

# Comorbid patterns of anaemia and diarrhoea among children aged under 5 years in Ghana: a multivariate complex sample logistic regression analysis and spatial mapping visualisation

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**Background:** Anaemia and diarrhoea are known independent causes of under-five morbidity and mortality. This study sought to investigate predictors of comorbid patterns of anaemia and diarrhoea using the 2014 Ghana Demographic and Health Survey (GDHS).

**Methods:** The study employed analysis of secondary data from the 2014 GDHS. We performed a multivariate complex sample logistic regression and spatial analysis.

**Results:** The weighted prevalence of comorbid anaemia and diarrhoea was 9.28% with the highest burden (16.45%) found in the Upper West region. Independent predictors (risk factors) of comorbid patterns of anaemia and diarrhoea were children aged 6–23 mo (OR=2.17, 95% CI 1.42 to 3.33), male gender (OR=1.50, 95% CI 1.04 to 2.16), history of fever (OR=4.37, 95% CI 2.94 to 6.50) and living in a household with two children aged <5 y (OR=1.80, 95% CI 1.14 to 2.84). Protective factors were having a father with secondary or higher education (OR=0.57, 95% CI 0.33 to 0.97), living in a household with ≥6 members (OR=0.46, 95% CI 0.28 to 0.75) and living in a richer household (OR=0.38, 95% CI 0.16 to 0.89). Surface maps revealed inter-regional and subregional variations.

**Conclusion:** The study shows that the independent predictors of comorbid patterns of anaemia and diarrhoea among children aged <5 y in Ghana are age, gender, history of fever, the number of children aged <5 y in the household, parental education, household size and household wealth. The study identified zones to be targeted for cost-effective policy interventions.

Keywords: comorbid anaemia and diarrhoea, children under five, Demographic and Health Survey, Ghana.

#### Introduction

Childhood diseases such as anaemia and diarrhoea are conditions of public health concern due to their adverse impact on child survival, morbidity and mortality. <sup>1-3</sup> Diarrhoea has been identified as the third leading cause of death among children aged <5 y. <sup>4</sup> Anaemia is also estimated to affect approximately 43% of young children (aged 6–59 mo) globally with 70% prevalence rate in Central and West Africa. <sup>5</sup> Evidence from literature shows that anaemia <sup>1,6</sup> and diarrhoea <sup>2,3</sup> independently affect underfive mortality.

Unfortunately, some children may concurrently develop anaemia with diarrhoeal illness or following a recent history of diarrhoea. One plausible explanation for this comorbid pattern is that inflammatory cytokines such as TNF- $\alpha$  and IL-6, which are elevated in diarrhoea, are also implicated in the inflammatory pathway of anaemia of chronic infection. 8-10

Dehydration resulting from severe diarrhoea can also lead to hypovolaemic shock with resulting mortality in children. Conversely, there is the potential for iatrogenic fluid overload during the management of dehydration in children, which can cause heart failure, and add to the complexities in clinical management of an anaemic child with diarrhoea. One meta-analysis found that children with acute malnutrition were more likely to die if they also had comorbid diarrhoea or anaemia. Another clinical study found that malnourished children with diarrhoea were 4.2 times as likely to die if they had severe anaemia. Thus, comorbid patterns of anaemia and diarrhoea may have a worse prognosis compared with the independent occurrence of either condition, which can have an adverse effect on the well-being of children aged <5 y.

Sustainable Development Goal 3.2 charges countries to end preventable deaths in children aged <5 y and to reduce under-five mortality to as low as 25 per every 1000 live births by 2030. Regrettably, despite numerous interventions having been instituted, such as rotavirus immunisation, the roll back malaria initiative, prevention of mother to child transmission of various infectious diseases and child welfare clinics, subregional disparities in under-five mortality are still a concern in Ghana. There are, however, no relevant current data on the specific national morbidity rates for comorbid anaemia and diarrhoea. Various child, parental and household level factors have been found to be associated with anaemia and diarrhoea in children. 9,14-19

Previous literature on anaemia and diarrhoea among underfives in Ghana have largely studied these conditions as separate outcomes. 14-16,18,19 In addition, some of these studies, which used nationality representative data such as the Demographic and Health Survey (DHS) and the Multiple Indicator Cluster Survey to study childhood anaemia and diarrhoea, did not employ complex survey data analysis to account for the complex sampling designs used in these surveys. 14,19 Moreover, there is a paucity of literature on the subregional variations in the burden of anaemia and diarrhoea among children in Ghana. Against this backdrop, the current study employs a multivariate complex survey analysis to investigate the prevalence and independent predictors of comorbid patterns of anaemia and diarrhoea in children aged <5 y in Ghana. This study also employs spatial analysis to provide detailed information on the high prevalence zones at the subregional level for targeted policy actions.

