


# Patterns of Frequently Diagnosed Pediatric Morbidities in Hospitalized Children in the Volta Region of Ghana

Global Pediatric Health  
Volume 6: 1–12  
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DOI: 10.1177/2333794X19889230  
journals.sagepub.com/home/gph



Samuel Mawuli Adadey, MPHIL<sup>1</sup>, Richmond Ayee, MPHIL<sup>1</sup>,  
Sylvester Languon, MSC<sup>1</sup>, Darius Quansah, BSC<sup>1</sup>, and  
Osbourne Quaye, PHD<sup>1</sup> 

## Abstract

**Background.** The aim of this study was to identify the frequently diagnosed pediatric diseases in the Volta Region of Ghana, as well as to examine the burden of these diseases. The top pediatric diseases that were frequently diagnosed were malaria, gastroenteritis, systemic infection, anemia, pneumonia, and respiratory tract infection. **Methods.** Clearance was obtained from the Volta Regional Directorate of the Ghana Health Service to collect primary data on pediatric hospitalizations in the major hospitals in the Region. Diseases with more than 1000 recorded cases of hospitalizations were considered among the top frequently diagnosed childhood morbidities. **Results.** The data suggest that the Northern sector had different seasonal patterns of recorded diagnosed pediatric cases compared with the Central and Southern sectors, which had similar patterns of the reported diseases. Most of the pediatric diseases in the Volta Region were more prevalent during the dry seasons compared with the rainy seasons and resulting in seasonal patterns of hospitalizations. **Conclusion.** Although the frequently diagnosed pediatric diseases can be prevented and/or treated, many children are hospitalized, with a proportion of them dying. It is, therefore, important that efforts are made to reduce the burden of pediatric hospitalization.

## Keywords

hospital diagnosis, pediatric hospitalizations, pediatric diseases, Volta Region of Ghana

Received February 22, 2019. Received revised August 19, 2019. Accepted for publication October 22, 2019.

## Introduction

The levels and trends in child mortality report published by the United Nations International Children's Emergency Fund in 2017 indicated that about 7000 new born babies died every day in 2016.<sup>1</sup> The launch of the Global Millennium Development Goal 4 (MDG4) in the year 2000, which was aimed at reducing child mortality by two thirds in the period between 1990 and 2015, has led to reduction in child mortality and morbidity worldwide. Globally, pediatric mortality has declined from 90.6 deaths per 1000 live births in 1990 to 42.5 in 2015.<sup>2</sup> The World Bank report in 2016 has also shown that global child mortality rate declined by 56% from 93 deaths per 1000 live births to 41 deaths per 1000 live births. A previous report by the African Development Bank has shown that child mortality rate in sub-Saharan African (SSA) countries has declined from 174 deaths per 1000 live births in 1990 to 141 deaths per 1000 live births in

2010.<sup>3</sup> Also, the United Nations in Ghana has reported that the country has experienced a decline in child mortality rate from 155 deaths per 1000 live births in 1990 to 60 per 1000 live births in 2014, representing 58% reduction in child mortality.<sup>4</sup>

Although much progress has been made to reduce global child mortality and morbidity, a great deal of effort is needed to achieve the MDG4, since a significant number of children still die before age 5.<sup>2</sup> Out of 6.3 million under-5 deaths recorded in 2013, 3.27 million were as a result of infectious diseases, with the occurrence of 2.76 million deaths within the neonatal

<sup>1</sup>University of Ghana, Accra, Ghana

### Corresponding Author:

Osbourne Quaye, Department of Biochemistry, Cell and Molecular Biology, College of Basic and Applied Sciences, University of Ghana, Volta Road, Accra, Ghana.  
Email: oquaye@ug.edu.gh



period.<sup>5</sup> In SSA, about 1 in 13 children die before reaching age 5, whereas in developed countries, the ratio is 1 in 189.<sup>1</sup> Previous reports have shown that out of 10.8 million global child mortalities estimated in 2000, 41% occurred in SSA and 34% in Southeast Asia.<sup>6</sup> There have been changes in the patterns and levels of child mortality and morbidity across countries in the world; for instance, in 2013, global child mortality ranged from 2.3 to 152.5 per 1000 live births between Singapore and Guinea Bissau, respectively.<sup>7</sup>

