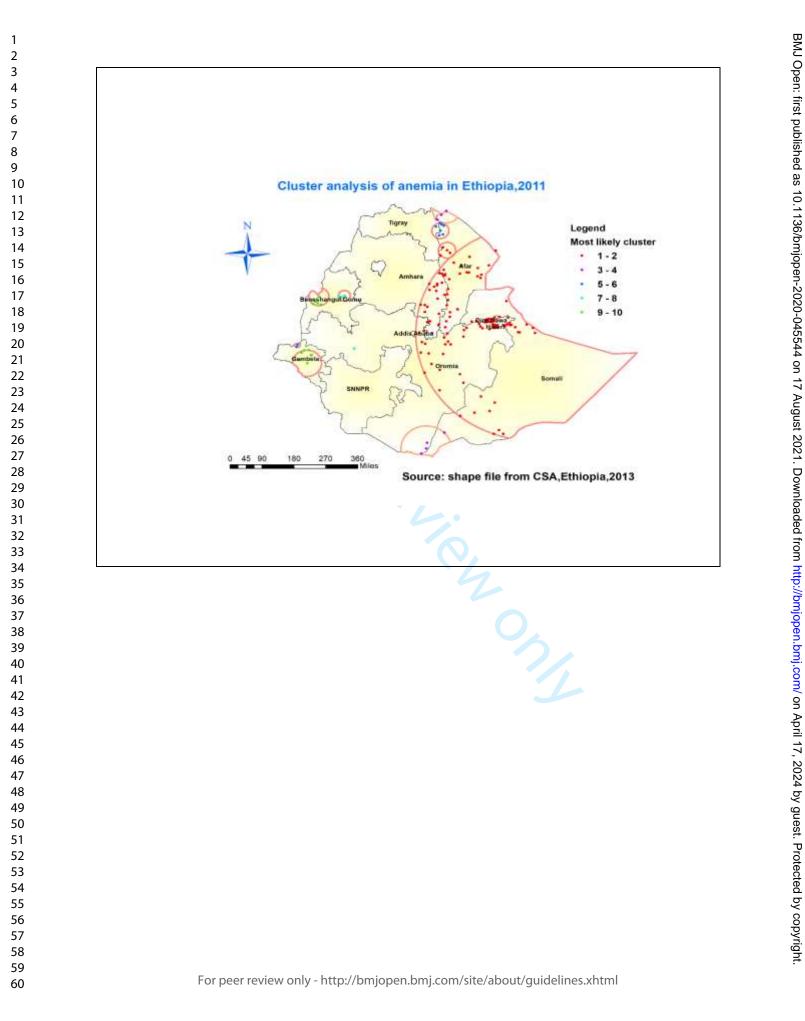
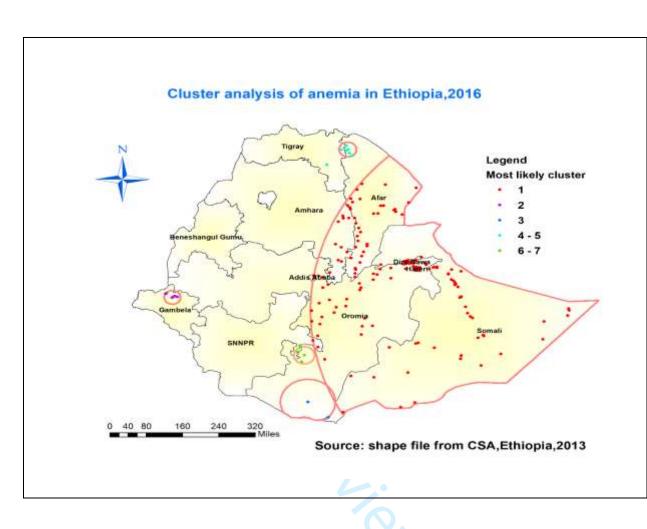
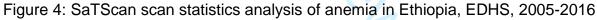


Figure 3: Ordinary Kriging interpolation of anemia in Ethiopia, EDHS 2005 to 2016











	Item No	Recommendation
Title and abstract	1	Cross-sectional study design
		Aimed Spatiotemporal distribution and factors associated to childhood anaemia
		Spatial analysis revealed that the spatial distribution of anaemia varied across the
		country
		In mixed effect model Child age, women age, maternal anaemia status, wealth index,
		birth order, fever, stunting, wasting status, and region were significant predictors of
		childhood anaemia.
Introduction		
Background/rationale	2	Though childhood anaemia is a major public health problem in Ethiopia, there is
		limited evidence on the spatio-temporal variability of childhood anaemia overtime.
		study attempts to fill the gap by investigating the spatio-temporal distribution of
		anaemia and its associated factors using multilevel model, since its hierarchical nature
Objectives	3	Therefore, this study aimed to assess the spatio-temporal distribution and associated
		factors of childhood anaemia using the Ethiopian Demographic and health survey
		(EDHS) data from 2005-2016
Methods		
Study design	4	Survey-based cross-sectional study design was employed for the EDHS
Setting	5	All nine regions and two city administrations of Ethiopia in 2005, 2011 and 2016.
Participants	6	The source population for this study was all 6–59 months of children in Ethiopia. A
		total of 21,302 children aged 6-59 months were included in this study.
Variables	7	Outcome measure: The outcome variable was child anaemia status
		Independent: sociodemographic (religion, mother age, marital status, educationa
		status, husband education, wealth index, mothers working status, numbers of unde
		five children) Maternal and Child- related (child sex, age, birth size, birth order
		maternal BMI, maternal anaemia, breastfeeding, fever, diarrhoea, vitamin supplement
		stunting and wasting). Community-level (residence, region, community women
		education and community women poverty).
Data sources/	8*	DHS program (Demographic and Health Survey)
measurement		website(www.measuredhsprogram.com) after obtaining the necessary permissions for
		the download and further analyses.
Bias	9	Cross-sectional nature of the data prevents causality from being inferred between the
	,	independent and dependent variables
Study size	10	A total of 21,302 children (3,868 in 2005, 8,958 - in 2011, and 8476 in 2016) were
		included in this study
Quantitative variables	11	Quantitative variables were handled in three level
		Level-0 intercept model
		Level-1 cluster with individual variables
		Level -2 community- level with cluster
		Level -3 mixed level individuals with community
Statistical methods	12	Multilevel model for associated factors, we use mixed effect to control confounding
		than traditional regression model.

		Spatial analysis was performed
		For associated factor predictors with missing dropped and for spatial analysis without
		spatial information was dropped
		Secondary data analysis and participants were selected based on a stratified two-stage
		cluster sampling technique
		Spatiotemporal pattern analysis was done for three-year data
Results		
Participants	13*	A total of 21,302 children
-		Secondary data analysis
		Simply we take from EDHS
Descriptive data	14*	A total of 21,302 children with known haemoglobin levels (3,868 in 2005, 8,958 in
-		2011, and 8467 in 2016) were included in this study. The prevalence of anaemia for
		the three consecutive surveys was 53.9%, 44.6%, and 57.6% in 2005, 2011, and 2016
		EDHS data respectively
		The majority of children were from rural residency in five years preceding the survey
		in three surveys. About 78.6%, 70%, and 67% of women were unable to read and
		write in 2005, 2011, and 2016 survey respectively. Children from poor and middle-
		class families were more anaemic than children from rich families across the three
		EDHS survey
		Husband educational level was missing data
Outcome data	15*	The dependent variable was child anaemia status, categorized as "anaemic/no
		anaemic" for this study.
Main results	16	The spatial distribution of childhood anaemia in Ethiopia was non-random in all three
		consecutive surveys. The global Moran's I test value was 0.176 (P-value <0.001)
		2005, 0.18 (P-value < 0.001) in 2011, and 0.09(P-value < 0.005) in 2016 Ethiopia
		Demographic and health surveys.
		In multivariable multilevel mixed-effect logistic regression analysis, individual-lev
		factors such as the age of the child, wealth index, mother age, maternal anaemic statu
		birth order, fever, stunting, and wasting status were significant predictor of childhoo
		anaemia.
		Not-applicable
		Not-applicable
Other analyses	17	Different spatial technique spatial autocreation, hotspot/cold spot analysis,
		interpolation, and sat scan analysis
Discussion		
Key results	18	This study tried to identify spatio-temporal distribution and predictors of childhood
		anaemia across the regions in Ethiopia. 2005, 2011, and, 2016 Ethiopian Demograph
		and Health Survey data were used. In this study, anaemia's trend was decreased from
		2005 to 2011, while the rate significantly increased from 2011 to 2016. The stud
		revealed that 57.56% [CL: 0.56-0.59] of children were anaemic in 2016, preceding th
		survey. This finding was in line with a study done in Gondar, Northwest Ethiop 58.6%

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		The spatial pattern shows the geographical inequality of anaemia by using sat scan and GIS spatial techniques like cluster mapping tools and interpolation techniques. The spatial analysis indicates that the distribution of childhood anaemia was non-random across the country with a global Moran's I index of 0.176 in 2005, 0.18 in 2011, and 0.09 in 2016 with a significant p-value, which indicates substantial-considerable clustering areas. This study's findings were in line with a study done in Nigeria,
		Malawi, Tanzania, and Uganda
Limitations	19	The cross-sectional nature of the data prevents causality from being inferred between the independent and dependent variables
		Respondents' without coordinate (longitude and latitude) were excluded from the spatial analysis, which could affect the generalizability of the findings
Interpretation	20	Prevalence of childhood anaemia decreased between the 2005-2011 survey while the prevalence increased from 2011-2016 EDHS. The spatial pattern of child anaemia in Ethiopia was non-random among the three consecutive surveys with the global Moran's I value of 0.176, 0.18, and 0.09 in EDHS 2005, 2011, and 2016. In line study done Cape Verde, west Africa, Nigeria, Malawi, Tanzania, and Uganda
Generalisability	21	Policymakers and health planners should design effective intervention strategies for the identified hot spot areas and individual and community-level factors to anaemia. For health care community, and researcher to alleviate the problem.
Other information		
Funding	22	No funding

\*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.

## Spatio-temporal distribution and associated factors of anaemia among children aged 6–59 months in Ethiopia: Based on the EDHS 2005- 2016: A spatial and multilevel analysis

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Manuscript ID	bmjopen-2020-045544.R2		
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Complete List of Authors:	Samuel, Hailegebreal; Arba Minch University, Department of Health Informatics Nigatu, Araya; University of Gondar, Department of Health Informatics, Institute of Public Health, University of Gondar, Ethiopia Mekonnen, Zeleke; Ethiopia Ministry of Health, Health System Directorate, Ministry of Health, Addis Ababa, Ethiopia; Endehabtu, Berhanu; University of Gondar, Department of Health Informatics, Institute of Public Health, University of Gondar, Ethiopia		
<b>Primary Subject Heading</b> :	Paediatrics		
Secondary Subject Heading:	Public health		
Keywords:	Anaemia < HAEMATOLOGY, PAEDIATRICS, Community child health < PAEDIATRICS		

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1	Spatio-temporal distribution and associated factors of anaemia among children aged 6-59
2	months in Ethiopia: Based on the EDHS 2005- 2016: A spatial and multilevel analysis
3	Samuel Hailegebreal <sup>1*</sup> , Araya Mesfin Nigatu <sup>2</sup> , Zeleke Abebaw Mekonnen <sup>2,3</sup> , Berhanu Fikadie
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1 2	22	Abstract						
3 4 5 6 7 8 9 10 11 2 13 14 15 16 17 18 19 20 1 22 3 24 25 26 27 8 9 30 31 32 33 4 35 36 37 38 9 40 4 1 2 43 44 45	23	Objectives: Anaemia is a global public health problem with major health and socio-economic						
	24	consequences. Though childhood anaemia is a major public health problem in Ethiopia, there						
	25	is limited evidence on the spatio-temporal variability of childhood anaemia overtime in the						
	26	country. Therefore, this study aimed to assess the spatio-temporal distribution and associated						
	27	factors of childhood anaemia using the Ethiopian Demographic and Health Survey (EDHS)						
	28	data from 2005-2016.						
	29	<b>Design:</b> Survey-based cross-sectional study design was employed for the EDHS.						
	30	Setting: Data were collected in all nine regions and two city administrations of Ethiopia in						
	31	2005, 2011 and 2016.						
	32	<b>Participants:</b> The source population for this study was all 6–59 months of children in Ethiopia.						
	33	A total of 21,302 children aged 6-59 months were included in this study.						
	34	Outcome measure: The outcome variable was child anaemia status.						
	35	Results: The prevalence of anaemia declined from 53.9% in 2005 to 44.6% in 2011, but it						
	36	showed an increment in 2016 to 57.6%. The spatial analysis revealed that the spatial						
	37	distribution of anaemia varied across the regions. The spatial scan statistics analysis indicated,						
	38	a total of 22 clusters (RR= 1.5, P-value < 0.01) in 2005, 180 clusters (RR = 1.4, P-value < 0.01)						
	39	in 2011, and 219 clusters (RR = 1.4, P-value < 0. 0.01) in 2016 significant primary clusters						
46 47	40	were identified. Child age, women age, maternal anaemia status, wealth index, birth order,						
48 49 50	41	fever, stunting, wasting status, and region were significant predictors of childhood anaemia.						
51 52 53	42	Conclusions: In this study, childhood anaemia remains a public health problem. The spatial						
54 55	43	distribution of childhood anaemia was significantly varied across the country. Individual-level						
56 57 58	44	and community-level factors were associated with childhood anaemia. Therefore, in regions 2						
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml						

with a high risk of childhood anaemia, individual and community level factors should be intensified by allocating additional resources and providing appropriate and tailored strategies. Keywords: Anaemia, Childhood, EDHS, Spatial, Multilevel, Ethiopia Strengths and limitations of this study This study applied different methods of spatial pattern, trend and a multilevel logistic regression models accounting for the nested nature of EDHS data The study was based on three consecutive EDHS dataset's representing the whole • country of Ethiopia The cross-sectional nature of the data prevents causality from being inferred between the independent and dependent variables Respondents without coordinate (longitude and latitude) were excluded from the spatial analysis, which could affect the generalizability of the findings 

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67 Background

Anaemia is a condition characterized by a low level of haemoglobin in the blood(1). Over 273 million under-five children suffer from anaemia worldwide(2). Sub-Saharan Africa is one of the most affected regions, accounting for about 53.8%(2). World Health Organization (WHO) had developed a classification system to facilitate international comparisons of anaemia as public health crises. The problem was considered severe if anaemia prevalence is  $\geq 40\%$ , moderate from 20% to 39.9%, and mild from 5% to 19.9%(3). The high prevalence of anaemia and its consequences on children's health, especially on their growth and development, have made it important public health problem. It also increases the risk of mortality and morbidity that come from other diseases(4,5). 

Anaemia is a public health problem that affects populations in both industrialized and non-industrialized countries which touches all segments of the population. It is frequently observed among children and pregnant women who are the most vulnerable group because their iron requirements are higher than any other group(6). Anaemia is defined as a haemoglobin level below 11.0 g/dl for children age 6-59 month. Childhood anaemia is mainly caused by dietary iron deficiency, foliate, vitamin B12, vitamin A deficiencies, chronic inflammation, parasitic infections, nutritional deficiencies, hemoglobinopathies and inherited disorders were contribute to childhood anaemia (7,8). 

The 2015 WHO report, from the global anaemia prevalence in 2011 showed that Africa, south east Asia, America, and European regions were,62.3%,53.8%,23.3%, and 22.9%, respectively(3). In Sub-Saharan Africa, anaemia is a significant public health problem associated with an increased risk of death and impaired cognitive development(9).

Various-studies showed that the prevalence of anaemia among 6-59-month children is high
and a severe public health problem. Evidence from various studies indicated that women age,

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residence, maternal education status(10), an introduction of complementary foods, poor breastfeeding practice, poor utilization of folic acid by mothers(11), maternal anaemia(12), unemployment of the parent, and presence of sickle haemoglobin, household wealth index, and sex of the child were associated with childhood anaemia(13). Few studies have been done on factors associated with anaemia in Ethiopia, to date; the risk areas (hot spot) of anaemia among children are not identified. Thus, this study aimed to assess the spatiotemporal patterns of anaemia among under five children in Ethiopia over the last one and half-decades to point out whether there was either the shift or improvement in anaemia risk areas following intervention programs in between the survey periods in Ethiopia. Geographical differences in the causes of anaemia can be partially explained by large-scale variability in environmental drivers, particularly nutritional and infectious causes(14). The risk of malaria is known to be associated with elevation and land surface temperature(15). Environmental drivers of anaemia tend to show a high degree of spatial dependency. Therefore, detecting the geographic variation of anaemia during childhood is important to 31 104 prioritize and design targeted intervention programs to reduce anaemia especially in those areas with a consistently higher risk of anaemia over time. Therefore, this study attempts to fill the gap by investigating the spatio-temporal distribution of anaemia and its associated factors 38 107 using multilevel model analysis in Ethiopia using the EDHS survey between 2005-2016 data. 