#### Methods

# Study design and sampling

The study employed analysis of secondary data obtained from the 2014 Ghana DHS (GDHS). The DHS is a prospective crosscountry survey that is conducted to ascertain the general health of individuals in selected countries. The 2014 GDHS was conducted by the Ghana Statistical Service together with local agencies of the Ghana Health Service with funding from the United States Agency for International Development among other international donor agencies and technical support from Inner City Fund (ICF) International. The sampling design used in the DHS employed multistage sampling. The first stage involved random selection of clusters. Clusters were enumeration areas that were defined during the 2010 Population and Housing Census in Ghana. The second stage involved systematic selection of households from those clusters chosen during the first stage. Sampling was also stratified to account for place of residence (i.e. rural vs urban households). In all, 427 clusters were selected, comprising 216 and 211 from urban and rural areas, respectively. On average,

30 households were chosen from each selected cluster, constituting a total of 12 831 selected households in the 2014 GDHS. All mothers of children gged <5 v in selected households who consented to participate were interviewed. Sociodemographic and health data were obtained from women of reproductive age, as well as information on all children aged <5 y. In half the selected households, blood samples for anaemia testing were obtained through heel prick and finger prick in children aged 6–11 and 12-59 mo, respectively. Successfully obtained blood samples were collected in microcuvettes and the analysis of Hb concentration was performed onsite using a battery-powered transportable HemoCue analyser (HemoCue, Ängelholm, Sweden). A child was diagnosed with anaemia if the Hb concentration was <11 g/dl. Anaemic children were further classified based on the ranges of Hb levels: mild (10.0–10.9 g/dl), moderate (7.0–9.9 g/dl) and severe < 7.0 a/dl). Diarrhoea status was assessed through interviews asking mothers if their child had diarrhoea within the last 2 wk preceding the survey. Further details can be found in the original 2014 GDHS report.<sup>20</sup>

# Data preparation

The 2014 GDHS child data (5884 cases) were downloaded after permission was sought by the primary author. Data is freely available after a simple online request at <a href="https://dhsprogram.com/data/dataset\_admin/login\_main.cfm">https://dhsprogram.com/data/dataset\_admin/login\_main.cfm</a>. Preliminary data cleaning and final analysis were performed in Stata/SE version 16, StataCorp LLC, Texas, USA. Only 2388 cases with available anaemia testing results were selected, from which 45 children who were not usually residents of the household at the time of the survey were excluded. Therefore a final sample of 2343 cases was analysed.

# Outcome variable

The main outcome variable was comorbid anaemia and diarrhoea status. The anaemia status variable, which was originally coded as an ordered variable with four levels—non-anaemic, mild, moderate and severe—was recategorised into a dichotomous variable, with non-anaemic as 'No', while mild, moderate and severe anaemia were grouped together as 'Yes'. 'No' and 'Yes' anaemia status was coded as '0' and '1', respectively. Diarrhoea status had a dichotomous response of either 'No' or 'Yes' and was also coded as '0' or '1', respectively. A child was defined as having comorbid anaemia and diarrhoea if the child had both anaemia and diarrhoea and then was coded as '1'. Children with only one of the conditions, or those with neither anaemia nor diarrhoea, had no comorbid condition and were coded as '0'.

# **Explanatory variables**

Explanatory variables were selected based on factors identified in the literature as associated with anaemia and diarrhoea. Explanatory variables at child level were age, gender, birth, fever status and vitamin A supplementation. Explanatory variables at the parental level were the age of the mother and educational levels of the mother and father. Household level explanatory variables were household wealth status, household size, the number of children aged <5 y, source of drinking water, main floor

Variable	VIF	Tolerance
Child's age (mo)	1.06	0.94
Child's gender	1.01	0.99
Birth order	2.55	0.39
History of fever	1.03	0.97
Vitamin A supplementation	1.05	0.95
Mother's age	2.17	0.46
Educational level of mother	1.78	0.56
Educational level of father	1.75	0.57
Household size	1.55	0.64
Number of children aged <5 y in the household	1.26	0.79
Household wealth status	3.27	0.30
Source of drinking water	1.16	0.86
Main floor material	1.12	0.89
Locality of residence	1.99	0.50
Region of residence	1.43	0.70

material and the region and locality of residence. Except for birth order, household size, the number of children aged <5 y in the household and source of drinking water, which were recoded, all the other explanatory variables were used as they were coded in the original dataset. For birth order, order 1–3 remained the same as in the original data, fourth and fifth birth order were categorised together, whereas birth orders  $\ge 6$  were put into one category. Likewise, household size was recoded into two categories, namely, households with 1–5 and  $\ge 6$  members. The number of children aged <5 y in a household was recoded as 1, 2 and  $\ge 3$  children. Source of drinking water was recoded into improved and unimproved based on the classifications in the 2012 WHO and UNICEF updated report on progress on drinking water and sanitation.  $^{21}$ 