Malnutrition and frequent exposure to infectious agents have been strongly linked to child mortality.<sup>1</sup> In developing countries in Africa, 20% of children below 5 years are malnourished,<sup>8</sup> and coupled with exposure to disease-causing pathogens, the morbidity and mortality of children are significantly high.<sup>6</sup>

Despite the existence of modern technologies and improved health care systems, children are still the most vulnerable to the leading causes of mortality, which are neonatal developmental disorders and infectious diseases.<sup>9</sup> A Child Health report published by the UN Inter-Agency Group for Child Mortality Estimation in 2013 indicated that pneumonia, preterm birth complications, intrapartum-related complications, diarrhea, and malaria contributed 17%, 15%, 10%, 9%, and 7%, respectively, to child mortality and morbidity.<sup>10</sup>

Africa is continuously burdened with under-5 deaths resulting from infectious diseases such as pneumonia, diarrhea, malaria, HIV, measles, and other causes.<sup>11</sup> Studies that have evaluated trends in child mortality and morbidity in Ghana suggest that malnutrition, malaria, diarrhea, pneumonia, HIV/AIDS, septicemia, measles, anemia, injuries, and neonatal disorders are the leading causes of death and morbidity among children.<sup>12-14</sup> However, these studies have been limited to 1 or 2 hospitals and do not give an extensive report of the trends of the causes of childhood morbidity and mortality. There is, therefore, the need for a more comprehensive evaluation that spans more study sites, to give a better estimate of the causes of childhood mortality and morbidity in Ghana. This study was designed to evaluate the leading causes of childhood morbidity in the Volta Region of Ghana.

## Methods

Pediatric diagnoses data were obtained from 23 major hospitals across the Volta Region of Ghana. The health centers provide primary, secondary, and/or tertiary health care services, which include general and specialized medicine, surgery, dentistry, and radiology among other services. The Volta Region of Ghana stretches from the upper part of the country to the lower part

(Figure 1) and has different vegetation and climate zones. Transmission of major diseases such as malaria are influenced by vegetation and climate.<sup>15-18</sup> The region was, therefore, separated into 3 main sectors based on geographical location, as well as climate and vegetation: Northern (savanna or Guinea savanna), Central (semi-deciduous forest zone and savanna woodland forest vegetation), and Southern (mangrove swamps, adjoining arid coastal plains, and coastal forest vegetation).<sup>19</sup>