Methods and materials 

Study design, setting and period 

The survey-based cross-sectional study design was employed using the 2005, 2011, and 2016 EDHS. Data access, extraction, and analysis were conducted from January to June 2020. 50 112 The study was conducted in Ethiopia located at the horn of Africa ( $3^{\circ}-14^{\circ}N$  and  $33^{\circ}-48^{\circ}E$ ). Administratively, the country is divided into nine regions and two city administrations. Each 

115	region is sub-divided into zones, districts, towns, and kebeles (the smallest administrative
116	units).
117	Source and study population
118	All 6-59 months children in Ethiopia were the source population for this study whereas all
119	children aged from 6-59 months in the selected enumeration areas within five years before the
120	survey were the study population.
121	Sample size and sampling technique
122	A total of 21,302 children (3,868 in 2005, 8,958 in 2011, and 8476 in 2016) were included in
123	this study. Children's record (KR) dataset was used for analysis. The survey covered all nine
124	regions and the two city administrations of Ethiopia. Participants were selected based on a
	stratified two-stage cluster sampling technique in each survey year. After excluding clusters
120	with zero coordinates and missing information, a total of 503 clusters in 2005, 569 clusters in
127	2011, and 615 clusters in 2016 were used for analysis. The detailed sampling procedure was
	available in each survey years report(16–18)
129	Data collection tools and procedures
130	The data for this analysis were extracted from Demographic and Health Survey (DHS) program
131	website (www.measuredhsprogram.com) after obtaining the necessary permissions for the
	download and further analyses. Similarly, spatial location data (latitude and longitudinal) were
133	extracted from the downloaded excel file. After extraction, the missing values for the significant
134	independent variables were excluded and the analysis was undertaken using a complete data
	set. In all survey years for all children age 6-59 month from whom consent was obtained from
150	their parents. Blood samples were drawn from the drop of blood taken from a finger prick or a
137	heel prick in the case of 6-11 month, and collected in a microcuvette. Haemoglobin analysis
	was carried out on-site using a battery-operated portable HemoCue analyzer.
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	<ol> <li>116</li> <li>117</li> <li>118</li> <li>119</li> <li>120</li> <li>121</li> <li>122</li> <li>123</li> <li>124</li> <li>125</li> <li>126</li> <li>127</li> <li>128</li> <li>129</li> <li>130</li> <li>131</li> <li>132</li> <li>133</li> <li>134</li> <li>135</li> <li>136</li> </ol>

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#### 20 147

## Key variables and measurements

140 Dependent variable: The study variables were grouped into dependent and independent 141 variables. The dependent variable is childhood anaemia status, categorized as "anaemic or 142 not-anaemic". Children whose haemoglobin level was less than 11g/dl were considered 143 anaemic and not anaemic otherwise.

## a 144 Independent variables:

sociodemographic (religion, women age, marital status, educational status, husband education, wealth index, women working status, numbers of under five children) Maternal and Child- related (child sex, age, birth size, birth order, maternal BMI, maternal anaemia, 22 148 breastfeeding, fever, diarrhoea, vitamin supplement, stunting and wasting). Community-level variables (residence, region, community women education and community women poverty). 27 150 We created community women education and community women poverty variables by 29 151 aggregating the individual characteristics within their clusters. The aggregates were computed using the median values of the proportions of women in each category of a given variable. We 

categorized the aggregate values of a cluster into groups based on national median values,
 since all aggregates were not normally distributed.

Community women's education: was defined as the proportion of women who attended 39 155 primary, secondary and higher education within the cluster. The aggregate of individual primary, secondary and higher educational attainment can show the overall educational and academic status of women within the cluster. They were categorized into two categories a 46 158 48 159 higher proportion of women's education within the cluster and a lower proportion of women education based on the national median value. 

Community women's poverty status: defined as the proportion of poor and poorest mothers
 within the cluster. For each cluster, the proportion of poor and poorest as-was aggregated and

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show overall poverty status within the cluster. It was categorized into two categories based on national median value as higher proportion of poor/poorest mother's and lower proportion of mothers within a cluster. Data management and analysis The data were cleaned using STATA 14.1 software and Microsoft excel. The data were weighted using sampling weight, primary sampling unit, and strata before any statistical analysis to restore the representativeness of the survey to take into account the sampling 15 169 design when calculating standard errors to get reliable statistical estimates. 20 171 **Spatial analysis** For the spatial analysis, ArcGIS V.10.7 software was used to evaluate whether the pattern was clustered, dispersed or random across the study area, and SaTScan<sup>™</sup> software, version 9.6.1, 27 174 was used for the local cluster detection analysis. It uses a circular window that moves

 $^{28}$  systematically throughout the study area to identify a significant spatial clustering of childhood  $^{31}_{32}$  176 anaemia.

#### <sup>34</sup> <sub>35</sub> 177 Spatial autocorrelation analysis

The spatial autocorrelation (Global Moran's I) statistic measures whether childhood anaemia 37 178 patterns were dispersed, clustered or randomly distributed in the study area. Moran's I output value ranges from (-1 to +1). Values close to -1 indicate anaemia dispersed, whereas Moran's I close to +1 indicate childhood anaemia clustered and distributed randomly if I value zero. Anselin Local Moran's I was used to indicate the local level cluster locations of anaemia positively correlated (high-high and low-low) clusters or negatively correlated (high-low and low-high). 

## <sup>53</sup><sub>54</sub> 185 Hot spot analysis (Getis-Ord Gi\* statistic)

Local Moran's I, Gettis-OrdGi\* statistics was computed to measure how spatial autocorrelation of anaemia among under-five children varies across different locations in Ethiopia. Hotspot analysis computes Z-score and p-value to determine the statistical significance of the clustering of anaemia over the study area at different significance levels simultaneously. Statistical output with high GI\* indicates "hotspot" whereas low GI\* means a "cold spot". hot spot areas showed that there was a high proportion of anaemia and the cold spot indicated a low proportion of anaemia. 15 192

#### Spatial interpolation 18 193

There are various deterministic and geostatistical interpolation methods. Among all of the methods, ordinary Kriging and empirical Bayesian Kriging are considered the best methods since they incorporate spatial autocorrelation and statistically optimize the weight. Ordinary 27 197 Kriging spatial interpolation method was used for this study for predictions of childhood anaemia in unobserved areas of Ethiopia since it had low mean square error and residual as compared to the other interpolation techniques. 

Spatial scan statistical analysis 

Spatial scan statistical analysis used to Identifying most likely(primary) and secondary spatial 37 201 clusters. This method is widely recommended as it is very important in detecting local clusters and has higher power than other available spatial statistical methods. Bernoulli based model was employed to test for statistically significant spatial clusters of anaemia using Kulldorff's SaTScan<sup>™</sup> version 9.6.1, software. Children with anaemia were taken as cases, and were not-anaemic as controls to fit the Bernoulli model. The default maximum spatial cluster size of <50% of the population was used. The scanning window with maximum likelihood was the most likely cluster, and the p-value was assigned to each cluster using Monte Carlo hypothesis 

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1 2	209	testing. The primary and secondary clusters were identified and assigned p-values and ranked
3 4	210	based on their likelihood ratio test, based on 999 Monte Carlo replications(19).
5 6 7 8	211	Associated factors of anaemia
9 10 11	212	Four models were fitted using melogit, a STATA command, the null model without predictors,
	213	model I with only individual-level variables, model II with only community-level variables, and
14 15	214	Model III both individual-level and community-level variables. Model comparison was
16 17 18	215	conducted by using deviance and likelihood ratio.
19 20		Intra-class correlation (ICC), median odds ratio (MOR), and proportional change in variance
21 22 23	217	(PCV) were computed to measure the variation between clusters. The intra-class correlation
23 24 25	218	coefficient (ICC) quantifies the degree of heterogeneity of childhood anaemia between clusters
26 27		(the proportion of the total observed individual variation in anaemia that is attributable between
28 29	220	cluster variations) calculated as
30 31 32 33	221	$ICC = \frac{6^2}{(6^2 + \sigma^2_b)}$ (20), where, $6^2$ is the community level variance and $\sigma^2_b$ indicates individual level
34 35 36	222	variance. The individual variance ( $\sigma_b^2$ ) equal to $\pi^2/3$ .
37 38	223	but MOR is quantifying the variation or heterogeneity in outcomes between clusters and is
39 40	224	defined as the median value of the odds ratio between the cluster at high risk of anaemia and
41 42 43	225	cluster at lower risk when randomly picking out two clusters (EAs).
44 45 46	226	$MOR = e^{(0.95 * \text{ sqrt}(6^2))}$ (21) where, $6^2$ indicates that cluster level variance.
47 48	227	PCV measures the total variation attributed by individual-level factors and community-level
	228	factors in the multilevel model compared to the null model PCV. In the multivariable multilevel
51 52 53	229	logistic regression analysis variables with a p-value of <0.05 were considered as statistically
54 55		significant. Adjusted Odds Ratio (AOR) with their corresponding 95% confidence interval was
58	231	determined to identify factors associated with anaemia. After comparing all models, a model 10
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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- with low deviance was considered a better fitted model. Multicollinearity was checked using
- the Variance Inflation Factor (VIF). VIF less than 10% was taken as no multicollinearity.

## Ethics and confidentiality

Ethical clearance was obtained from the ethical review board of the University of Gondar Institute of Public Health, CMHS. Permission for data access was obtained from the measure demographic and health survey through an online request by a written letter of objective and significance of the study from (http://www.dhsprogram.com) 

- Patient and public involvement
  - This study did not involve patients and the public

## **Results**

#### Descriptive characteristics of the study population

A total of 21,302 children with known haemoglobin levels (3,868 in 2005, 8,958 in 2011, and 8467 in 2016) were included in this study. The prevalence of anaemia for the three consecutive 32 244 34 245 surveys was 53.9%, 44.6%, and 57.6% in 2005, 2011, and 2016 EDHS data respectively. The majority of the participants were in the age group of 36-47 (23.7%), 36-47 (24.4%), and, 48-59 (22.9%) in EDHS 2005, 2011, and 2016 survey respectively. The mean age of children was 32.6 ±15.6-SD, 32.6±15.4-SD, and 31.7±15.6-SD in 2005, 2011, and 2016 respectively. 41 248 Among children involved in the analysis, male participants were higher in 2011 and 2016 EDHS compared to 2005 survey periods. The majority of children were from rural resident in three surveys. About 78.6%, 70.1%, and 67.1% of women were unable to read and write in 2005, 48 251 2011, and 2016 survey respectively. Children from poor and middle-class wealth index families were more anaemic than children from rich families across the three EDHS survey (Table 1). 

59

60

1 2	254	During the study period, the trends in the prevalence of childhood anaemia in Ethiopia, were				
2 3 4	255	fluctuates across regions (Fig.1)				
5 6 7 8 9	256 257	Table 1: Descriptive characteristics of study participants included in the analysis for childhood anaemia five years preceding the survey from EDHS 2005-2016 in Ethiopia				
10 11		Variables	2005 (N, 3868)	2011 (N, 8958)	2016 (N, 8476)	
12 13			Frequency (%)	Frequency (%)	Frequency (%)	
14 15 16		Sex of child				
17 18		Male	1,931(49.9)	4,500(51.4)	4,395(51.9)	
19 20 21		Female	1,937(50.1)	4,358(48.7)	4,081(48.2)	
21 22 23		Age of child in month				
24 25		6-11	418 (10.8)	1,029(11.5)	1,000(11.8)	
26 27 28		12-23	842 (21.76)	1,804(20.14)	1,902(22.4)	
29 30		24-35	825 (21.3)	1,895(21.2)	1,803(21.3)	
31 32		36-47	919 (23.7)	2,184(24.4)	1,832(21.6)	
33 34 35		48-59	864 (22.3)	2,047(22.9)	1,939(22.9)	
36 37		Mean ± SD	32.6 ±15.6	32.6±15.4	31.7±15.6	
38 39 40		Residence				
41 42		Urban	244 (6.3)	1,047(11.7)	857(10.1)	
43 44 45		Rural	3,624 (93.7)	7,911(88.3)	7,619(89.9)	
45 46 47		Religion				
48 49		Orthodox	1,624 (42.0)	3,416(38.1)	2,913(34.4)	
50 51 52		Muslim	1,276 (33.0)	3,108(34.7)	3,432(40.5)	
52 53 54 55 56		Protestant	836 (22.0)	2,151(24.0)	1,874(22.1)	

Others	133 (3.0)	283(3.2)	258(3.0)
Women age			
15-29	1,930(49.9)	4,908(54.9)	4,356(51.4)
30-39	1,474(38.1)	3,223(36.0)	3,335(39.3)
40-49	464(12.0)	828(9.1)	785(9.3)
Women education			
No education	3,042 (78.6)	6,285(70.1)	5,685(67.1)
Primary	684 (17.7)	2,389(26.7)	2,275(26.8)
Secondary	136 (3.5)	168(1.9)	346(4.1)
Higher	7 (0.2)	117(1.3)	170(2.0)
Marital status			
Single	7(0.2)	50(0.6)	45(0.5)
Married	3,704(95.7)	8,425(94.0)	8,129(95.9)
Widowed	80(2.1)	178(2.0)	93(1.1)
Divorced	78(2.0)	306 (3.4)	210(2.5)
Husband education			
No-education	2,235 (58.0)	4,532(50.9)	4, 33(51.1)
Primary	1,233(32.0)	3,710(41.7)	3,273(38.6)
Secondary	362(9.0)	412(4.6)	572(6.8)
Higher education	31(1.0)	255 (2.8)	300(3.5)
Wealth index			
Poor	1,697(43.7)	4,048(45.2)	3,977(46.9)
Middle	854(22.1)	1,873(20.9)	1,821(21.5)

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1 2	Rich	1,318(34.1)	3,038 (33.9)	2,678(31.6)
3 4	Women working status			
5 6 7	Not working	2,841(73.5)	5,793(64.7)	6,140(72.4)
8 9	Working	1,027(26. 5)	3,165(35.3)	2,336(27.6)
10 11	Total	3,868(100)	8,958(100)	8,476(100)
12 13 258 14				
15 16 259	Community-level characteris	tics of the study pop	ulation	
17 <sup>18</sup> 260	Findings from this study area		م ام محمل المالية مع	
19	Findings from this study revea	aled a regional variatio	on of childhood a	inaemia, with 83.3% in
20 21 261 22	Somali, 75.5%, in Afar, 74.5%	in Dire Dawa, and 6	8.8% in Harari. I	However, Amhara, and
22 23 262 24	Benishangul with 42.5%, which	was relatively low cor	mpared to other r	egions.
25 26 263	Childhood anaemia varies by u	irban-rural of residence	e Children resid	ing in communities with
27				
28 264 29	low women poverty level had a	lower percent of anaer	nia (51.2%) than l	high community poverty
$\frac{30}{31}$ 265	level (62.5%). Children from	low community wome	en education lev	el (59.5%) were more
32 33 266 34	anaemic than children resided	with high community v	women (53.6%) e	ducational level (Table
35 267 36	2).			
37 38 268	Table 2: Community-level fa	ctors of under five of	children particip	ated in EDHS (2016),
39 40 269	Ethiopia. (N, 8476)			
41 42 43	Community-level factors	Not-anaemic (%	) Anaemic (%)	Total (100%)
44 45	Residence			
46 47 48	Urban	435(50.6)	424(49.4)	857
49 50	Rural	3164(41.5)	4455(58.5)	7619
51 52	Region			
53 54	Tigray	263(46.0)	309(54.0)	572
55 56				
57 58				14
59	For poor review of	nly - http://bmionon.hmi.com	n/cita/about/guidalia	

1	Afar	21(25.3)	62(74.5)	83
2				
4 5	Amhara	950(57.5)	703(42.5)	1653
6 7	Oromia	1273(34.2)	2446(65.8)	3719
8 9	Somali	58(16.7)	290(83.3)	348
10 11	Beneshangul	51(56.6)	39(43.4)	90
12 13 14	SNNPR	875(49.1)	906(50.9)	1781
15 16	Gambela	8(42.1)	11(57.9)	19
17 18	Harari	5(31.2)	11(68.8)	16
19 20 21	Addis Ababa	82(50.9)	79(49.1)	161
22 23	Dire Dawa	9(28.1)	23(71.9)	32
24 25 26	Community women education			
27 28	Low	2281(40.5)	3358(59.5)	5639
29 30	High	1315(46.4)	1520(53.6)	2837
31 32 33	Community women poverty			
34 35	Low	1815(48.8)	1905(51.2)	3719
36 37 38	High	1782(37.5)	2974(62.5)	4756
<sup>39</sup> 270 40				
41 42 271 43	Spatio-temporal distribution of a	inaemia among chil	ldren age 6-59 r	nonths in Ethiopia
44 <sup>45</sup> 272	The spatial distribution of childhood	d anaemia varied ac	ross regions in a	ll surveys. The spatial
46 47 48 273	autocorrelation analysis result indi	icated that childhood	d anaemia had s	spatial dependency in
49 50 274	2005, 2011 and 2016 (Moran's I: 0	.176, 0.18, and 0.09	, respectively at	P-value < 0.01).
51 52 275 53	Hot spot analysis of the three su	irveys		
54 55				
56 57				
58 59				15
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The spatial distribution of childhood anaemia in Ethiopia was different in all the three survey periods. In EDHS 2005, a high proportion of childhood anaemia was detected in Dire Dawa, Harari, eastern Oromia, Beneshangul in Metekel zone, Gambela, southern and eastern Tigray, and Somali region mainly Liben, Afdar, and Fafna zone which was hotspot area within 95% confidence level. On the counterpart, GamoGofa, Wolayita, Hadiya, Southern Omo, and Segen zone of SNNPR, Addis Ababa, central Oromia, Jima, north Shewa zone were cold spot area. In EDHS 2011, a highly significant clustering of childhood anaemia was detected in 15 282 Somali, Dire Dawa, Harari, Afar, Gambela, Beneshangul, eastern Oromia, Bale, Arsi zone were the hotspot areas within 95% level of confidence. The low hotspot area of childhood anaemia was detected in central Tigray, East and West Gojam, North Gondar, a central part 24 286 of Oromia, Addis Ababa and SNNPR were areas identified as the low percentage of childhood anaemia in the 2011 EDHS survey. 