# Data analysis

Data analysis occurred in three stages. The first stage involved bivariate analysis between the outcome and predictor variables using the  $\chi^2$  test for independence. The second stage involved multivariate logistic regression estimations of the determinants of comorbid diarrhoea and anaemia in children aged <5 y in Ghana. To account for sampling design, stratification and weighting, a complex survey analysis was performed. To achieve this, the 'svyset' command was activated in Stata 16 to set the data in complex survey analysis. The primary sampling units, sample strata and sample weights, were all adjusted in univariate, bivariate and multivariate analysis. This helped to achieve correct estimates of confidence intervals and standard errors of predicted estimates, especially in the multivariate logistic regression model. Prior to the multivariate analysis, a collinearity diagnostics was performed to rule out multicollinearity. The variance inflation factors of most of the covariates were <2 with the maximum being 3.27 (Table 1), all of which were far less than the generic cutoff values of  $\geq 5$  or  $\geq 10.22$ 

#### Spatial analysis

The third stage involved spatial visualisation of the outcome using surface maps. Quantum Geographic Information Systems (QGIS) software was used to produce visual maps of comorbid diarrhoea prevalence by region. The regional level prevalence maps were generated using Ghana's shapefile with regional boundary demarcations obtained from the DHS program. Regional estimates were computed in STATA. The regional level estimates were added to existing variables in the shapefile and used to produce the maps in QGIS. The steps followed to produce the maps are described elsewhere. The steps followed to produce the maps are described elsewhere.

Further, we produced a spatial interpolated surface map of comorbid diarrhoea and anaemia prevalence in children aged <5 y to unravel intraregional distribution of the study outcome. The spatial interpolated map was produced using the prevR package in R freeware 3.5.3, which was purposely developed to generate surface maps based on DHS data.<sup>25</sup> Other R packages used include foreign, maptools and gaplot2.<sup>26</sup> We adopted the Gaussian kernel density estimator approach with adaptive bandwidths of equal numbers of people surveyed to generate the surface map.<sup>25</sup> The authors of the prevR package preferred the Gaussian kernel over finite extent kernels to generate the maps because of its practical suitability in situations where the distribution of points is highly uneven, particularly in regions where the number of observations is small.<sup>25</sup> The main surface is a weighted estimate of comorbid anaemia and diarrhoea prevalence with parameter N=133, a value chosen using the 'Noptim ()' function in the prevR package.<sup>25</sup> 'N' is a function of the observed national prevalence, the number of people assessed for comorbid anaemia and diarrhoea and the number of cluster surveys, which are the three parameters used to simulate a DHS dataset.<sup>25</sup> Before generating the surface maps, we estimated the weighted prevalence of comorbid diarrhoea and anaemia prevalence in children aged <5 y in each of the 427 clusters using the Ghana shapefile and the 2014 GDHS. The 'prevR.colors.red()' function was used to produce a colour gradation from white/yellow to red/dark with 15-point resolution. A step-by-step approach on how the prevR package can be used to obtain surface maps is reported elsewhere.<sup>27</sup>

#### Results

In total, 2343 children aged <5 y were included, 53% male and 47% female. The overall prevalence of comorbid anaemia and diarrhoea was 9.28%. Prevalence varied among different age groups of children, with the highest prevalence of 15.16% seen among children aged 12-23 mo. The lowest prevalence (4.96%) was seen among children aged 48-59 mo. Prevalence was higher among male (10.75%) compared with female children (7.60%). Prevalence was greatest among children whose birth order was sixth or higher compared with firstborn children (7.56%). The prevalence of comorbid anaemia and diarrhoea was 23.26% among children who had fever compared with 6.73% among those without fever. In summary, significant associations were found between the outcome and the following predictors: age of child, gender of child, fever status, age of the mother, educational levels of the mother and father, household wealth status, number of children aged <5 y and the main floor material (Table 2).