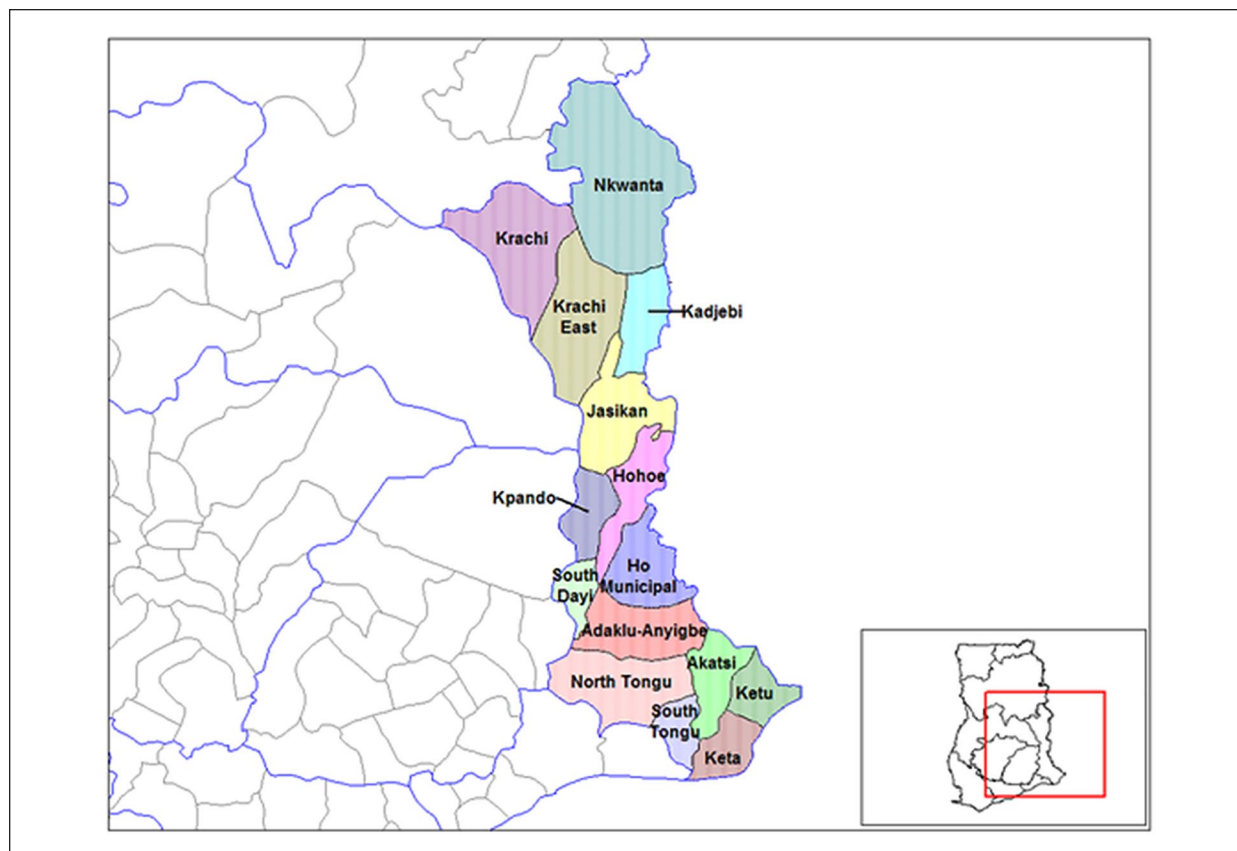
The patients considered for this study were children who were 5 years old and younger and were hospitalized in 1 of the 23 hospitals at the study site. The hospital diagnoses data from the records of the hospitals were analyzed to identify the frequently diagnosed disease conditions, and the conditions with more than 1000 patients were considered as frequently diagnosed pediatric conditions and selected for further analysis. The data for the study were obtained from the District Health Information Management System (DHIMS) II database in Microsoft Excel format and analyzed with IBM SPSS version 20 and GraphPad Prism 6. Frequency distribution, means, and percentages were used to compare the age groups, gender, hospitals, and hospitalization outcomes. Stacked column graphs were used to analyze the monthly distributions and pattern of hospitalization for the frequently diagnosed diseases. One-way analysis of variance and Tukey's multiple comparisons test were used to compare the yearly hospitalizations from 2012 to 2014 for all the frequently diagnosed diseases, and *P* values less than .05 (95% confidence level) were considered statistically significant.

## Ethical Approval and Informed Consent

Ethical approval and informed consent were not needed for the study. This was because the study posed no known risk since the data collected were in the nonidentifiable form and the patients cannot be reidentified, and the data were part of the routine health services provided by the hospitals. The data sets used for the study were hospital records data that had nothing to do with patient identity or contact. In addition, administrative clearance was obtained from the Volta Regional Directorate of the Ghana Health Services to collect pediatric diagnoses data from 23 major hospitals across the Region.