In EDHS-2016 sampled data, hot spot (high risk) regions for childhood anaemia were observed in Somali, Dire Dawa, Harari, Gambela, eastern, and Southern part of Oromia, However, 34 290 Amhara, Beneshangul, and SNNPR were identified as cold spot (low risk) regions for childhood anaemia within a 95% confidence interval (Fig.2) 

Spatial interpolation 

Based on EDHS-2005 sampled data, the geostatistical analysis predicts that the highest prevalence of childhood anaemia (65.75%-88.89%) was detected in east Oromia, Ilubabur, Arsi, some parts of Beneshangul, Agnuak zone in Gambela, north Shewa Amhara region, south and central Tigray, Afar in zone2, some parts of Dire Dawa and Somali. In EDHS-2011 Geostatistical analysis, a high percentage of anaemia was detected in Afar, most parts of Somali, Oromia in east Harerge and Borena, some part of Dire Dawa, and the Meketel zone in Beneshangul. In 2016 EDHS most of Somali, some parts of Gambela, Guji and some parts 

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of Borena, ast Shewa, East Harerge and Arsi in Oromia and part of Dire Dawa were highly prevalent areas in childhood anaemia (Fig.3)

### **Spatial scan statistics**

In 2005 EDHS, a total of 3 significant clusters were identified, one most likely (primary) cluster and two were secondary clusters of spatial scan analysis. The primary cluster spatial window was located in Somali, which was centered at (9.018373 N, 43.110635 E) of geographic location with a 97.93 km radius, and Log-Likelihood ratio (LLR) of 20.03, at p < 0.01 which was detected as the most likely cluster with maximum likelihood. It showed that children within the spatial window had 1.5 times more likely a higher risk of anaemia than the children outside the spatial window areas. The secondary clusters scanning window was located in the southern part of Somali region, which was centered at (3.998656 N, 41.240691 E) with a 92.08 km radius and LLR of 1.7 at p-value < 0.01. It showed that children within the spatial window had

In 2011 EDHS, 10 clusters were identified and five of them were significant clusters with a pvalue <0.05. A total of 180 locations/spots with a total sampled population of 2478 were found</li>
in the primary cluster spatial window with a significant p-value < 0.01. The primary cluster</li>
spatial window was located mainly in Somali, Afar, eastern Oromia, Dire Dawa, and Harari.
The primary cluster spatial window was centered at (8.975207 N, 43.790264 E) / 540.29 km,
with a relative risk (RR) of 1.4 and a log-likelihood ratio (LLR) of 127.79. It showed that children
within the spatial window areas. The secondary cluster spatial window was located mainly in
Afar region. The secondary cluster spatial window was centered at (12.758587 N, 40.175990
E) / 39.58 km, with a relative risk (RR) of 1.7 and a log-likelihood ratio (LLR) of 21.5 Pvalue<0.01.</li>

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In 2016 EDHS, 7 clusters (one most likely cluster) were located in Somali, Afar, eastern Oromia, Dire Dawa, and Harari. The cluster window was centered with a radius at (7.650693) N, 47.007920 E) / 912.19 km with a relative risk (RR) of 1.4. The Log-Likelihood ratio (LLR) for the most likely cluster was 182.86, P-value<0.01. It showed that children within the spatial window had a 1.4 times higher risk of anaemia than outside the window. Secondary clusters were located in Gambela which was centered at (8.195862 N, 34.289837 E) with a radius of 29.01 km, and LLR of 18.80 at p-value < 0.01(Fig.4). 15 330 

#### **Multilevel Analysis** 18 331

21 332 The intra-cluster correlation coefficient (ICC) in the empty model indicated that 19% of the total variability for childhood anaemia was due to differences between clusters. The remaining unexplained 81% were attributable to individual differences. The median odds ratio for anaemia was 2.3 in the null model, indicating variation between clusters. If we randomly select children from two different clusters children at the cluster with a higher risk of anaemia had 2.3 30 336 times higher odds of experiencing anaemia than children at the cluster with a lower risk of anaemia. 

Bi-variable multilevel logistic regression analysis was done to identify variables for multivariable multilevel logistic analysis, and variable with a p-value less than 0.25 were 40 340 42 341 considered for multivariable analysis. 

#### Individual-level predictors for anaemia

48 343 In multivariable multilevel mixed-effect logistic regression analysis, individual-level factors such as the age of the child, wealth index, mother age, maternal anaemia status, birth order, fever, stunting, and wasting status were significant predictor of childhood anaemia. 

Children age between 12–23 months (AOR = 0.66, 95%CI = 0.53-0.81), between 24–35 months (AOR= 0.35, 95% CI = 0.28-0.43), between 36–47 months (AOR = 0.23-95% CI = 0.19-0.29), and between 48–59 months (AOR = 0.15, 95%Cl = 0.12-0.19) were less likely to develop anaemia compared with children age between 6–11 months. The likelihood of developing anaemia for those children residing with the family wealth index of middle and rich were lower by 21% (AOR=0.79, 95%CI = 0.67-0.94), and 23% (AOR=0.77, 95%CI = 0.65-0.91), respectively as compared with children with low wealth index. Children whose mother's age were between 40-49 had 25% decreased odds of developing childhood 18 353 20 354 anaemia compared to age 15-29, (AOR=0.75, 95%CI = 0.59-0.95). 23 355 The odds of experiencing anaemia for those birth orders 4-5, six and above six were 1.22 times (AOR=1.22, 95%CI = 1.01-1.47) and, 1.35 times (AOR=1.35, 95%CI = 1.08-1.67) higher as compared with first-order respectively. The odds of developing anaemia of children born from anaemia history mother were 1.39 higher more elevated than those born from not anaemic 30 358 history before. Children who had fever were 39% (AOR =1.39, 95% CI: 1.24-1.58) more likely to develop anaemia than their counterparts. Children with moderate and severe stunting status were 35% (AOR=1.35, 95% CI: 1.17-1.54) and, 96% (AOR=1.95, 95% CI: 1.68-2.28), more 37 361 likely to develop anaemia respectively, compared to no stunting status. Similarly, children who had to sever wasting status were 51% more (AOR =1.51, 95% CI: 1.07-2.12) likely to develop anaemia compared with those children who had no wasting. Community-level predictors for anaemia The multivariable multilevel logistic regression analysis region was significantly associated with 52 367 community-level factors for childhood anaemia. Odds of children live in Somali were 5.65 times (AOR=5.65, 95% CI: 3.92-8.16), Dire Dawa 3.45 times (AOR=3.45, 95% CI: 2.27-5.26), Afar 3 times (AOR=3.00, 95% CI: 2.09-4.34), and 

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Oromia 2.34 times (AOR=2.34, 95% CI: 1.73-3.18) had more likely to develop childhood anaemia compared to Amhara region. Similarly, the odds of developing anaemia in Addis Ababa were 2 times (AOR=2.00, 95% CI: 1.40-3.16), Gambella 1.94 times (AOR=1.94, 95% CI: 1.32-2.84), and Tigray 1.46 times (AOR=1.46, 95% CI: 1.08-1.98), more likely as compared to Amhara region. Beneshangul and SNNPR had not significantly different in the prevalence of anaemia than the reference region Amhara (Table 3). 

#### Table 3: Multilevel logistic regression analysis result of both individual and community-15 376 level factors associated with anaemia in Ethiopia, EDHS 2016

Variables	Null	Model I	Model II	Model III
	Model	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
	Individua	al-level factors		
Age of child in mor	nth			
6-11	-	10,	-	1
12-23	-	0.66[0.54-0.82] **	· -	0.66 [0.53-0.81]
24-35	-	0.35[0.28-0.44] **	4	0.35 [0.28-0.43]
36-47	-	0.23[0.18-0.28] **	0	0.23 [0.19-0.29]
48-59	-	0.15[0.12-0.19] **	5,	0.15 [0.12-0.19]
Religion			1	
Orthodox	-	1	-	1
Muslim	-	2.07[1.77-2.47] **	-	1.21 [0.97-1.46]
Protestant		1.20 [1.00-1.48] *		1.10 [0.86-1.37]
Others	-	1.55[1.07-2.32] *	-	1.44[0.96-2.13]
Wealth status				
Poor	-	1	-	1

Middle	-	0.71[0.61-0.84] **	-	0.79 [0.67-0.94] *
Rich	-	0.72[0.63-0.85] **	-	0.77 [0.65-0.91] *
Child size at birth				
Small	-	1	-	1
Average	-	0.96[0.84-1.09]	-	0.93 [0.80-1.07]
Large	-	0.94[0.81-1.08]	-	0.96 [0.84-1.10]
Birth order			-	
1 <sup>st</sup>	0,	1	-	1
2-3	-	1.09[0.94-1.28]	-	1.13[0.97-1.32]
4-5	-	1.17[0.97-1.40]	-	1.22 [1.01-1.47] *
6 and above	-	1.30[1.05-1.62]	-	1.35 [1.08-1.67] **
No of children unde	er 5			
1-2 children	-	1	-	1
≥ 3 children	-	1.22[1.1-1.4] *	<b>)</b> , -	1.09 [0.94-1.27]
Maternal anaemia			2	
Not anaemic	-	1	0	1
Anaemic	-	1.51[1.34, 1.72] **	-//	1.39 [1.24-1.58] **
Maternal BMI				
≥18.5 kg/m2	-	1	-	1
<18.5 kg/m2	-	1.12[0.97-1.26]	-	1.05 [0.92-1.19]
Women working sta	atus			
Not-working	-	1	-	1
-			1	1

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Women age				
15-29	-	1		1
30-39	-	0.91[0.71-1.06]	-	0.90 [0.78-1.04]
40-49	-	0.75[0.59-1.12] *	-	0.75 [0.59-0.95]
Breastfeeding				
No	-	1	-	
Yes		0.92[0.81-1.04]	-	0.98 [0.87-1.12]
Vitamins in last 6 m	onth			
No	-	1	-	
Yes	-	0.90[0.81-1.09]	-	0.93 [0.84-1.05]
Diarrhea last 2 weel	k	- C		
No	-	1	-	1
Yes	-	0.88[0.73, 1.04]	•	0.90 [0.76-1.07]
Fever in last 2 week	(S		0	
No	-	1	2-	1
Yes	-	1.35[1.15-1.59] **	0,	1.32 [1.13-1.56]
Stunting status			- 7/.	
No-stunting	-	1		1
Moderate stunting	-	1.27[1.10-1.46] **	-	1.35 [1.17-1.54]
Severely stunting	-	1.81[1.55-2.11] **	-	1.96 [1.68-2.28]
Wasting status				
No-wasting	-	1	-	1
Moderate wasting		1.27[1.11-1.45]		0.98 [0.80-1.19]

Page	24	of	3	8
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Severe wasting	-	1.68[1.55-2.10] *	-	1.51 [1.07-2.12] *
	Commu	inity/cluster-level fac	tors	
Region				
Amhara	-	-	1	1
Tigray	-	-	1.46[1.09-1.97] **	1.46 [1.08-1.98] **
Afar	-	-	3.90 [2.84-5.35] **	3.00 [2.09-4.34] **
Oromia		-	2.48 [1.89-3.25] **	2.34 [1.73-3.18] **
Somali	0,	-	6.34[4.65-8.63]	5.65 [3.92-8.16] **
Beneshangul	-	5	0.86 [0.62-1.17]	0.81 [0.58-1.15]
SNNPR	-	6	1.33 [1.00-1.76]	1.30 [0.94-1.80]
Gambela	-		1.93 [1.38-2.69] **	1.94 [1.32-2.84] **
Harari	-	6	3.08 [2.15-4.43] **	2.98 [1.99-4.46] **
Addis Ababa	-	- 2	1.91[1.29-2.83] **	2.10 [1.40-3.16] **
Dire dawa	-	-	3.92 [2.67-5.77] **	3.45 [2.27-5.26] **
Residence			2	
Urban	-	-	0	1
Rural	-	-	1.40[1.12-1.78]	1.28 [0.99-1.64]
Community women	education			
Low	-	-	1	1
High	-	-	1.07[0.90-1.26]	1.13[0.94-1.34]
Community women	poverty			1
Low	-	-	1	1
High	-	-	1.41[1.17-1.68] *	1.15[0.94-1.40]

	Model comparison	and randor	n effect		
	ICC	0.19	0.12	0.08	0.07
	Log-likelihood	-4981.63	-4513.17	-4836.83	-4436.60
		0000.00	0000.04	0070.00	0070.00
	Deviance	9963.26	9026.34	9673.66	8873.20
	MOR	2.30	1.72	1.42	1.38
	More	2.00	1.72	1.72	1.00
	PVC (%)	Ref	41.20	60.10	62.59
	*Key:	1: reference	e group; p-valu	e 0.05-0.01 *: p-valu	ue < 0.01 **
	Multicollinearity				
	,				
	Multicollinearity was	checked	for those variat	ples included in the	final model using VIF.
	Accordingly, the \///	- for all p	adiatar variabla	included in the fin	al madal waa balaw 10
	Accordingly, the vil	- for all pr	edictor variables	s included in the fin	al model was below 10
	indicating the absen	ce of multic	collinearity among	g the predictor variab	oles.
	<b>J</b>				
Comparison of models					
	Devience was used				
Deviance was used to compare the models, and the lowest value of deviance (Model III) was					
considered the better mode.					
	Discussion				
	This study tried to i	dentify spa	tio-temporal dist	ribution and predicto	ors of childhood anaemia
	across the regions in	Ethionia -	The 2005 2011	and 2016 Ethiopian	Demographic and Health
	across the regions in	i Lunopia.	ine 2003, 2011,		Demographic and riealt
	Survey data were us	ed. In this	study, anaemia t	rend was decreased	from 2005 to 2011, while
	-		•		
	the rate significantly	increased	from 2011 to 201	6. The study revealed	ed that 57.56% [CL: 0.56-
	0 501 of obildrop wo	o onoomio	in 2016 proced	ing the survey. This	finding was in line with a
			ili 2010, pieceu	ing the survey. This	infulling was in fine with a
	study done in Gonda	ar, Northwe	est Ethiopia 58.6°	%(22), whereas high	er than the study done ir
	,		·	0	5
	cape Verde, west	Africa 51.8	%(23), and sout	thern Ethiopia(24).	Among children of 6–59
	monthe charmic is	otill oppoid	rad a aignificant	nublic boolth problem	n in Ethionia. Though the
	monuns, anaemia is		ereu a signilicant	public riealtri probler	n in Ethiopia. Though the
					-
					24

levels of anaemia among children vary by background characteristics like region and lowest household wealth index and maternal related factors, more of the children in Ethiopia were suffering anaemia. 