**Table 2.** Prevalence of comorbid diarrhoea and anaemia in children aged <5 y Comorbid diarrhoea and anaemia, n (%) Category No Yes Total, N (%) p-value Age (mo) 6-11 235 (90.03) 29 (9.97) 264 (100) 12-23 472 (84.84) 94 (15.16) 566 (100) 24-35 465 (88.32) 71 (11.68) 536 (100) 36-47 473 (96.13) 23 (3.87) 496 (100) 48-59 456 (95.04) 25 (4.96) 481 (100) < 0.001 Total 2101 (90.72) 242 (9.28) 2343 (100) Gender of child Male 1073 (89.24) 149 (10.76) 1222 (100) Female 1028 (92.40) 93 (7.60) 1121 (100) Total 2101 (90.72) 242 (9.279) 2343 (100) 0.02 Birth order 1 451 (92.44) 46 (7.56) 497 (100) 2 412 (90.88) 48 (9.12) 460 (100) 3 375 (91.48) 37 (8.52) 412 (100) 4-5 538 (91.20) 56 (8.80) 594 (100) >6 325 (86.08) 55 (13.92) 380 (100) 0.07 Total 2101 (90.72) 242 (9.28) 2343 (100) Fever No 1804 (93.27) 148 (6.73) 1952 (100) Yes 297 (76.74) 94 (23.26) 391 (100) < 0.001 2101 (90.72) 242 (9.28) 2343 (100) Vitamin A supplementation No 796 (90.97) 78 (9.03) 874 (100) 1291 (90.49) 1454 (100) Yes 163 (9.51) 0.75 Total 2087 (90.67) 241 (9.33) 2328 (100) Age of mother (y) 15-19 46 (74.73) 19 (25.27) 65 (100) 20-24 333 (89.32) 41 (10.68) 374 (100) 25-29 524 (92.13) 55 (7.87) 579 (100) 30-34 519 (92.44) 51 (7.56) 570 (100) 35-39 403 (89.69) 50 (10.31) 453 (100) ≥40 276 (91.23) 26 (8.77) 302 (100) 0.007 Total 2101 (90.72) 242 (9.28) 2343 (100) Highest education of mother 855 (100) No education 743 (86.74) 112 (13.26) 424 (88.55) 56 (11.45) 480 (100) Primary Secondary and higher 934 (93.85) 74 (6.15) 1008 (100) < 0.001 2101 (90.72) 242 (9.28) 2343 (100) Highest education of father No education 589 (85.24) 100 (14.76) 689 (100) 28 (10.24) 265 (100) Primary 237 (89.76) Secondary and higher 1133 (93.02) 95 (6.98) 1228 (100) < 0.001 Total 1959 (90.82) 223 (9.18) 2182 (100) Household wealth Poorest 675 (87.2) 89 (12.8) 764 (100) Poorer 446 (88.35) 59 (11.65) 505 (100) Middle 376 (87.81) 59 (12.19) 435 (100) Richer 324 (95.54) 22 (4.46) 346 (100) Richest 280 (96.15) 13 (3.85) 293 (100) < 0.001 Total 2101 (90.72) 242 (9.28) 2343 (100)

Category	Comorbid diarrhoea	Comorbid diarrhoea and anaemia, n (%)		
	No	Yes	Total, N (%)	p-value
Household size, members				
1–5	1122 (90.58)	130 (9.42)		
<u>≥</u> 6	979 (90.90)	112 (9.10)		
	2101 (90.72)	242 (9.28)	2343 (100)	0.81
Number of children aged <	5 y			
0–1	885 (93.16)	87 (6.84)	972 (100)	
2	872 (88.86)	111 (11.14)	983 (100)	
≥3	344 (89.32)	44 (10.68)	388 (100)	
	2101 (90.72)	242 (9.28)	2343 (100)	0.02
Source of drinking water				
Improved	1753 (90.93)	204 (9.07)	1957 (100)	
Unimproved	340 (89.12)	38 (10.88)	378 (100)	
·	2093 (90.69)	242 (9.31)	2335 (100)	0.46
Main floor material				
Sand	166 (84.25)	25 (15.75)	191 (100)	
Ceramic tiles	107 (97.11)	3 (2.89)	110 (100)	
Cement	1455 (89.87)	183 (10.13)	1638 (100)	
Woollen carpet	137 (95.76)	9 (4.24)	146 (100)	
Rubber carpet	192 (91.29)	20 (8.71)	212 (100)	
Total	2057 (90.66)	240 (9.34)	2297 (100)	0.0130
Locality of residence				
Urban	858 (92.38)	89 (7.62)	947 (100)	
Rural	1243 (89.30)	153 (10.70)	1396 (100)	
Total	2101 (90.72)	242 (9.28)	2343 (100)	0.07
Region of residence				
Western	216 (92.58)	20 (7.42)	236 (100)	
Central	225 (91.56)	24 (8.44)	249 (100)	
Greater	172 (95.00)	10 (5.00)	182 (100)	
Volta	171 (91.49)	15 (8.51)	186 (100)	
Eastern	179 (87.84)	26 (12.16)	205 (100)	
Ashanti	204 (90.88)	21 (9.12)	225 (100)	
Brong Ahafo	244 (88.24)	31 (11.76)	275 (100)	
Northern	329 (87.84)	47 (12.16)	376 (100)	
Upper East	199 (90.48)	18 (9.52)	217 (100)	
Upper West	162 (83.55)	30 (16.45)	192 (100)	
Total	2101 (90.72)	242 (9.28)	2343 (100)	0.27