## Results

The study reviewed hospital diagnosis data from the DHIMS II database for 36 892 children aged 5 years and younger, who reported to the 23 hospitals in the Volta Region of Ghana (Table S1, available online). Out of the 36 892 children, 20 158 were males and 16 734 were



**Figure 1.** Districts in the Volta Region of Ghana captured in the study. Adopted from Ghana Broadcasting Cooperation (GBC; <https://www.gbcghana.com/1.11022657>).

females (Table S2, available online). We analyzed a total of 58 diagnosed diseases over the period of 3 years (2012-2014; Table S1). The frequently diagnosed diseases that resulted in at least 1000 hospitalization in the Region over the 3-year period were malaria, gastroenteritis, systemic infection, anemia, pneumonia, and respiratory tract infection (RTI), which sum up to a total of 31 838 hospitalizations (Table 1). Out of the 31 838 hospitalizations, a total of 12 638 hospitalizations were recorded in Southern sector of the Volta Region, 14 402 in the Central sector, and 4 798 in Northern sector (Table S3, available online). There was a sharp increase in the number of hospitalizations from age 0 to 1 year, and a gradual decrease from age 1 to 5 years (Table S2). Overall, the frequently diagnosed diseases contributed between 1.0% and 1.2% deaths in children of 5 years and younger in each of the 3 sectors in the Volta Region of Ghana (Table 1).

There was no statistically significant difference in the yearly number of malaria cases diagnosed in the Northern and Central sectors across the 3 years investigated (Figure 2A and B). However, the diagnosed malaria cases increased significantly from 2012 to 2014

in the Southern sector ( $P$  value of .0331), with 2014 recording the highest number of cases (Figure 2C). The first and fourth quarters of the years (dry seasons) had the highest number of malaria diagnoses in the Northern sector of the Volta Region (Figure 2D), whereas the second and third quarters (rainy season) had the highest number of malaria diagnoses in the Southern and Central sectors of the Region (Figure 2E and F).