The spatial pattern shows the geographical inequality of anaemia by using different spatial analysis techniques like cluster mapping tools and interpolation techniques. The spatial analysis indicates that the distribution of childhood anaemia was non-random across the country with a global Moran's I index of 0.176 in 2005, 0.18 in 2011, and 0.09 in 2016 with a significant p-value <0.01, which indicates substantial-considerable clustering areas. This 18 404 20 405 findings were in line with a study done in Nigeria, Malawi, Tanzania, and Uganda (25,26).

The spatial pattern of scan statistical analysis showed that Eastern Somali region were primary (most likely) cluster and secondary cluster also located in the southern part of Somali in 2005 sat scan analysis. In 2011 Somali, Afar, Eastern Oromia, Dire Dawa, and Harari were located in the primary window and centered at (8.975207 N, 43.790264 E/ 540.29 km with a significant 30 409 p-value. Similarly, spatial sat scan analysis showed that Somali, Afar, Eastern Oromia, Dire Dawa, Harari were hotspot areas in the 2016 EDHS spatial analysis. In addition, this study revealed that eastern parts of the country had similar spatiotemporal trend over the study 37 412 <sup>39</sup> 413 periods. 

42 414 The spatial analysis indicated the hotspots areas of anaemia were situated in the East. Northeast, and Western parts, whereas, Central area, and South, and Northwest parts were cold spot parts of Ethiopia. The observed variability of childhood anaemia might be attributed 49 417 to the regional deference of economy, healthcare facility and food availability(27). 

52 418 This study indicated that children age 12-59 months were less affected by childhood anaemia. This finding was consistent with studies conducted in Ethiopia and Togo (28–30). This could be explained by the fact that children who are getting older receive a richer and complete diet, 

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with a sufficient intake of iron which could prevent the occurrence of iron deficiency anaemia. The deficiency may result from inadequate dietary intake of iron, malabsorption of iron an increased iron demand during rapid growth might it be the possible reason (31). The finding of this study indicated that children whose women age was between 40-49 were less anaemic as compared to age 15-29. This finding was consistent with other studies conducted in Sub-Saharan Africa and Ghana (12,32). 

This group consists of more at-risk population segments (Adolescent) for anaemia. They are vulnerable to malnutrition because they are growing faster than at any time after their first year 18 428 20 429 of life which contributes to the intergenerational cycle of malnutrition and most common forms of malnutrition among Ethiopian adolescent girls is iron deficiency anaemia. Aside from, growing adolescent mother and her baby's bodies may compete for nutrients, raising the 27 432 infant's risk of low birth weight; however, the lack of such nutrients might lead to anaemia. 

Children from households of middle and rich wealth indexes were less affected by childhood 30 433 anaemia as compared to children from a poor household. This finding in line with similar studies in Nigeria and Northern Ethiopia (25,33). This is due to the reason that children from poor households are less likely to get iron-rich foods like animal foods and vitamin-rich foods 37 436 <sup>39</sup> 437 especially vitamins A and C which are very important for iron absorption. 

42 438 Maternal anaemia was highly associated with the occurrence of childhood anaemia. This finding was in line with a study done in South Africa. Haiti, and India(34–36). 

This might be explained that mothers and children share a common home environment, socioeconomic, and dietary conditions, and maternal and child anaemia may reflect the 52 442 household common nutritional status, and poor maternal iron intake during pregnancy, reduce breast milk might be the possible reason. 

The EDHS data set indicated that the incidence of fever had an impact on childhood anaemia. This is in line with studies done in Ghana and South Ethiopia Wolaita (24,37). This result showed that children who had a fever in the last two weeks before the survey had had a higher likelihood of anaemia than the counterpart. This could be attributed to the infectious cause of childhood fever mainly malaria, tuberculosis, and Leishmaniasis which cause anaemia by destructing red blood cells or other related mechanisms. 

The nutritional status of children had a significant association with childhood anaemia. The stunting status of children had significant association with childhood anaemia. This finding in 18 451 20 452 line with previous similar finding conducted in South Africa(36), Bangladesh(38,39), and Ethiopia(40,41). This might be explained that children suffering from nutritional deficiency were more likely to have weak immune systems, making them vulnerable to various illnesses and 27 455 healthiness such as parasitic infections or chronic inflammation; many of these conditions reduce the haemoglobin level in the blood leading to increased childhood anaemia(42) 

Furthermore, severely wasting children were more likely to be anaemic than their counterpart. Consistent with other previous studies (43,44). This is due to the fact that malnutrition leads to both macronutrient and micronutrient deficiencies, such as protein, iron, and vitamin A, which 37 459 are responsible for iron deficiency. Odds of experiencing anaemia for those birth order four up to five and six and greater than six were higher than those of the first order. This finding was similar to a studies done in Indian(12,45). This could be due to the distribution of scarce 46 463 resources within the family and related to the maternal exhaustion of micronutrient feeding practices. 

In a multivariable multilevel analysis, the odds of developing childhood anaemia were higher among children who lived in Somali, Dire Dawa, Afar, and Gambela compared to Amhara region. This might be due to the unavailability and inaccessibility of health facilities as 56 467

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compared to the regions. Regional variation in the nutrient intake can cause significant health disparity, and this variability may be mediated by factors such as food availability, food customs, and culture. 

This study, used different methodologies; spatial pattern, trends, and a multilevel regression model because of nested or cluster samples to show the effect of individual predictors and 11 472 community-level variables on the outcome variable. The study was based on a large dataset representing the whole country of Ethiopia and which was weighted to make it nationally representative and adjusted for the design to get a reliable estimate. However, there were 18 475 20 476 some limitations to this study. The cross-sectional nature of the data prevents causality from being inferred between the independent and dependent variables. Also, respondents' data that didn't have files (longitude and latitude) were excluded from the spatial analysis which could 27 479 affect the overall result and the generalizability of the findings. 

#### Conclusion

through declining prevalence of childhood anaemia was observed from 2005 to 2011, it increases from 2011-2016 survey. Besides, it was spatially clustered across regions in 35 482 Ethiopia. The most prominent risk areas of anaemia were detected in Afar, Somali, Dire Dawa and Oromia regions more or less consistently overtime in the last one and half-decade. Child age, women age, wealth index, maternal anaemia, fever, birth order, stunting, wasting and 42 485 region were significant predictors among 6-59 months. Therefore, public health intervention actions intended in a targeted approach to bearing high-risk populations as well as geographic regions were vital to reduce childhood anaemia in Ethiopia. 49 488

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1 2	491	Abbreviations
3 4 5	492	AOR-Adjusted Odds Ratio, CSA-Central Statics Agency, CI-Confidence Interval, CMHS-
5 6 7	493	College of Medicine and Health Science COR-Crude Odds Ratio, EDHS-Ethiopia
8 9	494	Demographic and Health Survey, GPS-Global Positioning System, ICC-Intra Class Correlation
10 11 12	495	Coefficient, LLR-Log-Likelihood Ratio, MOR-Median odds ratio, OR-Odds Ratio, RR-Relative
	496	Risk, PVC-Proportional Change in Variance, SNNPR- Southern Nations, Nationalities, and
15 16	497	Peoples' Region.
17 18 19 20	498	Declarations
23	499	Onset to participate
24 25 26	500	The institutional ethical review committee board approved the study. Ethical clearance was
	501	obtained from ethical review board of the University of Gondar. Upon this clearance, the study
29 30	502	was conducted. The congeniality of the data was maintained by using the extracted data only
31 32 33	503	for the study purpose and keeping the data from a third party.
34 35 36	504	Consent for publication
37 38 39	505	Not-applicable
40 41	506	Data sharing statement
42 43	507	The data in which the authors used to produce this manuscript are available upon reasonable
44	508	request
45 46	509	Competing interests
47 48	510	The authors declare that they have no competing interests.
49	511	Funding
50 51	512	No funding
52		
53 54	513	Contributors
55 56		
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514	Proposal preparation, acquisition of data, analysis, and interpretation of data was done by SH,
515	AM, ZM and BF guided the study design data collection and analysis. SH drafted the
516	manuscript and all authors have a substantial contribution in revising and finalizing the
517	manuscript. All authors read and approved the final manuscript.
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521	files for this study.
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Figure 1: Trends in anaemia overtime across the regions in Ethiopia, EDHS 2005 to 2016 681

1 2 3	682 683	Figure 2: Hot spot and cold spot analysis of anaemia in Ethiopian, EDHS 2005 to 20016 Figure 3: Ordinary Kriging interpolation of anaemia in Ethiopia, EDHS 2005 to 2016
4 5	684	Figure 4: Spatial scan statistics analysis of anaemia in Ethiopia, EDHS, 2005-2016
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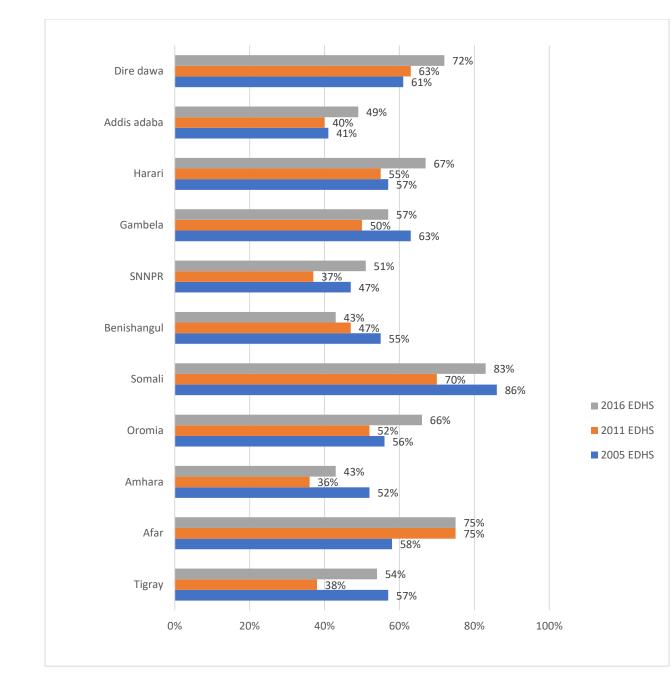
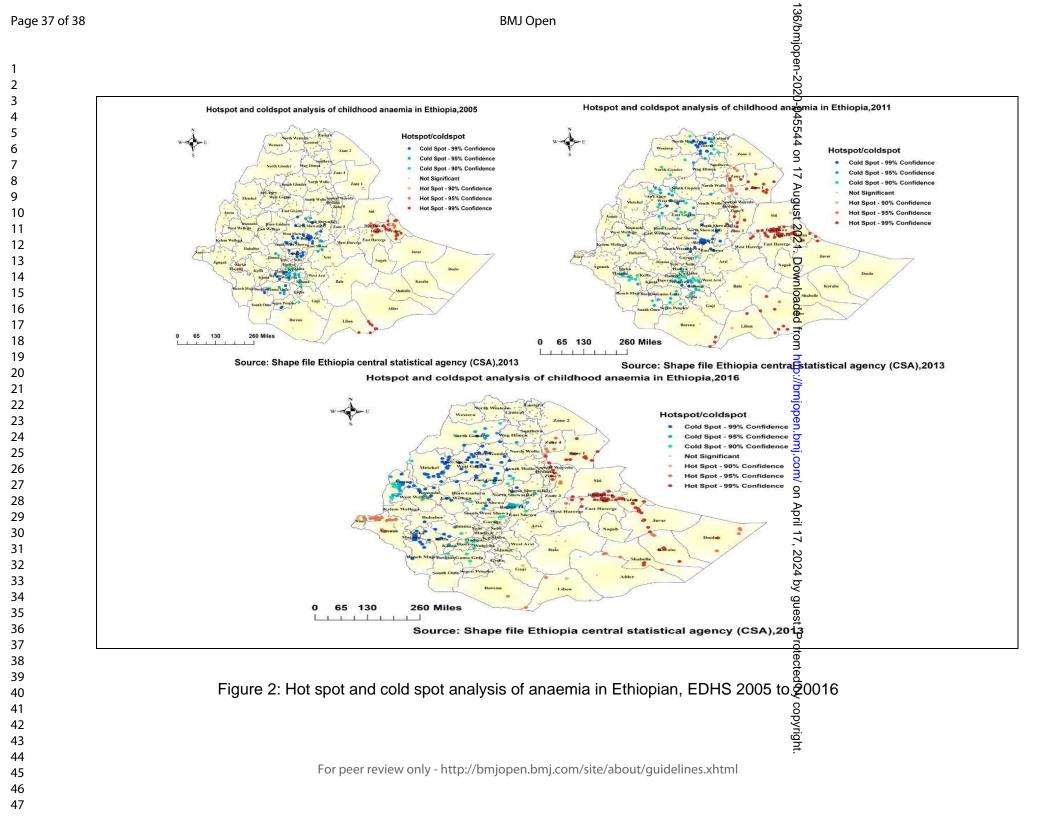
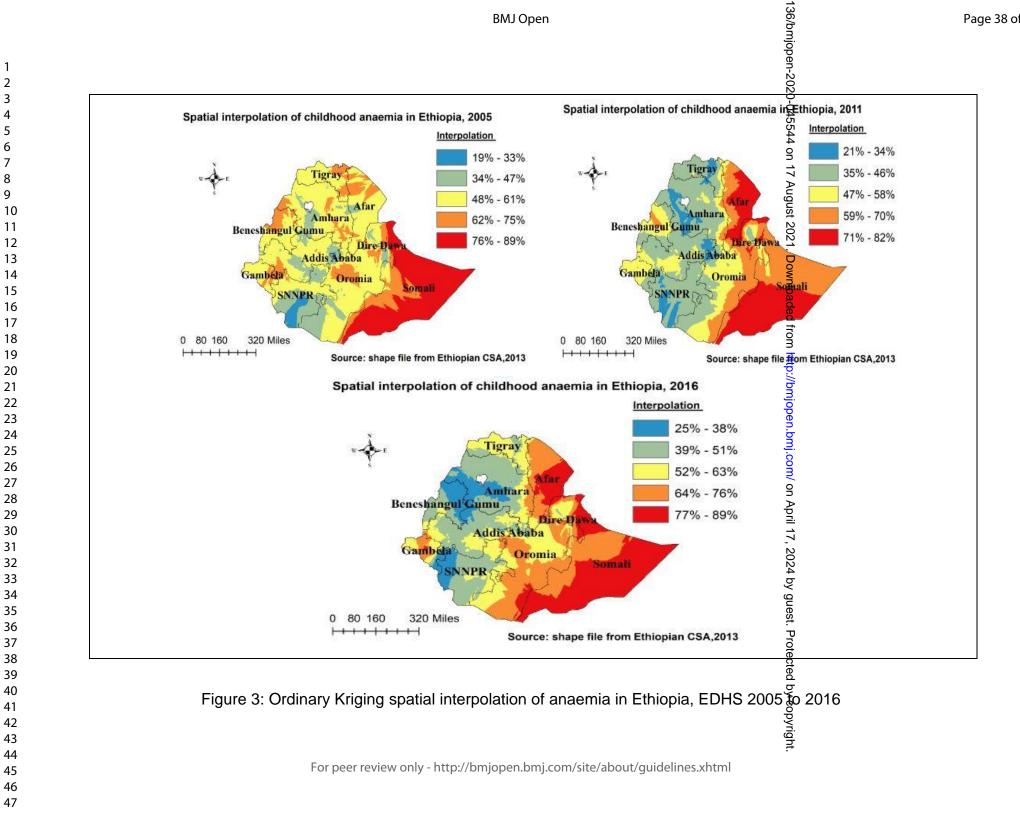