The strength of association was assessed using a single multivariate logistic regression model. The model adjusted for age of child, gender of child, birth order, fever status, vitamin A supplementation, age of the mother, educational levels of the mother and father, household wealth status, household size, number of children aged <5 y, source of drinking water, main floor material, locality and region of residence. The odds of being diagnosed with comorbid anaemia and diarrhoea was 2.17 times greater in children aged 6–23 mo compared with those aged 24–59 mo (OR=2.17, 95% CI 1.42 to 3.33). Likewise, male children were 50% more likely to have comorbid anaemia and diarrhoea compared with female children (OR=1.50, 95% CI 1.04 to 2.16). Compared with children who had no fever,

children who had fever had 4.37 times greater odds of being diagnosed with comorbid diarrhoea and anaemia (OR=4.37, 95% CI 2.94 to 6.50). Relative to children whose fathers had no education, those whose fathers had attained secondary and higher education were 43% less likely to be diagnosed with comorbid anaemia and diarrhoea (OR=0.57, 95% CI 0.33 to 0.97) (Table 3).

The odds of comorbid anaemia and diarrhoea decreased by 54% among children from households with a size of  $\geq$ 6 members compared with children from households with 1–5 members (OR=0.46, 95% CI 0.28 to 0.75). Children from households with two children aged <5 y had 80% increased odds of having comorbid anaemia and diarrhoea (OR=1.80, 95% CI 1.14 to 2.84).

Table 3. Multivariate complex sample logistic regression estimates of the child and parental level predictors of comorbid anaemia and diarrhoea

Child and parental level predictors		p-value	95% CI	
	OR		Lower	Upper
Child's age (mo)				
24–59	Ref.			
6-23	2.17	<0.001**	1.42	3.33
Child's gender				
Male	1.50	0.031**	1.04	2.16
Birth order				
1	Ref			
2	1.33	0.407	0.67	2.64
3	1.29	0.486	0.63	2.63
4–5	1.36	0.484	0.57	3.26
≥6	2.47	0.08	0.90	6.81
History of fever				
No	Ref.			
Yes	4.37	<0.001**	2.94	6.50
Vitamin A supplementation				
No	Ref.			
Yes	0.93	0.726	0.61	1.41
Mother's age, y				
15-19	Ref.			
20-24	0.51	0.292	0.15	1.78
25–29	0.36	0.121	0.10	1.31
30-34	0.40	0.19	0.10	1.58
35–39	0.46	0.282	0.11	1.90
≥40	0.30	0.114	0.07	1.34
Educational level of mother	0.50	0.111	0.07	1.5 1
No formal education	Ref.			
Primary	1.03	0.927	0.57	1.85
Secondary education and higher	0.63	0.095	0.36	1.09
Educational level of father	0.05	0.033	0.50	1.05
No formal education	Ref.			
Primary	0.65	0.209	0.33	1.27
Secondary and higher	<b>0.57</b>	0.039**	0.33	0.97
				0.57

<sup>\*\*</sup>statistical significance at 0.05 alpha level.

The model estimates were adjusted for age of child, gender of child, birth order, fever status, vitamin A supplementation, age of mother, educational levels of mother and father, household wealth status, household size, number of children aged <5 y, source of drinking water, main floor material, region and place of residence.

Values in bold shows statistical significance at 0.05 alpha level.

Relative to children from the poorest households, those from richer households had 62% decreased odds of being diagnosed with comorbid anaemia and diarrhoea (OR=0.38, 95% CI 0.16 to 0.89) (Table 4).

# Spatial maps of comorbid anaemia and diarrhoea prevalence

Regional disparities were observed in the prevalence of comorbid anaemia and diarrhoea among under-five children in Ghana. The Upper West region recorded the highest prevalence of anaemia and diarrhoeal comorbid cases, whereas the Greater Accra region recorded the lowest (Figure 1). The spatial interpolated

map revealed that there were disparities in comorbid anaemia and diarrhoeal prevalence within each region, and that these disparities were more pronounced in the Upper West, Brong Ahafo and Ashanti regions (Figure 2).