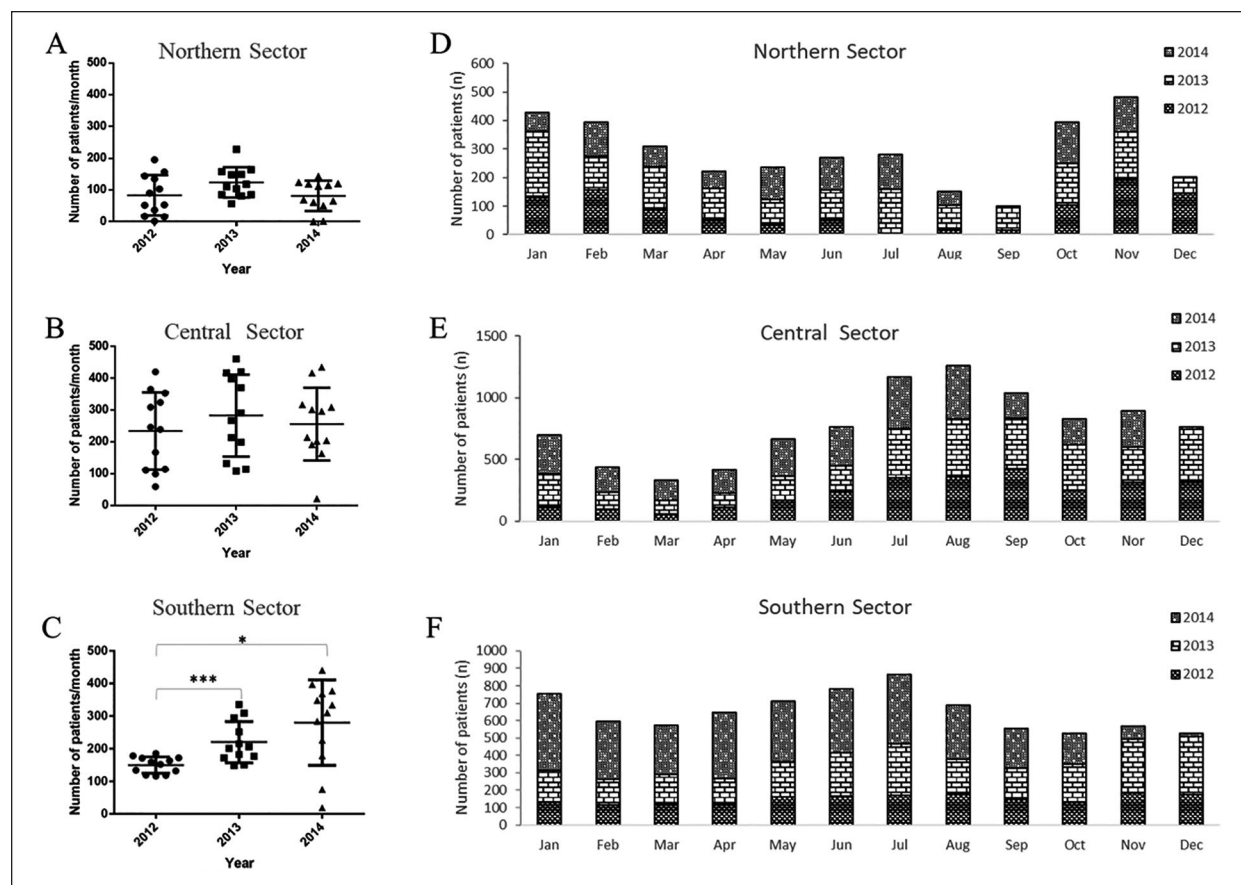
The yearly analyses of the hospitalization data did not show any significant difference in the monthly average number of gastroenteritis from 2012 to 2014. Although there was no significance difference in the monthly averages, a trend was observed in that the Central and Southern sectors recorded the highest average number of cases in 2013 (Figure 3A-C). There were higher number of gastroenteritis cases diagnosed in the dry season than in the wet season in the Northern sector of the Volta Region (Figure 3D), whereas the Central and Southern sectors had similar numbers in both seasons (Figure 3E and F).

There was also no statistically significant difference in the monthly average number of systemic infection cases from 2012 to 2014 in the Northern sector of the