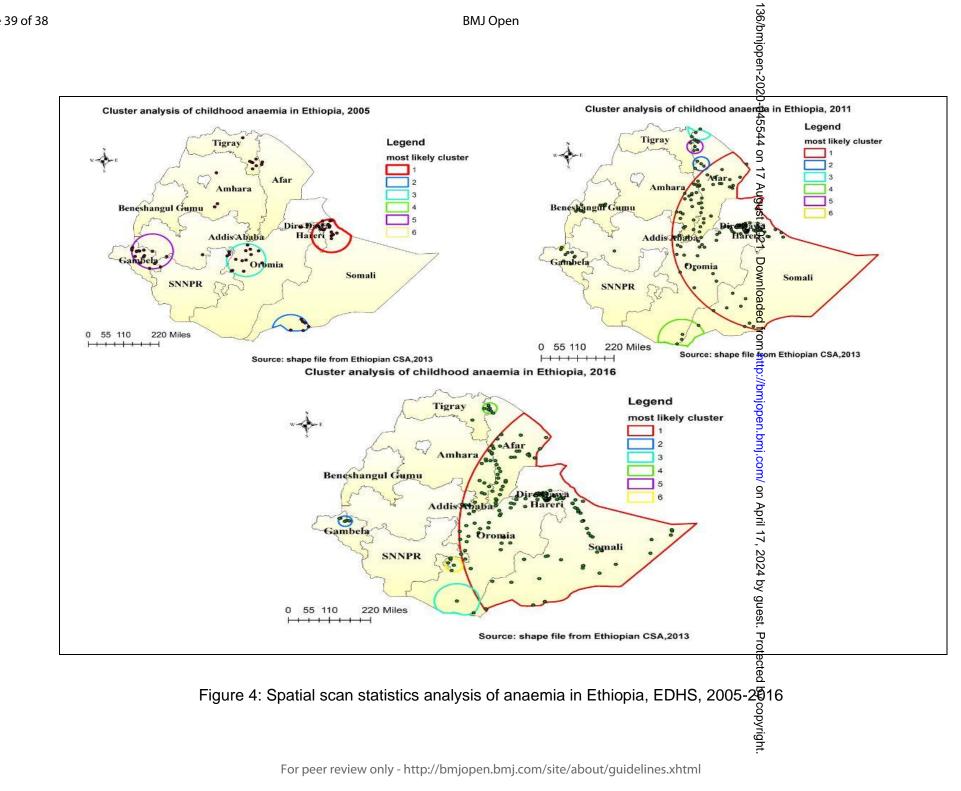
Figure 1: Trends in anaemia overtime across the regions in Ethiopia, EDHS 2005 to 2016



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### Spatio-temporal distribution and associated factors of anaemia among children aged 6–59 months in Ethiopia: a spatial and multilevel analysis based on the EDHS 2005-2016

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1 2	1	Spatio-temporal distribution and associated factors of anaemia among children aged 6–59
2 3 4 5	2	months in Ethiopia: a spatial and multilevel analysis based on the EDHS 2005- 2016
6 7	3	Samuel Hailegebreal <sup>1*</sup> , Araya Mesfin Nigatu <sup>2</sup> , Zeleke Abebaw Mekonnen <sup>2,3</sup> , Berhanu Fikadie
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1 2	22	Abstract
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	23	Objectives: Anaemia is a global public health problem with major health and socio-economic
	24	consequences. Though childhood anaemia is a major public health problem in Ethiopia, there
	25	is limited evidence on the spatio-temporal variability of childhood anaemia over time in the
	26	country. Therefore, this study aimed to assess the spatio-temporal distribution and associated
	27	factors of childhood anaemia using the Ethiopian Demographic and Health Survey (EDHS)
	28	data from 2005-2016.
	29	Design: Survey-based cross-sectional study design was employed for the EDHS.
	30	Setting: Data were collected in all nine regions and two city administrations of Ethiopia in
23 24 25	31	2005, 2011 and 2016.
26 27 28	32	Participants: The source population for this study was all 6–59 months of children in Ethiopia.
29 30	33	A total of 21,302 children aged 6-59 months were included in this study.
31 32 33	34	Outcome measure: The outcome variable was child anaemia status.
34 35 26	35	Results: The prevalence of anaemia declined from 53.9% in 2005 to 44.6% in 2011, but it
36 37 38	36	showed an increase in 2016 to 57.6%. The spatial analysis revealed that the spatial distribution
39 40	37	of anaemia varied across the regions. The spatial scan statistics analysis indicated a total of
41 42	38	22 clusters (RR= 1.5, P-value < 0.01) in 2005, 180 clusters (RR = 1.4, P-value < 0.01) in 2011,
43 44 45	39	and 219 clusters (RR = 1.4, P-value < 0. 0.01) in 2016 significant primary clusters were
46 47	40	identified. The child's age, age of the mother, maternal anaemia status, wealth index, birth
48 49	41	order, fever, stunting, wasting status, and region were significant predictors of childhood
50 51 52	42	anaemia.
52 53 54	43	Conclusions: In this study, childhood anaemia remains a public health problem. The spatial
55 56 57	44	distribution of childhood anaemia varied significantly across the country. Individual-level and

1 2	45	community-level factors were associated with childhood anaemia. Therefore, in r	egions with a				
2 3 4	46	high risk of childhood anaemia, individual and community level factors should be intensified by					
5 6	47	allocating additional resources and providing appropriate and tailored strategies.					
7 8 9 10	48	Keywords: Anaemia, Childhood, EDHS, Spatial, Multilevel, Ethiopia					
11 12	49	Strengths and limitations of this study					
13 14	50	• This study applied different methods to analyses spatial patterns, trend	ds, and used				
15 16 17	51	multilevel logistic regression models, accounting for the nested nature of	EDHS data				
18 19 20	52	• The study was based on three consecutive EDHS datasets representi	ng the whole				
21 22	53	country of Ethiopia					
23 24	54	• The cross-sectional nature of the data prevents causality from being infe	rred between				
25 26 27	55	the independent and dependent variables					
27 28 29	56	Respondents without coordinate (longitude and latitude) were excluded free	om the spatial				
30 31	57	57 analysis, which could affect the generalizability of the findings					
32 33	58						
34 35	59						
36 37 38	60						
39 40	61						
41 42	62						
43 44	63						
45 46	64						
47 48	65						
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# 69 Background

Anaemia is a condition characterized by a low level of haemoglobin in the blood(1). Over 273 million children age under five years suffer from anaemia worldwide(2). Sub-Saharan Africa is one of the most affected regions, accounting for 53.8% of childhood anaemia(2). World Health Organization (WHO) had developed a classification system to facilitate international comparisons of anaemia as public health crises. The problem is considered severe if anaemia prevalence is  $\geq$ 40%, moderate from 20% to 39.9%, and mild from 5% to 19.9%(3). The high prevalence of anaemia and its consequences for child health, especially on their growth and development, have made it an important public health problem. Anaemia also increases the risk of mortality and morbidity that come from other diseases(4,5). 

Anaemia is a public health problem that affects populations in both industrialized and nonindustrialized countries which touches all segments of the population. It is frequently observed among children and pregnant women who are the most vulnerable group because their iron requirements are higher than any other group(6). Anaemia is defined as a haemoglobin level below 11.0 g/dl for children age 6-59 months. Childhood anaemia is mainly caused by dietary iron deficiency, foliate, vitamin B12, vitamin A deficiencies, chronic inflammation, parasitic infections, nutritional deficiencies, hemoglobinopathies and inherited disorders (7,8).

A report from WHO in 2015 regarding global anaemia prevalence, using data for 2011, has shown that prevalence for Africa, southeast Asia, America and the European regions was 62.3%,53.8%,23.3%, and 22.9% respectively(3). In Sub-Saharan Africa, anaemia is a significant public health problem associated with an increased risk of death and impaired cognitive development(9).

Various studies showed that the prevalence of anaemia among children aged 6-59-months
was high and a severe public health problem. Evidence from various studies indicated that age

of the mother, residence, maternal education status(10), an introduction of complementary foods, poor breastfeeding practice, poor utilization of folic acid by mothers(11), maternal anaemia(12), unemployment of the parent, and presence of sickle haemoglobin, household wealth index, and sex of the child were associated with childhood anaemia(13). Few studies have been done on factors associated with anaemia in Ethiopia, to date; the risk areas (hot spot) of anaemia among children are not identified. Thus, this study aimed to assess the spatiotemporal patterns of anaemia among children aged under five years in Ethiopia over the last 15 years to evaluate whether there have been improvements in anaemia risk areas following intervention programs in between the survey periods in Ethiopia. Geographical differences in the causes of anaemia can be partially explained by large-scale variability in 24 103 environmental drivers, particularly nutritional and infectious causes(14). The risk of malaria is known to be associated with elevation and land surface temperature(15). Environmental drivers of anaemia tend to show a high degree of spatial dependency. Therefore, detecting the geographic variation of anaemia during childhood is important to prioritize and design targeted intervention programs to reduce anaemia especially in those areas with a consistently higher risk of anaemia over time. Therefore, this study attempts to fill the gap by investigating the spatio-temporal distribution of anaemia and its associated factors using multilevel model 38 109 analysis in Ethiopia using the EDHS survey between 2005-2016 data. 

Methods and materials 

Study design, setting and period 

A cross sectional survey data from three consecutive EDHS (2005, 2011 and 2016) were used for this study. The surveys were conducted at 5-year interval at the national level. Ethiopia is situated in the Horn of Africa (3°-14°N and 33° – 48°E). Administratively, the country is divided 53 115 <sup>55</sup> 116 into nine regions (Afar, Amhara, Benishangul-Gumuz, Gambela, Harari, Oromia, Somali, 

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Southern Nations, Nationalities, and People's Region (SNNPR), and Tigray) and two cities administration (Addis Ababa and Dire-Dawa). Each region is sub-divided into zones, districts, towns, and kebeles (the smallest administrative units). Source and study population All children aged 6-59-months in Ethiopia were the source population for this study whereas 14 122 all children aged 6-59 months in the selected enumeration areas within five years before the survey were the study population. Sample size and sampling technique For the current study, a total of 21,302 children aged 6-59-months were extracted from three surveys and included in the analysis. Children's record (KR) datasets were used for this analysis. The survey covered all nine regions and the two city administrations of Ethiopia. 26 127 Participants were selected based on a stratified two-stage cluster sampling technique in each survey year. After excluding clusters with zero coordinates and missing information, a total of 503 clusters in 2005, 569 clusters in 2011, and 615 clusters in 2016 were used for analysis. 33 130 The detailed sampling procedure was available in each survey years report(16–18) Data collection tools and procedures The data for this analysis were extracted from Demographic and Health Survey (DHS) program website (www.measuredhsprogram.com) after obtaining the necessary permissions for the download and further analyses. Similarly, spatial location data (latitude and longitudinal) were extracted from the DHS website. After extraction, the missing values for the significant independent variables were excluded and the analysis was undertaken using a complete data 52 138 set. Blood specimens for anaemia testing were collected from all children age 6-59 months for whom consent was obtained from their parents or other adults responsible for them. Blood samples were drawn from a drop of blood taken from a finger prick or a heel prick in the case 

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of children age 6-11 months and collected in a microcuvette. Haemoglobin analysis was carried

out on-site using a battery-operated portable HemoCue analyser. 

Key variables and measurements 

**Dependent variable**: The study variables were grouped into dependent and independent variables. The dependent variable is childhood anaemia status, categorized as "anaemic or not-anaemic". Children whose haemoglobin level was less than 11g/dl were considered anaemic and not anaemic otherwise. 15 147

Independent variables: 

20 149 sociodemographic (religion, age of mother, marital status, educational status, husband 22 150 education, wealth index, mothers working status, numbers of under five children) Maternal and Child- related (child's sex, child's age, birth size, birth order, maternal BMI, maternal anaemia <sub>27</sub> 152 status, breastfeeding, fever, diarrhoea, vitamin supplement, stunting status and wasting 29 153 status). Community-level variables (residence, region, community women education and community women poverty). 

We created community women education and community women poverty variables by aggregating the individual characteristics within their clusters. The aggregates were computed 36 156 using the median values of the proportions of women in each category of a given variable. We categorized the aggregate values of a cluster into groups based on national median values, 43 159 since all aggregates were not normally distributed.

46 160 Community women education: was defined as the proportion of women who attended 48 161 primary, secondary, and higher education within the cluster. The aggregate of individual primary, secondary, and higher educational attainment can show the overall educational and academic status of women within the cluster. They were categorized into two categories a 

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higher proportion of women education within the cluster and a lower proportion of women education based on the national median value. 

**Community women poverty status:** defined as the proportion of poor and poorest mothers within the cluster. For each cluster, the proportion of poor and poorest as-was aggregated and show overall poverty status within the cluster. It was categorized into two categories based on national median value as higher proportion of poor/poorest mother's and lower proportion of mothers within a cluster. 15 170

#### Data management and analysis

The data were cleaned using STATA version 14.1 software and microsoft excel. The data were weighted using sampling weight, primary sampling unit, and strata before any statistical 24 174 analysis to restore the representativeness of the survey and take into account the sampling design to obtain reliable statistical estimates.

#### **Spatial analysis**

For the spatial analysis, ArcGIS V.10.7 software, and SaTScan V.9.6 software were used. 

The spatial scan statistics uses a circular scanning window that moves across the study area to identify a significant spatial clustering of childhood anaemia. 37 179

#### 40 180 Spatial autocorrelation analysis

42 181 The spatial autocorrelation (Global Moran's I) statistic measures whether childhood anaemia patterns were dispersed, clustered or randomly distributed in the study area. Moran's I is a 47 183 spatial statistic used to measure spatial autocorrelation by taking the entire dataset and produce a single output value that ranges from -1 to +1. Moran's I values close to -1 indicate the spatial distribution of anaemia was dispersed, whereas Moran's I close to +1 52 185 indicate the spatial distribution of anaemia was clustered, and an I value of 0 means anaemia 

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is distributed randomly. Anselin's Local Moran's / (ALMI) identifies High-High clusters, Low-

Low clusters, and spatial outliers (High-Low and Low-High).

# 189 Hot spot analysis (Getis-Ord Gi\* statistic)

Local Moran's I, Gettis-OrdGi\* statistics was computed to measure how spatial autocorrelation
of anaemia among children age under five years varies across the regions. In this analysis,
Z-score and p-value were computes to determine the statistical significance of the clustering.
Statistical output with high GI\* indicates 'hotspot' (high-risk areas) of childhood anaemia,
whereas low GI\* shows a 'cold spot' (low-risk areas) of anaemia in Ethiopia.

### 195 Spatial interpolation

The unsampled areas of Ethiopia were also predicted by using data from sampled locations through the spatial interpolation technique. There are various deterministic and geostatistical interpolation methods. Among all of the methods, ordinary Kriging and empirical Bayesian Kriging are considered the best methods since they incorporate spatial autocorrelation and statistically optimize the weight. Ordinary Kriging spatial interpolation method was used for this study for predictions of childhood anaemia in unobserved areas of Ethiopia since it had low mean square error and residual as compared to the other interpolation techniques.

### 203 Spatial scan statistical analysis

Spatial scan statistical analysis was employed to Identifying most likely(primary) and secondary spatial clusters of childhood anaemia. This method is widely recommended as it is very important in detecting local clusters and has higher power than other available spatial statistical methods. Bernoulli based model was employed to test for statistically significant spatial clusters of anaemia using Kulldorff's SaTScan V.9.6 software. Children age under five years with anaemia were taken as cases, and those who are not-anaemic as controls to fit the Bernoulli model. The default maximum spatial cluster size of <50% of the population was used.

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The scanning window with maximum likelihood was the most likely cluster, and the p-value was assigned to each cluster based on Monte Carlo hypothesis testing(19). Associated factors of anaemia Four models were constructed for multilevel logistic regression analysis using melogit STATA command. The first model (a random intercept model) was null model without predictors to 12 215 determine the extent of cluster variations in anaemia. The second model (model I) was adjusted with individual-level variables. The third model (model II) was adjusted for community-19 218 level variables, while the fourth model (model III) was fitted with both individual-level and community-level variables simultaneously. For model comparison, we used Log-Likelihood Ratio (LLR) and deviance. Intra-class correlation (ICC), median odds ratio (MOR), and proportional change in variance (PCV) were computed to measure the variation between clusters. The intra-class correlation coefficient (ICC) quantifies the degree of heterogeneity of childhood anaemia between clusters (the proportion of the total observed individual variation in anaemia that is attributable between cluster variations) calculated as  $ICC = \frac{6^2}{(6^2 + \sigma_b^2)}$  (20), where,  $6^2$  is the community level variance and  $\sigma_b^2$  indicates individual level 39 226 variance. The individual variance ( $\sigma_b^2$ ) equal to  $\pi^2/3$ . 42 227 Median Odds Ratio (MOR) is guantifying the variation of the odds ratio between the cluster at high risk of anaemia and cluster at lower risk when randomly picking out two clusters (EAs).  $MOR = e^{(0.95 * \text{ sqrt}(6^2))}$  (21) where,  $6^2$  indicates that cluster level variance. Proportional Change in Variance (PCV) the proportion of the total observed individual variation of childhood anaemia that is attributable to between cluster variations. In the multivariable

multilevel logistic regression analysis variables with a p-value of <0.05 were considered as statistically significant. Adjusted Odds Ratio (AOR) with their corresponding 95% confidence interval was determined to identify factors associated with anaemia. Multicollinearity was checked using the variance inflation factor (VIF), which indicates that there is no multicollinearity because all variables have VIF less than 10%. The final model was the best fitted model since it had the highest log-likelihood and the lowest deviance value.