#### **Discussion**

In developing countries, childhood diseases remain a significant concern for primary healthcare providers and families. The concern is greater with comorbid patterns of childhood diseases due to the high risk of mortality. <sup>11,12</sup> This indicates the seriousness with which such patterns should be investigated in children and

Table 4. Multivariate logistic regression estimates of the household level predictors of comorbid anaemia and diarrhoea

Household level predictors			95% CI	
	OR	p-value	Lower	Upper
Household size, members				
1–5	Ref.			
≥6	0.46	0.002**	0.28	0.75
Number of children aged <5 y in the house	hold			
0–1	Ref.			
2	1.80	0.012**	1.14	2.84
≥3	1.69	0.134	0.85	3.37
Household wealth status				
Poorest	Ref.			
Poorer	0.89	0.669	0.51	1.55
Middle	1.18	0.595	0.64	2.20
Richer	0.38	0.025**	0.16	0.89
Richest	0.39	0.138	0.11	1.36
Source of drinking water				
Unimproved	Ref			
Improved	1.13	0.679	0.63	2.02
Main floor material				
Sand	Ref.			
Ceramic	0.59	0.551	0.11	3.34
Cement	0.64	0.172	0.33	1.22
Woollen/synthetic carpet	0.35	0.092	0.11	1.19
Rubber carpet	0.71	0.509	0.26	1.96
Locality of residence				
Urban	Ref.			
Rural	0.71	0.2	0.43	1.20
Region of residence				
Greater Accra	Ref.			
Western	0.73	0.657	0.18	2.92
Central	1.06	0.919	0.36	3.11
Volta	0.56	0.325	0.18	1.78
Eastern	1.08	0.895	0.37	3.14
Ashanti	1.27	0.606	0.51	3.16
Brong Ahafo	0.81	0.686	0.29	2.26
Northern	0.74	0.592	0.24	2.26
Upper East	0.58	0.394	0.17	2.02
Upper West	0.82	0.745	0.24	2.75
Model detail				
Population size	2024.84			
Number of observations	2116			
Number of strata	20			
Number of primary sampling units	408			
Design df	388			
F (39, 350)	4.87			
Prob. > F	0.000			
McKelvey and Zavoina's R <sup>2</sup>	0.267			

<sup>\*\*</sup>statistical significance at 0.05 alpha level. The model estimates were adjusted for age of child, gender of child, birth order, fever status, vitamin A supplementation, age of mother, educational levels of mother and father, household wealth status, household size, number of children aged <5 y, source of drinking water, main floor material, region and place of residence.

Values in bold shows statistical significance at 0.05 alpha level.

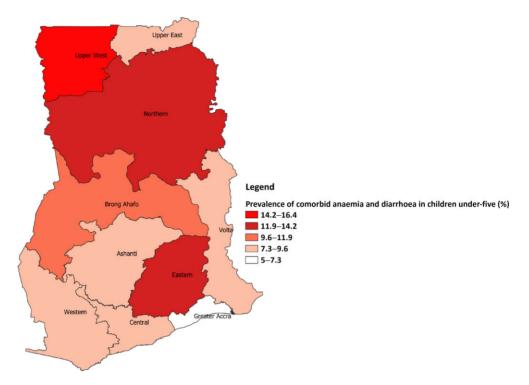


Figure 1. Regional prevalence of under-five comorbid anaemia and diarrhoea.

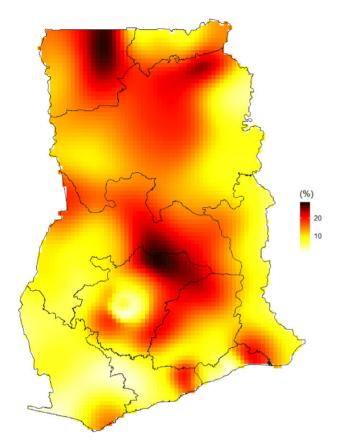
their risk factors identified. In Ghana, there is a paucity of literature on the comorbid patterns of anaemia and diarrhoea. Our findings reveal that the prevalence of comorbid anaemia and diarrhoea among children aged <5 y in Ghana was 9.28%. This is very low compared with the independent prevalence of anaemia (66.81%) and diarrhoea (12.66%) in the same sample.