**Table 1.** Frequently Diagnosed Diseases in the Volta Region and Disease Outcome<sup>a</sup>.

Volta Region	Admission Outcome	Malaria	Systemic Infections			Gastroenteritis	Pneumonia	Respiratory Tract Infection		Anemia	Total
			Systemic Infections	Gastroenteritis	Pneumonia			Respiratory Tract Infection			
Northern sector	Discharged	3414 (88.5%)	87 (70.7%)	356 (89.7%)	84 (72.4%)	98 (91.6%)	173 (88.3%)	4212 (87.8%)			
	Died	36 (0.9%)	3 (2.4%)	2 (0.5%)	2 (1.7)	1 (0.9%)	8 (4.1%)	52 (1.1)			
	Transferred	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	Absconded	11 (0.3%)	0 (0.0%)	1 (0.3%)	1 (0.9%)	0 (0.0%)	2 (1.0%)	15 (0.3%)			
	N/A	398 (10.3%)	33 (26.8%)	38 (9.6%)	29 (25.0%)	8 (7.5%)	13 (6.6%)	519 (10.8%)			
Total	3859 (100.0%)	123 (100.0%)	397 (100.0%)	116 (100.0%)	107 (100.0%)	196 (100.0%)	4798 (100.0%)				
Central sector	Discharged	9173 (88.8%)	756 (94.6%)	1136 (94.8%)	597 (95.8%)	508 (92.7%)	796 (88.1%)	12966 (90%)			
	Died	57 (0.6%)	39 (4.9%)	10 (0.8%)	18 (2.9%)	4 (0.7%)	26 (2.9%)	154 (1.1%)			
	Transferred	14 (0.1%)	3 (0.4%)	6 (0.5%)	5 (0.8%)	3 (0.5%)	3 (0.3%)	34 (0.2%)			
	Absconded	15 (0.1%)	0 (0.0%)	2 (0.2%)	1 (0.2%)	2 (0.4%)	4 (0.4%)	24 (0.2%)			
	N/A	1071 (10.4%)	1 (0.1%)	44 (3.7%)	2 (0.3%)	31 (5.7%)	75 (8.3%)	1224 (8.5%)			
Total	10330 (100.0%)	799 (100.0%)	1198 (100%)	623 (100.0%)	548 (100.0%)	904 (100%)	14402 (100.0%)				
Southern sector	Discharged	7723 (85.1%)	890 (91.5%)	1090 (93.3%)	597 (91.4%)	329 (93.4%)	360 (84.9%)	10983 (86.9%)			
	Died	35 (0.4%)	37 (3.8%)	11 (0.9%)	20 (3.1%)	4 (1.2%)	6 (1.4%)	113 (0.9%)			
	Transferred	22 (0.2%)	5 (0.5%)	9 (0.8%)	8 (1.2%)	0 (0.0%)	6 (1.4%)	50 (0.4%)			
	Absconded	12 (0.1%)	1 (0.1%)	2 (0.2%)	2 (0.3%)	1 (0.3%)	2 (0.5%)	20 (0.2%)			
	N/A	1282 (14.1%)	40 (4.1%)	56 (4.8%)	26 (4.0%)	18 (5.2%)	50 (11.8%)	1472 (11.6%)			
Total	9074 (100.0%)	973 (100.0%)	1168 (100.0%)	653 (100.0%)	346 (100.0%)	424 (100.0%)	12638 (100.0%)				

<sup>a</sup>The outcome of the hospitalization of the frequently diagnosed disease are presented as percentages of the sum in each disease category (in parenthesis). N/A represents the hospitalizations that do not have documented admission outcome.



**Figure 2.** Pattern of malaria diagnoses in the Volta Region: the variation in the annual diagnosis of malaria in the Northern (A), Central (B), and Southern (C) sectors were analyzed using 1-way analysis of variance. The significance levels are represented as  $* < .5$ ,  $** < .1$ ,  $*** < .01$ , respectively. The monthly patterns of malaria diagnoses from 2012 to 2014 are represented in stacked bar graphs: (D) Northern, (E) Central, and (F) Southern sectors.

Volta Region (Figure 4A), but the average number of cases recorded in the Central and Southern sectors in 2013 were significantly different (with  $P$  values of .0001 and .0002) for the Central and Southern sectors, respectively, when compared with the average number of cases in 2012 and 2014 (Figure 4B and C). There is relatively similar number of diagnosis of systemic infections in the Central and Southern sectors during both the dry and rainy seasons, but the diagnoses in the Northern sector increased and decreased in the dry and rainy seasons, respectively (Figure 4D-F).

The yearly analysis of the monthly average number of anemia cases showed no statistically significant differences in the 3 sectors (Figure 5A-C). The highest number of anemia cases were recorded between the second and third quarters of the year (rainy season) for all the 3 sectors (Figure 5D-F).