16 239 Patient and public involvement

240 This study did not involve patients and the public

**Results** 

# 24 242 **Descriptive characteristics of the study population**

A total of 21,302 children with known haemoglobin levels (3,868 in 2005, 8,958 in 2011, and 8467 in 2016) were included in this study. The prevalence of anaemia for the three consecutive surveys was 53.9%, 44.6%, and 57.6% in 2005, 2011, and 2016 EDHS data respectively. The majority of the participants were in the age group of 36-47 (23.7%), 36-47 (24.4%), and, 48-59 34 246 (22.9%) in EDHS 2005, 2011, and 2016 survey respectively. The mean age of children was 32.6 ±15.6-SD, 32.6±15.4-SD, and 31.7±15.6-SD in 2005, 2011, and 2016 respectively. 41 249 Among the three survey, male participants were higher in 2011 and 2016 compared to 2005 EDHS survey. The majority of children were from rural resident in three surveys. The educational status of women was 78.6%, 70.1%, and 67.1% were unable to read and write in 2005, 2011, and 2016 survey years respectively. Children from poor and middle class wealth 48 252 50 253 index families were more anaemic than children from rich families across the three EDHS survey years (Table 1). In this study, the trends in the childhood anaemia rate were fluctuates <sub>55</sub> 255 across regions (Fig.1). 

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2	Table 1: Descriptive characteristics of study participants included in the analysis for childhood anaemia five years preceding the survey from EDHS 2005-2016 in Ethiopia			
4 5	Variables	2005 (N, 3868)	2011 (N, 8958)	2016 (N, 8476)
6 7 8		Frequency (%)	Frequency (%)	Frequency (%)
9 10 11	Sex of child			
12 13	Male	1,931(49.9)	4,500(51.4)	4,395(51.9)
14 15 16	Female	1,937(50.1)	4,358(48.7)	4,081(48.2)
17 18	Age of child in month			
19 20	6-11	418 (10.8)	1,029(11.5)	1,000(11.8)
21 22 23	12-23	842 (21.76)	1,804(20.14)	1,902(22.4)
23 24 25	24-35	825 (21.3)	1,895(21.2)	1,803(21.3)
26 27	36-47	919 (23.7)	2,184(24.4)	1,832(21.6)
28 29 30	48-59	864 (22.3)	2,047(22.9)	1,939(22.9)
31 32	Mean ± SD	32.6 ±15.6	32.6±15.4	31.7±15.6
33 34	Residence			
35 36 37	Urban	244 (6.3)	1,047(11.7)	857(10.1)
38 39	Rural	3,624 (93.7)	7,911(88.3)	7,619(89.9)
40 41 42	Religion			
43 44	Orthodox	1,624 (42.0)	3,416(38.1)	2,913(34.4)
45 46 47	Muslim	1,276 (33.0)	3,108(34.7)	3,432(40.5)
47 48 49	Protestant	836 (22.0)	2,151(24.0)	1,874(22.1)
50 51	Others	133 (3.0)	283(3.2)	258(3.0)
52 53 54	Women age			
55 56 57	15-29	1,930(49.9)	4,908(54.9)	4,356(51.4)
58 59	<b>F</b> arman 1			12

30-39	1,474(38.1)	3,223(36.0)	3,335(39.3)
40-49	464(12.0)	828(9.1)	785(9.3)
Women education			
No education	3,042 (78.6)	6,285(70.1)	5,685(67.1)
Primary	684 (17.7)	2,389(26.7)	2,275(26.8)
Secondary	136 (3.5)	168(1.9)	346(4.1)
Higher	7 (0.2)	117(1.3)	170(2.0)
Marital status			
Single	7(0.2)	50(0.6)	45(0.5)
Married	3,704(95.7)	8,425(94.0)	8,129(95.9)
Widowed	80(2.1)	178(2.0)	93(1.1)
Divorced	78(2.0)	306 (3.4)	210(2.5)
Husband education			
No-education	2,235 (58.0)	4,532(50.9)	4, 33(51.1)
Primary	1,233(32.0)	3,710(41.7)	3,273(38.6)
Secondary	362(9.0)	412(4.6)	572(6.8)
Higher education	31(1.0)	255 (2.8)	300(3.5)
Wealth index			
Poor	1,697(43.7)	4,048(45.2)	3,977(46.9)
Middle	854(22.1)	1,873(20.9)	1,821(21.5)
Rich	1,318(34.1)	3,038 (33.9)	2,678(31.6)
Women working status			
Not working	2,841(73.5)	5,793(64.7)	6,140(72.4)

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1	Working	1,027(26. 5)	3,165(35.3)	2,336(27.6)		
2 3	Total	3,868(100)	8,958(100)	8,476(100)		
4 5		0,000(100)	0,000(100)	0,0(100)		
6 258 7						
8 9 259 10	Community-level characteristi	cs of the study pop	oulation This stu	dy revealed that there		
11 260 12	was a significant regional varia	tion of childhood and	aemia, with 83.3	%, 75.5%,74.5%, and		
<sup>13</sup> 261 14	68.8% in Somali, Afar, Dire Dawa and Harari respectively. However, Amhara, and Benishangul					
15 16 262	regions were relatively low compared to other regions.					
17 18 263 19	Also, childhood anaemia varies by place of residence. Children residing in communities with					
<sup>20</sup> 264 21	low women poverty level had a lower percent of anaemia (51.2%) than high community poverty					
22 23 265	level (62.5%). Children from low community women education (59.5%) were more anaemic					
24 25 266 26	than children resided from high community women educational (53.6%) (Table 2).					
27 28 267	Table 2: Community-level factors of under five children participated in EDHS (2016),					
<sup>29</sup> 30268	Ethiopia. (N, 8476)					
31 32 33	Community-level factors	Not-anaemic (%)	Anaemic (%)	Total (100%)		
34 35	Residence					
36 37	Urban	435(50.6)	424(49.4)	857		
38 39 40	Rural	3164(41.5)	4455(58.5)	7619		
41 42	Region					
43 44	Tigray	263(46.0)	309(54.0)	572		
45 46 47	Afar	21(25.3)	62(74.5)	83		
47 48 49	Amhara	950(57.5)	703(42.5)	1653		
50 51	Oromia	1273(34.2)	2446(65.8)	3719		
52 53	Somali	58(16.7)	290(83.3)	348		
54 55 56			200(00.0)			

Beneshangul	51(56.6)	39(43.4)	90	
SNNPR	875(49.1)	906(50.9)	1781	
Gambela	8(42.1)	11(57.9)	19	
Harari	5(31.2)	11(68.8)	16	
Addis Ababa	82(50.9)	79(49.1)	161	
Dire Dawa	9(28.1)	23(71.9)	32	
Community women education				
Low	2281(40.5)	3358(59.5)	5639	
High	1315(46.4)	1520(53.6)	2837	
Community women poverty				
Low	1815(48.8)	1905(51.2)	3719	
High	1782(37.5)	2974(62.5)	4756	
Spatio-temporal distribution of a	naemia among chil	dren age 6-59 n	nonths in Ethiopia	
opatio-temporal distribution of allaelina among children age 0-00 months in Ethiopia				
The spatial distribution of childhood anaemia varied across regions in all surveys. The spatial				
autocorrelation analysis result indicated that childhood anaemia had spatial dependency in				
2005, 2011, and 2016 (Moran's I: 0.176, 0.18, and 0.09, respectively at P-value < 0.01).				
Hot spot analysis of the three surveys				
The spatial distribution of childhood anaemia in Ethiopia was different in all the three survey				
periods. In EDHS 2005, a high proportion of childhood anaemia was detected in Dire Dawa,				
Harari, eastern Oromia, Beneshangul in Metekel zone, Gambela, southern and eastern Tigray,				
and Somali region mainly Liben, Afdar, and Fafna zone which was hotspot area within 95%				
confidence level. On the counterpart, GamoGofa, Wolayita, Hadiya, Southern Omo, and				
			15	
For peer review only - I	nttp://bmjopen.bmj.com/s	ite/about/guidelines		
	SNNPR Gambela Harari Addis Ababa Dire Dawa Community women education Low High Community women poverty Low High Spatio-temporal distribution of a The spatial distribution of childhood autocorrelation analysis result indi 2005, 2011, and 2016 (Moran's I: 0 Hot spot analysis of the three su The spatial distribution of childhood periods. In EDHS 2005, a high pro Harari, eastern Oromia, Beneshang and Somali region mainly Liben, A	SNNPR875(49.1)Gambela8(42.1)Harari5(31.2)Addis Ababa82(50.9)Dire Dawa9(28.1)Community women education2281(40.5)High1315(46.4)Community women poverty1315(46.4)Low1815(48.8)High1782(37.5)Spatio-temporal distribution of childhood anaemia varied actautocorrelation analysis result indicated that childhood2005, 2011, and 2016 (Moran's I: 0.18, and 0.09)Hot spot analysis of the three surveysThe spatial distribution of childhood anaemia in Ethiopperiods. In EDHS 2005, a high portion of childhood anaemia in Ethiopaud Somali region mainly Liben, Atdar, and Fafna zonconfidence level. On the counterpart, GamoGofa, W	SNNPR875(49.1)906(50.9)Gambela8(42.1)11(57.9)Harari5(31.2)11(68.8)Addis Ababa82(50.9)79(49.1)Dire Dawa9(28.1)23(71.9)Community women education1315(46.4)3358(59.5)High1315(46.4)1520(53.6)Community women poverty1815(48.8)1905(51.2)Low1815(48.8)1905(51.2)High1782(37.5)2974(62.5)The spatial distribution of childhood anaemia varied arrest regions in a autocorrelation analysis result indicated that childhood anaemia had as 2005, 2011, and 2016 (Moran's I: vite, 0.18, and 0.09. vitespectively at Hot spot analysis of the three surversThe spatial distribution of childhood anaemia in Ethiopia was different periods. In EDHS 2005, a high provision of childhood anaemia in Sthiopia was different periods. In EDHS 2005, a high provision of childhood anaemia ware area anaemia was a at a anaemia ware and a anaemia ware anaemia	

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Segen zone of SNNPR, Addis Ababa, central Oromia, Jima, north Shewa zone were cold spot area. In EDHS 2011, a highly significant clustering of childhood anaemia was detected in Somali, Dire Dawa, Harari, Afar, Gambela, Beneshangul, eastern Oromia, Bale, Arsi zone were the hotspot areas within 95% level of confidence. The low hotspot area of childhood anaemia was detected in central Tigray, East and West Gojam, North Gondar, a central part of Oromia, Addis Ababa and SNNPR were areas identified as the low percentage of childhood anaemia in the 2011 EDHS survey. 15 286

In2016 EDHS sampled data, hot spot (high risk) regions for childhood anaemia were observed 18 287 20 288 in Somali, Dire Dawa, Harari, Gambela, eastern, and Southern part of Oromia. However, Amhara, Beneshangul, and SNNPR were identified as cold spot (low risk) regions for childhood anaemia within a 95% confidence interval (Fig.2) 

#### **Spatial interpolation**

Based on 2005 EDHS sampled data, the geostatistical analysis predicts that the highest 30 292 prevalence of childhood anaemia (65.75%-88.89%) was detected in east Oromia, Ilubabur, Arsi, some parts of Beneshangul, Agnuak zone in Gambela, north Shewa Amhara region, south and central Tigray, Afar in zone2, some parts of Dire Dawa and Somali. In EDHS-2011 37 295 Geostatistical analysis, a high percentage of anaemia was detected in Afar, most parts of Somali, Oromia in east Harerge and Borena, some part of Dire Dawa, and the Meketel zone in Beneshangul. In 2016 EDHS most of Somali, some parts of Gambela, Guji and some parts of Borena, ast Shewa, East Harerge and Arsi in Oromia and part of Dire Dawa were highly prevalent areas in childhood anaemia (Fig.3) 

#### Spatial scan statistics

In 2005 EDHS, a total of 3 significant (one most likely/primary and two secondary) clusters were identified in spatial scan analysis. The primary cluster spatial window was located in 56 303

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Somali. it was centered at (9.018373 N, 43.110635 E) with a radius of 97.93 km, a relative risk (RR) of 1.5, a Log-Likelihood ratio (LLR) of 20.03, at p < 0.01. It showed that children within the spatial window had 1.5 times more likely a higher risk of anaemia than thechildren outside the spatial window areas. The secondary clusters scanning window was located in the southern part of Somali region. It was centered at (3.998656 N, 41.240691 E) with a radius of 92.08 km, a relative risk (RR) of 1.7 at p-value < 0.01. It showed that children within the spatial window had a 1.7 times higher risk of anaemia than children outside the window. 15 310

In 2011 EDHS, 10 clusters were identified and five of them were significant clusters at a p-18 311 20 312 value <0.05. A total of 180 locations/spots with a total sampled population of 2478 were found in the primary cluster spatial window with a significant p-value < 0.01. The primary cluster spatial window was located mainly in Somali, Afar, eastern Oromia, Dire Dawa, and Harari. It 27 315 was centered at (8.975207 N, 43.790264 E) with a radius of 540.29 km, a relative risk (RR) of 1.4, a log-likelihood ratio (LLR) of 127.79 at p-value < 0.01. It showed that children within the spatial window had 1.4 times more likely a higher risk of anaemia than the children outside the 34 318 spatial window areas. The secondary cluster spatial window was located mainly in Afar region. It was centered at (12.758587 N, 40.175990 E) with a radius of 39.58 km a relative risk (RR) of 1.7,a log-likelihood ratio (LLR) of 21.5 at P-value<0.01. 

In 2016 EDHS, 7 clusters (one most likely cluster) located in Somali, Afar, eastern Oromia, Dire Dawa, and Harari. It was centered at (7.650693 N, 47.007920 E) with a radius 912.19 km, 46 323 a relative risk (RR) of 1.4 and a Log-Likelihood ratio (LLR) of 182.86 at P-value<0.01. It showed that children within the spatial window had a 1.4 times higher risk of anaemia than outside the window. Secondary clusters spatial window was located in Gambela. It was centered at 53 326 (8.195862 N, 34.289837 E) with a radius of 29.01 km, a log-likelihood ratio (LLR) of 18.80 at p-value < 0.01(Fig.4).

The intra-cluster correlation coefficient (ICC) in the null model indicated that 19% of the total variability for childhood anaemia was due to differences between clusters. The remaining unexplained 81% were attributable to individual differences. The median odds ratio for anaemia was 2.3 in the null model, indicating variation between clusters. If we randomly select 11 332 children from two different clusters children at the cluster with a higher risk of anaemia had 2.3 times higher odds of experiencing anaemia than children at the cluster with a lower risk of anaemia. A bivariable analysis was done to identify variables for multivariable multilevel logistic 18 335 20 336 analysis. A variable with a p-value < 0.25 were considered for multivariable logistic regression analysis.

### Individual-level predictors for anaemia

In multivariable multilevel mixed-effect logistic regression analysis child's age, wealth index, age of mother, maternal anaemia status, birth order, fever, stunting, and wasting status were significant predictor of childhood anaemia. 33 341

Children age between 12-23 months (AOR = 0.66, 95%CI = 0.53-0.81), between 24-35 36 342 months (AOR= 0.35, 95% CI = 0.28-0.43), between 36–47 months (AOR = 0.23-95% CI = 0.19-0.29), and between 48–59 months (AOR = 0.15, 95%CI = 0.12-0.19) were less likely to develop 43 345 anaemia compared with children age between 6–11 months.