Children gaed 6-23 mo were found to have greater odds of comorbid anaemia and diarrhoea compared with children aged ≥24 mo. This finding is consistent with previous studies that independently investigated risk factors of anaemia<sup>9,15</sup> and diarrhoea<sup>18,28,29</sup> in children. Children aged <2 y have immature immune systems compared with older children. In addition, the potential for contamination during complementary feeding in younger children may put them at higher risk of infections and subsequent development of diarrhoea and anaemia. Another plausible attributable factor is the changes in physiological processes as children grow. Under normal physiological conditions, there is rapid body growth and a compensatory decline of neonatal iron stores within the first 2 y of life. These deficits are higher during late infancy than at any other stage in life.<sup>30</sup> Some children aged <2 y with a high aversion to specific foods tend to be deprived of essential nutrients necessary for growth and development. This, coupled with poor feeding practices, may cause anaemia in children. While this appears seemingly unchallenging in the Western world, malnutrition in sub-Saharan Africa is on the rise.31 In light of this, it is essential to include iron-fortified nutrients in the diets of young children.<sup>30</sup>

In agreement with previous studies that investigated child-hood anaemia and diarrhoea, 9,18,19,32 we also report greater odds of comorbid anaemia and diarrhoea for male children compared with their female counterparts. This can be ex-

plained by the gender variations in levels of Hb, ferritin, transferrin receptors and erythrocyte mean cell volume during the age of 3–9 mo, which ostensibly increases the prevalence of iron deficiency anaemia in male children.<sup>30,33</sup> However, another studies did not find any relationship between diarrhoea and gender.<sup>29</sup>

History of fever was also found to be associated with greater odds of comorbid anaemia and diarrhoea. This finding is congruent with that of a previous study, which reported high associations between fever, diarrhoea and anaemia in children aged <5 y.<sup>7</sup> However, this contradicts the findings of Howard et al.,<sup>9</sup> who found no significant association between fever and anaemia after adjusting for current diarrhoea and other variables. In malaria-endemic regions such as Ghana, fever in children is often attributable to malaria, which can cause haemolysis of red blood cells, eventually leading to anaemia. The effect of malaria fever on comorbid anaemia and diarrhoea cannot be underestimated in malaria-endemic countries such as Ghana. We were, however, unable to control for malaria in this study. The best proxy for malaria was fever. However, using fever as a proxy of malaria may have its limitations as fever can also be a symptom associated with an array of microbial infections. The inflammatory cytokines such as IL-6 that are associated with febrile response<sup>34</sup> are also involved in the development of diarrhoea and anaemia of chronic infection.<sup>8-10</sup> Cytokines are known to shorten the lifespan of erythrocytes and impair erythropoiesis. 10 Thus, irrespective of the underlying cause of fever, the physiological changes associated with it and/or its resultant pathology appears to partly explain the aetiological process of comorbid anaemia and diarrhoea. Our finding suggests that fever in children aged <5 y should be given a higher priority by parents and health providers as it could be



**Figure 2.** Prevalence (%) of under-five comorbid anaemia and diarrhoea estimated by Guassian kernel estimator approach.

associated with comorbid conditions, which can adversely affect the overall health of children.

Consistent with the results of previous studies, <sup>14,28,32</sup> higher parental education was found to be associated with decreased odds of comorbid anaemia and diarrhoea in children aged <5 y. As with the case of other West African countries, higher education is a factor for social mobility in Ghana. Highly educated parents are more likely to have stable employment, which translates into better economic and living conditions, which can impact child health. In addition, children of highly educated parents are more likely to have access to a consistent diet, which can reduce the odds of anaemia associated with malnutrition. Moreover, it may be that highly educated parents are more likely to have knowledge on appropriate childcare skills such as handwashing prior to key activities such as meal preparation and childfeeding; this can help reduce those infections that can potentially cause diarrhoea and anaemia.

Likewise, children from households with two children aged <5 y were found to be associated with higher odds of having comorbid anaemia and diarrhoea compared with their counterparts from households with just one child aged <5 y. One plausible explanation for this is that with more children aged <5 y in a household, parental attention to childcare will probably be divided, which can negatively affect child health indicators.

We unexpectedly found that larger household size was associated with lower odds of anaemia in children aged <5 y in Ghana. This finding is contradictory to a previous study that found

a positive association between household crowding and anaemia in sub-Saharan Africa.<sup>17</sup> This finding is also in conflict with a Jordanian study that found a positive association between household crowding index and the prevalence of diarrhoea.<sup>35</sup> One assumption is that a large household size is associated with poor diarrhoea-prevention practices.<sup>36</sup> In our opinion, this conflicting finding can be explained by the fact that a large household size potentially entitles parents nursing several children aged <5 y to childcare support services such as cleaning, feeding and bathing. Moreover, one would have to interpret the findings in context, given that we have adjusted for many other variables whose presence may have caused household size to be seen a protective factor for comorbid anaemia and diarrhoea.

In congruence with previous studies, <sup>9,19,35</sup> children from richer households were found to have decreased odds of having comorbid anaemia and diarrhoea. Children from richer households are likely to live in cleaner and affluent neighbourhoods with good sanitation and access to clean water and consistent meals, which decreases the likelihood of diarrhoea and anaemia.

One key contribution of this paper is the spatial visualisation of the burden of comorbid anaemia and diarrhoea in children aged <5 y in Ghana. The spatial analysis revealed that national estimates can mask regional variations as well as potential subregional variations of childhood illnesses. The regional variations in childhood illness may be partly explained by the varying social, economic and environmental factors existing across the different regions in Ghana. Although the Upper West region of Ghana was found to have the highest average prevalence, we found zones of equally high prevalence of anaemia and diarrhoea in some clusters in virtually all the other regions of Ghana. Likewise, even although the Greater Accra region was seen to generally have the lowest regional burden, we found zones with a higher prevalence of comorbid anaemia and diarrhoea above the national average in the same region. These observations may be attributable to local factors at subregional levels that render the clusters different to one another, even clusters in the same region. This heterogeneity in the burden of comorbid anaemia at the subregional level has implications for policy and practice. Public health practitioners at the district level must adapt national policies on child health within the context of each subregional population. Our findings imply the need to identify high-risk zones at the subregional level for targeting to ensure efficient and effective public health interventions to address the burden of comorbid angemia and diarrhoea in children. This highlights the benefit of using spatial analysis in ensuring the precision of public health policy interventions.

# Strengths and limitations of the study

The findings from this study will be very useful for targeted interventions aimed at empowering the health sector and they also provide relevant data to add to the 'national statistical repertoire' since little is known about the subregional distribution regarding this subject. The study used nationally representative 2014 GDHS data, hence our findings can be generalised. The study also employed a complex sample design to account for the complexities in sampling design used during GDHS data collection. Spatial analysis also helped to identify observations made that were masked in national and regional estimates. Despite

these strengths, one limitation of the study is that it used crosssectional data, hence the associations we observed do not infer causality. The malaria status of the children included in the survey was not available in the dataset used in the current study. This limitation is worth mentioning, as the burden of malaria would have provided further insight into the findings we have reported, especially given that the study was conducted in a child population living in a malaria-endemic country. Nevertheless, as with the case of other secondary data reviews, our analysis was restricted to those variables available in the DHS data. Moreover. during the spatial mapping, only the Global Positioning System (GPS) coordinates of the central points of the clusters were available in the spatial shape file, rather than the precise locations of individual households. Additionally, there was a random angular displacement of up to 2 km in the GPS coordinates for urban clusters and up to 5 km angular displacement in the GPS coordinates for clusters in rural areas. This is carried out by the DHS program before spatial shape files are made publicly available in order to prevent identification of individual households. However, this can potentially affect the accuracy of spatial mapping. Additionally, a further limitation of employing spatial mapping is that it is dispersed across all pixels, as though entire areas in a cluster had a population settlement. This limitation was partly addressed by the use of population-weighted prevalence in the surface maps.

#### Conclusions

Our findings highlight the presence of intraregional variations in the burden of comorbid patterns of anaemia and diarrhoea in Ghana. The study identified zones with an extreme burden of comorbid anaemia and diarrhoea in children within each region for targeted policy interventions. Independent predictors of comorbid patterns of anaemia and diarrhoea among children aged <5 y in Ghana were a child's age, the gender of the child, history of fever, the number of children aged <5 y in the household, parental education, household size and household wealth. Our findings revealed socioeconomic disparities at both the parental and household level affecting child health in Ghana. This implies the need for holistic policy interventions to address disparities at various levels of society to improve health outcomes among children aged <5 y in Ghana.

**Authors' contributions:** HOD, BO, IA, CEA and PA designed the study; HOD, CEA, IA and BO wrote the introduction; HOD and PA wrote the methodology, and performed the data analysis and interpretation. HOD drafted the manuscript; HOD, CEA, IA, BO and PA critically revised the manuscript for intellectual content. All the authors read and approved the final manuscript. HOD and PA are the guarantors of the paper.

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**Ethical approval:** The procedures/protocols used to collect data during the 2014 GDHS were reviewed and approved by the Ethical Review Committee of the Ghana Health Service and the Institutional Review Board of ICF International. Informed consent from participants was obtained by trained enumerators on behalf of the Ghana Statistical Service (GSS) dur-

ing primary data collection. No additional consent was obtained for the analysis of de-identified secondary data.

**Data availability:** Data used for the study is freely available after a simple online request at https://dhsprogram.com/data/dataset\_admin/login\_main.cfm.

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