46 346 The likelihood of developing anaemia for those children residing with the family wealth index 48 347 of middle and rich were lower by 21% (AOR=0.79, 95%CI = 0.67-0.94), and 23% (AOR=0.77, 95%CI = 0.65-0.91), respectively as compared with children with low wealth index. Children whose mother age were between 40-49 had 25% decreased odds of developing childhood anaemia compared to age 15-29, (AOR=0.75, 95%CI = 0.59-0.95). 55 350 

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1 2	351	The odds of experiencing anaemia for those birth orders 4-5, six and above six were 1.22 times
3 4	352	(AOR=1.22, 95%CI = 1.01-1.47) and, 1.35 times (AOR=1.35, 95%CI = 1.08-1.67) higher as
5 6	353	compared with first-order respectively. The odds of developing anaemia of children born from
7 8 9	354	anaemia history mother were 1.39 higher more elevated than those born from not anaemic
9 10 11	355	history before. Children who had fever were 39% (AOR =1.39, 95% CI: 1.24-1.58) more likely
12 13	356	to develop anaemia than their counterparts. Children with moderate and severe stunting status
	357	were 35% (AOR=1.35, 95% CI: 1.17-1.54) and, 96% (AOR=1.95, 95% CI: 1.68-2.28), more
16 17 18	358	likely to develop anaemia respectively, compared to no stunting status. Similarly, children who
19 20	359	had to sever wasting status were 51% more (AOR =1.51, 95% CI: 1.07-2.12) likely to develop
21 22	360	anaemia compared with those children who had no wasting.
23 24		
25	361	Community-level predictors for anaemia
26 27 28	362	The multivariable multilevel logistic regression analysis region was significantly associated with
	363	community-level factors for childhood anaemia.
31 32 33	364	Odds of children live in Somali were 5.65 times (AOR=5.65, 95% CI: 3.92-8.16), Dire Dawa
34 35	365	3.45 times (AOR=3.45, 95% CI: 2.27-5.26), Afar 3 times (AOR=3.00, 95% CI: 2.09-4.34), and
	366	Oromia 2.34 times (AOR=2.34, 95% CI: 1.73-3.18) had more likely to develop childhood
38 39 40	367	anaemia compared to Amhara region. Similarly, the odds of developing anaemia in Addis
40 41 42	368	Ababa were 2 times (AOR=2.00, 95% CI: 1.40-3.16), Gambella 1.94 times (AOR=1.94, 95%
	369	CI: 1.32-2.84), and Tigray 1.46 times (AOR=1.46, 95% CI: 1.08-1.98), more likely as compared
45 46 47	370	to Amhara region. Beneshangul and SNNPR had not significantly different in the prevalence
47 48 49	371	of anaemia than the reference region Amhara (Table 3).
50 51	372	Table 3: Multilevel logistic regression analysis result of both individual and community-
52 53	373	level factors associated with anaemia in Ethiopia, EDHS 2016
54	274	
55 56	374	
57		
58 59		19
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Age of child in mo 6-11 12-23		AOR (95% CI) ual-level factors	AOR (95% CI)	AOR (95% CI)
6-11		ual-level factors		
6-11	nth -			
	-			
12-23		1	-	1
	-	0.66[0.54-0.82] **	-	0.66 [0.53-0.81] **
24-35	-	0.35[0.28-0.44] **	-	0.35 [0.28-0.43] **
36-47	-	0.23[0.18-0.28] **	-	0.23 [0.19-0.29] **
48-59	-	0.15[0.12-0.19] **	-	0.15 [0.12-0.19] **
Religion				
Orthodox	•	1	-	1
Muslim	-	2.07[1.77-2.47] **	-	1.21 [0.97-1.46]
Protestant		1.20 [1.00-1.48] *		1.10 [0.86-1.37]
Others	-	1.55[1.07-2.32] *	-	1.44[0.96-2.13]
Wealth status				
Poor	-	1	-	1
Middle	-	0.71[0.61-0.84] **	-	0.79 [0.67-0.94] *
Rich	-	0.72[0.63-0.85] **	-	0.77 [0.65-0.91] *
Child size at birth				
Small	-	1	-	1
Average	-	0.96[0.84-1.09]	7-	0.93 [0.80-1.07]
Large	-	0.94[0.81-1.08]	O	0.96 [0.84-1.10]
Birth order				
<b>1</b> st	-	1	-	1
2-3	-	1.09[0.94-1.28]	_	1.13[0.97-1.32]
4-5	-	1.17[0.97-1.40]	-	1.22 [1.01-1.47] *
6 and above	-	1.30[1.05-1.62]	-	1.35 [1.08-1.67] **
No of children und	ler 5			
1-2 children	-	1	-	1
≥ 3 children	-	1.22[1.1-1.4] *	-	1.09 [0.94-1.27]
Maternal anaemia				
Not anaemic	-	1	-	1
Anaemic	-	1.51[1.34, 1.72] **	-	1.39 [1.24-1.58] **
				20

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Maternal BMI				
≥18.5 kg/m2	-	1	-	1
<18.5 kg/m2	-	1.12[0.97-1.26]	-	1.05 [0.92-1.19]
Women working sta	itus			
Not-working	-	1	-	1
Working	-	0.88[0.77-0.99] *	-	0.92 [0.81-1.04]
Women age				
15-29	-	1		1
30-39	-	0.91[0.71-1.06]	-	0.90 [0.78-1.04]
40-49 🧹	-	0.75[0.59-1.12] *	-	0.75 [0.59-0.95] *
Breastfeeding				
No	-	1	-	
Yes	-	0.92[0.81-1.04]	-	0.98 [0.87-1.12]
Vitamins in last 6 m	onth			
No	-	1	-	
Yes	-	0.90[0.81-1.09]	-	0.93 [0.84-1.05]
Diarrhea last 2 weel	k			
No	-	1	-	1
Yes	-	0.88[0.73, 1.04]	-	0.90 [0.76-1.07]
Fever in last 2 week	S			
No	-	1	-	1
Yes	-	1.35[1.15-1.59] **	O,	1.32 [1.13-1.56] *
Stunting status				
No-stunting	-	1	-	1
Moderate	-	1.27[1.10-1.46] **	-	1.35 [1.17-1.54] **
stunting				
Severely	-	1.81[1.55-2.11] **	-	1.96 [1.68-2.28] **
stunting				
Wasting status				
No-wasting	-	1	-	1
Moderate	-	1.27[1.11-1.45]	-	0.98 [0.80-1.19]

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1 51	[1.07-2.	121 *
1.01	[1.07 2.	14

1	Severe wasting	-	1.68[1.55-2.10] *	-	1.51 [1.07-2.12] *
2 3		Comm	unity/cluster-level f	actors	
4 5	Region				
6	Amhara	-	-	1	1
7 8	Tigray	-	-	1.46[1.09-1.97] **	1.46 [1.08-1.98] **
9 10	Afar	-	-	3.90 [2.84-5.35] **	3.00 [2.09-4.34] **
11 12	Oromia	-	-	2.48 [1.89-3.25] **	2.34 [1.73-3.18] **
13	Somali	-	-	6.34[4.65-8.63]	5.65 [3.92-8.16] **
14 15	Beneshangul	-	-	0.86 [0.62-1.17]	0.81 [0.58-1.15]
16 17	SNNPR	-	-	1.33 [1.00-1.76]	1.30 [0.94-1.80]
18 19	Gambela	•	-	1.93 [1.38-2.69] **	1.94 [1.32-2.84] **
20	Harari	-	-	3.08 [2.15-4.43] **	2.98 [1.99-4.46] **
21 22	Addis Ababa	-	<u> </u>	1.91[1.29-2.83] **	2.10 [1.40-3.16] **
23 24	Dire dawa	-	-	3.92 [2.67-5.77] **	3.45 [2.27-5.26] **
25	Residence				
26 27	Urban	-	-	1	1
28 29	Rural	-		1.40[1.12-1.78]	1.28 [0.99-1.64]
30 31	Community wome	en educatio	on 🖌		
32	Low	-	-	1	1
33 34	High	-	-	1.07[0.90-1.26]	1.13[0.94-1.34]
35 36	Community wome	en poverty			
37 38	Low	-	-		1
39	High	-	-	1.41[1.17-1.68] *	1.15[0.94-1.40]
40 41	Model comparisor	n and rand	om effect		
42 43	ICC	0.19	0.12	0.08	0.07
44 45	Log-likelihood	-4981.63	-4513.17	-4836.83	-4436.60
46	Deviance	9963.26	9026.34	9673.66	8873.20
47 48	MOR	2.30	1.72	1.42	1.38
49 50	PVC (%)	Ref	41.20	60.10	62.59
51 375 52 53 376 54 377 55 377 56 378 57 58 59	-			.05-0.01 *: p-value <	22
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### Discussion

This study tried to identify spatio-temporal distribution and predictors of childhood anaemia across the regions in Ethiopia. The 2005, 2011, and, 2016 Ethiopian Demographic and Health Survey data were used for this analysis. The anaemia trend over these years was decreased from 2005 to 2011, while the rate significantly increased from 2011 to 2016. The study revealed that 57.56% [CL: 0.56-0.59] of children were anaemic in 2016. This finding is in line with a study done in Gondar, Northwest Ethiopia 58.6% (22), higher than the study done in cape Verde, west Africa 51.8%(23), and southern Ethiopia(24). Among children aged 6-59-months, anaemia is still considered as a significant public health problem in Ethiopia, and consequent 20 387 22 388 by various factors. Childhood anaemia in this study was influenced by background characteristics such as child's age, age of the mother, region, wealth status, and maternal related factors. 

The spatial analysis found that the spatial pattern of childhood anaemia across the country was substantially varied. The spatial autocorrelation analysis result indicated that childhood 32 392 anaemia had spatial dependency in 2005, 2011, and 2016 (Moran's I: 0.176, 0.18, and 0.09, respectively at P-value < 0.01). These findings are in line with a studies done in Nigeria, Malawi, Tanzania, and Uganda (25,26). 39 395

Scan statistical analysis showed that Eastern Somali and the southern part of Somali region 42 396 were primary (most likely) and secondary clusters in 2005 respectively. Whereas, in 2011 the spatial window was located in Somali, Afar, Eastern Oromia, Dire Dawa, and Harari region. It was centered at (8.975207 N, 43.790264 Ewith radius of 540.29 km with a significant p-value. Similarly, spatial sat scan analysis showed that Somali, Afar, Eastern Oromia, Dire 54 401 Dawa, and Harari regions were hotspot areas in the 2016 EDHS survey. In addition, this study

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The spatial analysis indicated the hotspots areas of anaemia were situated in the East,
 Northeast, and Western parts, whereas, Central area, and South, and Northwest parts were
 cold spot parts of Ethiopia. The observed variability of childhood anaemia might be attributed
 to the regional deference of economy, healthcare facility and food availability(27).

This study indicated that children age 12-59 months were less affected by childhood anaemia. This finding was consistent with studies conducted in Ethiopia and Togo (28–30)(31). This could be explained by the fact that children who are getting older receive a richer and complete 23 411 diet, with a sufficient intake of iron which could prevent the occurrence of iron deficiency anaemia. The finding of this study indicated that children whose women age was between 40-49 were less anaemic as compared to age 15-29. This finding was consistent with other studies conducted in Sub-Saharan Africa and Ghana (12,32). 30 414

Women with the age group of 15-29 are consists adolescent population group who are more 33 415 at-risk population segments for anaemia. They are vulnerable to malnutrition because they are growing faster than at any time after their first year of life which contributes to the 40 418 intergenerational cycle of malnutrition. Iron deficiency is one of the most common forms of 42 419 malnutrition among Ethiopian adolescent girls that result iron deficiency anaemia. Aside from, growing adolescent mother and her baby's bodies may compete for nutrients, raising the infant's risk of low birth weight; however, the lack of such nutrients might lead to anaemia. 

Children from households of middle and rich wealth indexes were less affected by childhood 52 423 anaemia as compared to children from a poor household. This finding is in line with studies in Nigeria and Northern Ethiopia (25,33). This is due to the reason that children from poor households are less likely to get iron-rich foods like animal foods and vitamin-rich foods 

especially vitamins A and C which are very important for iron absorption. 

Maternal anaemia was highly associated with the occurrence of childhood anaemia. This finding was in line with a study done in South Africa, Haiti, and India(34–36). This might be explained that mothers and children share a common home environment, socioeconomic, and dietary conditions, and maternal and child anaemia may reflect the household common nutritional status, and poor maternal iron intake during pregnancy, reduce breast milk might be the possible reason. 

The findings from this study data set indicated that the incidence of fever had an impact on childhood anaemia. This is in line with studies done in Ghana and South Ethiopia Wolaita (24,37). This could be attributed to the infectious cause of childhood fever mainly malaria, tuberculosis, and Leishmaniasis which cause anaemia by destructing red blood cells or other related mechanisms. 

The nutritional status of children had a significant association with childhood anaemia. The 33 439 stunting status of children had significant association with childhood anaemia. This finding is in line with previous studies conducted in South Africa(36), Bangladesh(38,39), and Ethiopia(40,41). This might be explained that children suffering from nutritional deficiency were 40 442 more likely to have weak immune systems, making them vulnerable to various illnesses and 42 443 healthiness such as parasitic infections or chronic inflammation; many of these conditions reduce the haemoglobin level in the blood leading to increased childhood anaemia(42) 

Furthermore, severely wasting children were more likely to be anaemic than their counterpart. This finding is consistent with previous studies (43,44). This is due to the fact that malnutrition 52 447 leads to both macronutrient and micronutrient deficiencies, such as protein, iron, and vitamin A, which are responsible for iron deficiency anaemia. Birth order of four up to five and six and greater than six were higher than those of the first order. This finding was similar to a studies 

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done in Indian(12,45). This could be due to the distribution of scarce resources within the family and related to the maternal exhaustion of micronutrient feeding practices. 

In the multilevel analysis, different individual and community factors were significantly associated with anaemia. Among the community-level variables, it was found that the odds of anaemia among children lived in the Somali, Dire Dawa, Afar, and Gambela were higher than in the Amhara region. This might be due to the regional variation in the nutrient intake can cause significant health disparity, and this variability may be mediated by factors such as food availability, food customs, and culture. 18 457

The potential strength of our study is the use of different methodologies spatial pattern, trends, and a multilevel regression model because of nested or cluster samples to show the effect of individual predictors and community-level variables on the outcome variable. The study was based on a large dataset representing the whole country of Ethiopia and which was weighted to make it nationally representative and adjusted for the design to get a reliable estimate. 30 462 However, there were some limitations to this study. The cross-sectional nature of the data prevents causality from being inferred between the independent and dependent variables. Also, respondents' data that didn't have files (longitude and latitude) were excluded from the spatial analysis which could affect the overall result and the generalizability of the findings.

## Conclusion

Though, declining prevalence of childhood anaemia was observed from 2005 to 2011, it increases from 2011-2016 survey. Besides, it was spatially clustered across regions in 52 471 Ethiopia. The most prominent risk areas of anaemia were detected in Afar, Somali, Dire Dawa and Oromia regions more or less consistently over the last 15 years. child's age, age of the mother, wealth index, maternal anaemia, fever, birth order, stunting, wasting and region were 

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significant predictors among 6-59 months. Therefore, public health intervention actions intended in a targeted approach to bearing high-risk populations as well as geographic regions were vital to reduce childhood anaemia in Ethiopia. 

#### Abbreviations

AOR-Adjusted Odds Ratio, CSA-Central Statics Agency, CI-Confidence Interval, CMHS-14 479 College of Medicine and Health Science COR-Crude Odds Ratio, EDHS-Ethiopia 16 480 Demographic and Health Survey, GPS-Global Positioning System, ICC-Intra Class Correlation Coefficient, LLR-Log-Likelihood Ratio, MOR-Median odds ratio, OR-Odds Ratio, RR-Relative Risk, PVC-Proportional Change in Variance, SNNPR- Southern Nations, Nationalities, and , Der 23 483 Peoples' Region.

26 484 **Declarations** 

> **Ethics statements**

Patient consent for publication

Not required.

#### Ethics approval

Permission for data access was obtained from a major Demographic and Health Survey through an online request at (http://www.dhsprogram.com). The data used for this study were publicly available with no personal identifier. Our study was based on secondary data from 46 491 <sup>48</sup> 492 Ethiopian Demographic and Health Survey and we have secured the permission letter from the main Demographic Health and Survey. 

### **Consent for publication**

#### Not-applicable

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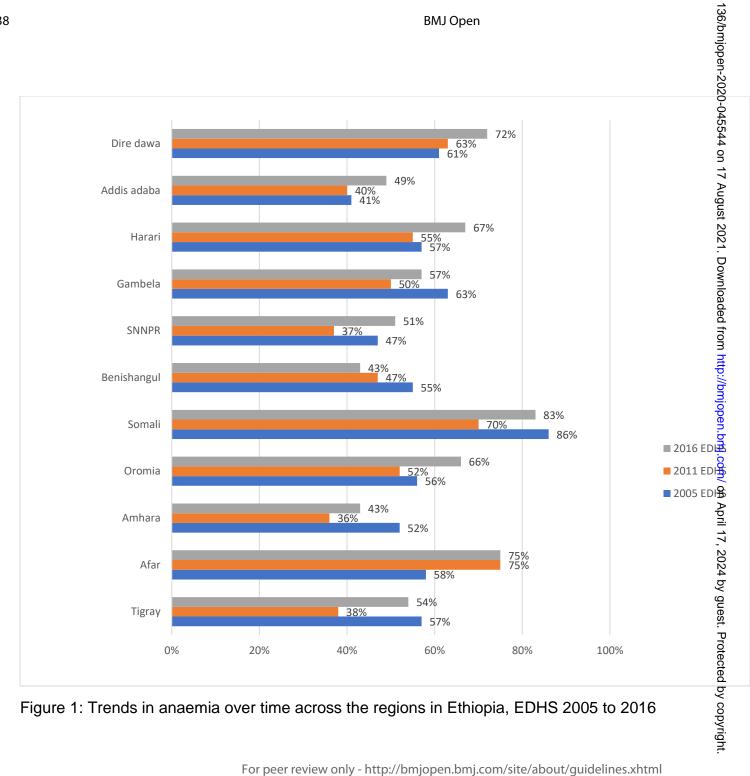
1	496	Data sharing statement
2 3	497	The data in which the authors used to produce this manuscript are available upon reasonable
4	498	request
5 6	499	Competing interests
7 8	500	The authors declare that they have no competing interests.
9 10	501	Funding
10 11 12	502	No funding
	503	Contributors
15 16 17	504	Proposal preparation, acquisition of data, analysis, and interpretation of data was done by SH,
18 19	505	AM, ZM and BF guided the study design data collection and analysis. SH drafted the
20 21 22	506	manuscript and all authors have a substantial contribution in revising and finalizing the
	507	manuscript. All authors read and approved the final manuscript.
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30 31 32	510	also thank the Ethiopian Central Statistics Agency for providing us with the data and shape
	511	files for this study.
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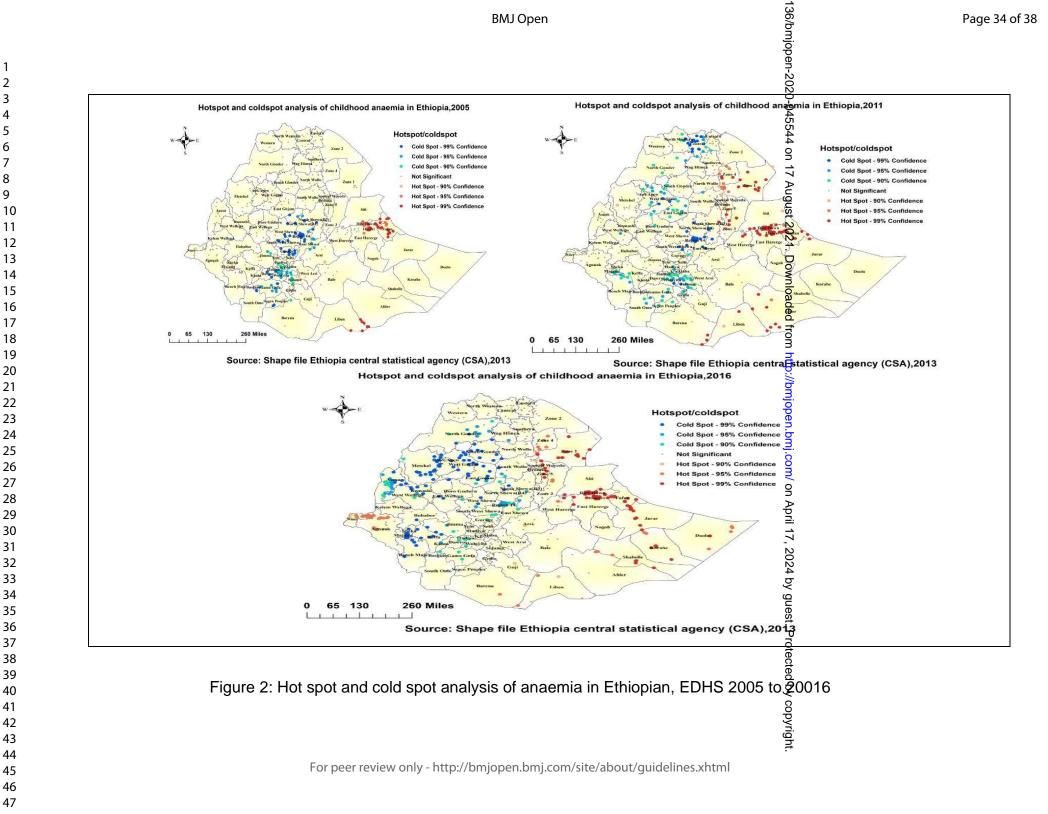
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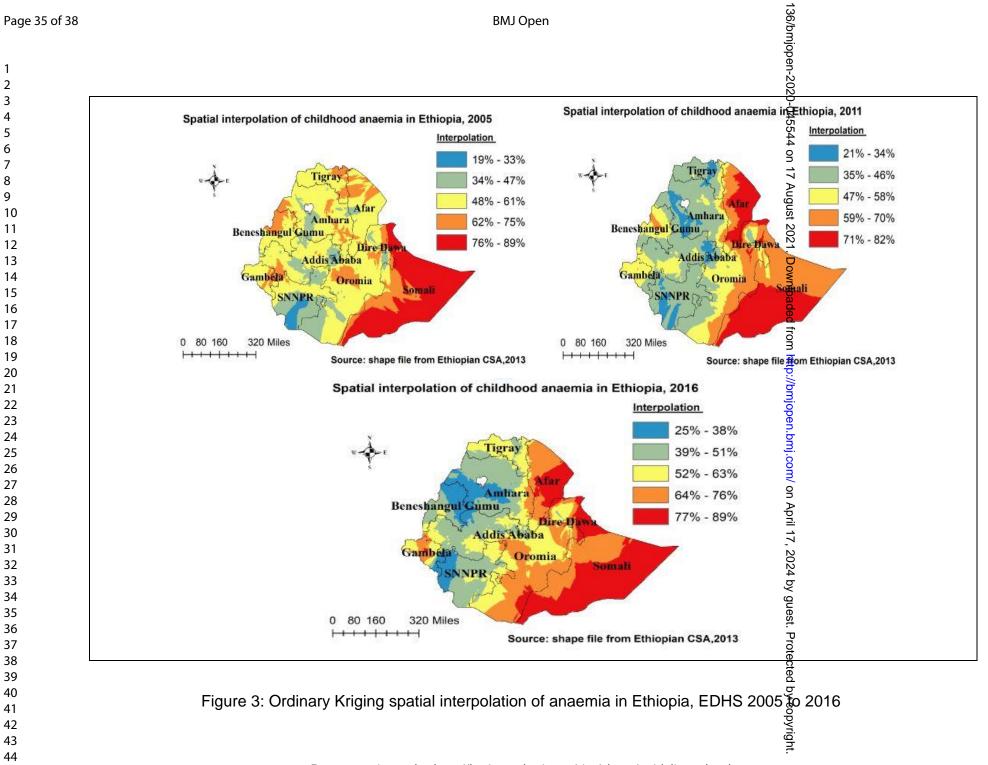
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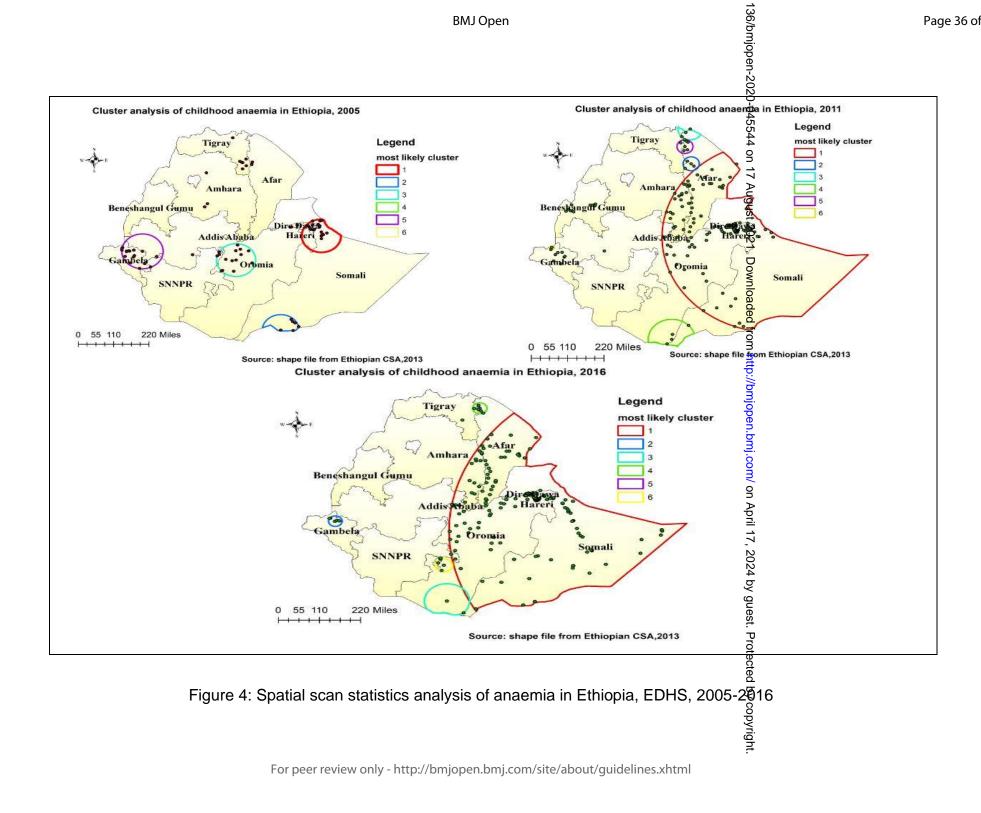
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47 48	660	Figur	e legend/caption	
	661	Figure	e 1: Trends in anaemia overtime across the regions in Ethiopia, EDHS 2005 to 2016	
51 52	662	Figure	e 2: Hot spot and cold spot analysis of anaemia in Ethiopian, EDHS 2005 to 20016	
53 54	663	Figure	e 3: Ordinary Kriging interpolation of anaemia in Ethiopia, EDHS 2005 to 2016	
	664	Figure	e 4: Spatial scan statistics analysis of anaemia in Ethiopia, EDHS, 2005-2016	
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	Item No	Recommendation	
Title and abstract	1	Spatio-temporal distribution and associated factors of anaemia among	Page1
		children aged 6-59 months in Ethiopia: a spatial and multilevel analysis	
		based on the EDHS 2005- 2016	
		Therefore, this study aimed to assess the spatio-temporal distribution and	Page2
		associated factors of childhood anaemia using the Ethiopian Demographic	
		and Health Survey (EDHS) data from 2005-2016.	
		In mixed effect model Child age, age of mother, maternal anaemia status,	
		wealth index, birth order, fever, stunting, wasting status, and region were	
		significant predictors of childhood anaemia.	
Introduction			
Background/rationale	2	Childhood anaemia is a major public health problem in Ethiopia, there is	Page 5
		limited evidence on the spatio-temporal variability of childhood anaemia	
		over time, study attempts to fill the gap by investigating the spatio-temporal	
		distribution of anaemia and its associated factors using multilevel model, since its hierarchical nature.	
Objectives	3	Therefore, this study aimed to assess the spatio-temporal distribution and	Page 5
Objectives	5	associated factors of childhood anaemia using the Ethiopian Demographic	
		and health survey (EDHS) data from 2005-2016	
Methods			
Study design	4	Survey-based cross-sectional study design was employed for the EDHSAll nine regions and two city administrations of Ethiopia in 2005, 2011 and	Page 5
Setting	5	2016.	rage.
Participants	6	The source population for this study was among children aged 6–59 months	Page 6
		in Ethiopia. A total of 21,302 children aged 6-59 months were included in	
		this study.	
Variables	7	Outcome measure: The outcome variable was child anaemia status	Page '
		Independent: sociodemographic (religion, mother age, marital status,	
		educational status, husband education, wealth index, mothers working status,	
		numbers of under five children) Maternal and Child- related (child sex, age,	
		birth size, birth order, maternal BMI, maternal anaemia, breastfeeding, fever,	
		diarrhoea, vitamin supplement, stunting and wasting). Community-level	
		(residence, region, community women education and community women	
		poverty).	
Data sources/	8*	DHS program (Demographic and Health Survey)	Page 6
measurement		website( <u>www.measuredhsprogram.com</u> ) after obtaining the necessary	
		permissions for the download and further analyses.	
Bias	9	Cross-sectional nature of the data prevents causality from being inferred	Page 2
		between the independent and dependent variables	
Study size	10	A total of 21,302 children (3,868 in 2005, 8,958 - in 2011, and 8476 in 2016)	Page 1

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		were included in this study	
Quantitative	11	Quantitative variables were handled in three level	Page 10
variables		Four models were constructed for multilevel logistic regression analysis	
		using melogit STATA command. The first model (a random intercept	
		model) was null model without predictors to determine the extent of cluster	
		variations in anaemia. The second model (model I) was adjusted with	
		individual-level variables. The third model (model II) was adjusted for	
		community-level variables, while the fourth model (model III) was fitted	
		with both individual-level and community-level variables simultaneously.	
Statistical methods	12	Multilevel model for associated factors, we use mixed effect to control	Page 10-
		confounding than traditional regression model.	11
		Spatial analysis was performed	
		For associated factor predictors with missing dropped and for spatial analysis	
		without spatial information was dropped	
		Secondary data analysis and participants were selected based on a stratified	
		two-stage cluster sampling technique	
		Spatiotemporal pattern analysis was done for three-year data	
Results	1		
Participants	13*	A total of 21,302 children Secondary data analysis, simply we take from EDHS	Page 11
Descriptive data	14*	A total of 21,302 children with known haemoglobin levels (3,868 in 2005,	Page 11
1		8,958 in 2011, and 8467 in 2016) were included in this study. The	12
		prevalence of anaemia for the three consecutive surveys was 53.9%, 44.6%,	
		and 57.6% in 2005, 2011, and 2016 EDHS data respectively	
		The majority of children were from rural residency in five years preceding	
		the survey in three surveys. About 78.6%, 70%, and 67% of women were	
		unable to read and write in 2005, 2011, and 2016 survey respectively.	
		Children from poor and middle-class families were more anaemic than	
		children from rich families across the three EDHS survey	
		Husband educational level was missing data	
Outcome data	15*	The dependent variable was child anaemia status, categorized as	Page 7
		"anaemic/not-anaemic" for this study.	0
Main results	16	The spatial distribution of childhood anaemia varied across regions in all	Page 15
		surveys. The spatial autocorrelation analysis result indicated that childhood	17
		anaemia had spatial dependency in 2005, 2011, and 2016 (Moran's I: 0.176,	1/
		0.18, and 0.09, respectively at P-value <0.01). In multivariable multilevel	
		mixed-effect logistic regression analysis, individual-level factors such as the	
		age of the child, wealth index, mother age, maternal anaemic status, birth	
		order, fever, stunting, and wasting status were significant predictor of	
		childhood anaemia.	
		Not-applicable	
		Not-applicable	
Other analyses	17	Different spatial technique spatial autocreation, hotspot/cold spot analysis,	Page 15
Outor analysis			

Key results	18	This study tried to identify spatio-temporal distribution and predictors of	Page
		childhood anaemia across the regions in Ethiopia. 2005, 2011, and, 2016	26
		Ethiopian Demographic and Health Survey data were used. In this study,	
		anaemia's trend was decreased from 2005 to 2011, while the rate	
		significantly increased from 2011 to 2016. The study revealed that 57.56%	
		[CL: 0.56-0.59] of children were anaemic in 2016, preceding the survey.	
		This finding was in line with a study done in Gondar, Northwest Ethiopia	
		58.6%	
		The spatial pattern shows the geographical inequality of anaemia by using	
		sat scan and GIS spatial techniques like cluster mapping tools and	
		interpolation techniques. The spatial analysis indicates that the distribution	
		of childhood anaemia was non-random across the country with a global	
		Moran's I index of 0.176 in 2005, 0.18 in 2011, and 0.09 in 2016 with a	
		significant p-value, which indicates substantial-considerable clustering areas.	
		This study's findings were in line with a study done in Nigeria, Malawi,	
		Tanzania, and Uganda	
Limitations	19	The cross-sectional nature of the data prevents causality from being inferred	Page 2
		between the independent and dependent variables. Also, respondents' data	
		that didn't have files (longitude and latitude) were excluded from the spatial	
		analysis which could affect the overall result and the generalizability of the	
		findings.	
Interpretation	20	Prevalence of childhood anaemia decreased between the 2005-2011 survey	Page 2
		while the prevalence increased from 2011-2016 EDHS. The spatial pattern	
		of child anaemia in Ethiopia was non-random among the three consecutive	
		surveys with the global Moran's I value of 0.176, 0.18, and 0.09 in EDHS	
		2005, 2011, and 2016.	
		In line study done Cape Verde, west Africa, Nigeria, Malawi, Tanzania, and	
		Uganda	
Generalisability	21	Policymakers and health planners should design effective intervention	Page 2
		strategies for the identified hot spot areas and individual and community-	
		level factors to anaemia.	
		For health care community, and researcher to alleviate the problem.	
Other information	22	No funding	
Funding	22		

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.