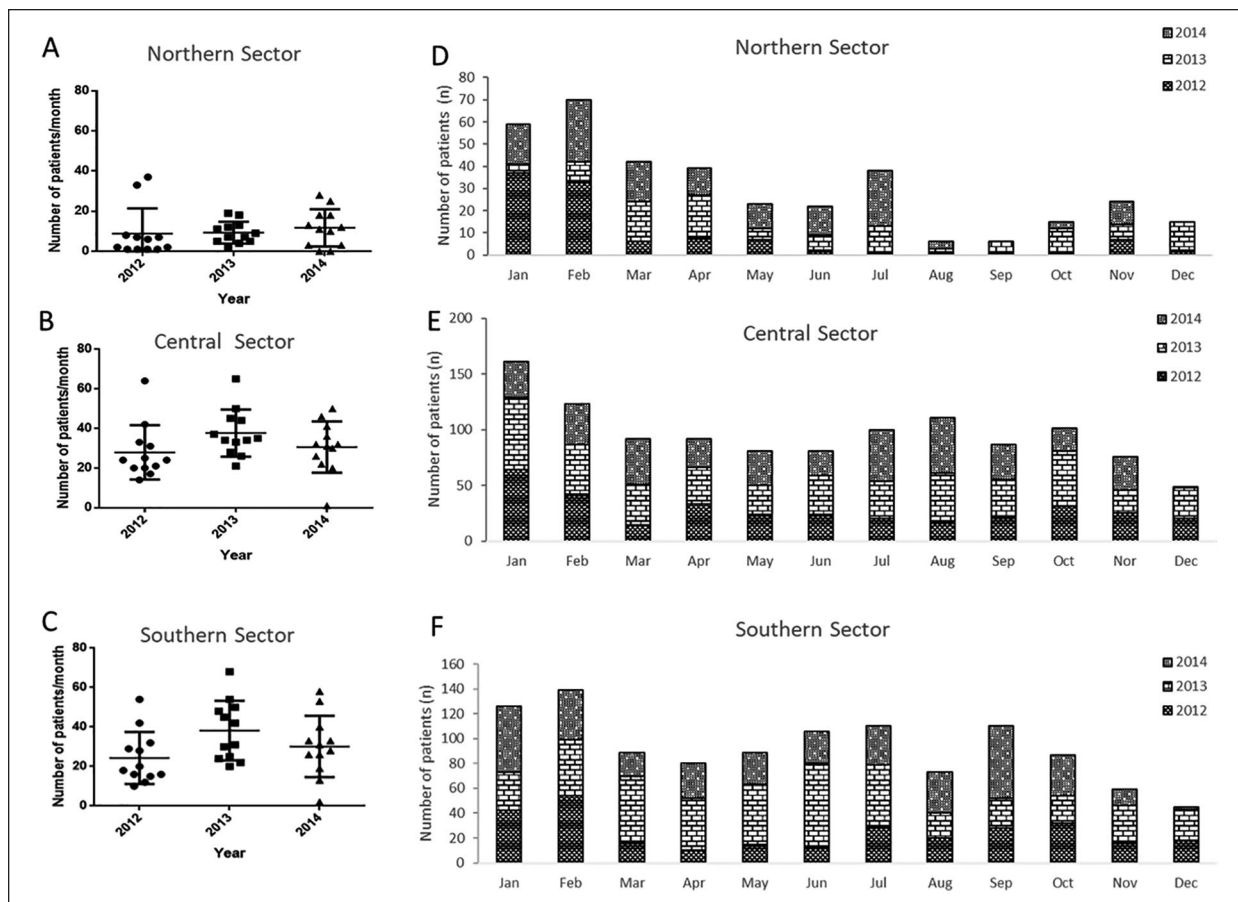
The monthly average number of pneumonia diagnoses did not show statistically significant difference from

2012 to 2014 in the Northern and Central sectors, but a significant difference was observed between 2012 and 2013 in the Southern sector with a  $P$  value of .01 (Figure 6A-C). Even though the seasonality was not well defined, there were more diagnoses of pneumonia cases in the dry season than in the rainy season for all the 3 sectors in the Volta Region (Figure 6D-F).

There was no statistically significant difference in the monthly average number of diagnoses of RTI from 2012 to 2014 in all the 3 sectors (Figure 7A-C), and no clear seasonality pattern was observed for the diagnoses of the infection in the 3 sectors, even though there were higher diagnoses in the dry season in the Northern sector (Figure 7D-F).

## Discussion

Although improved health facilities and life-saving interventions are currently available in most parts of the



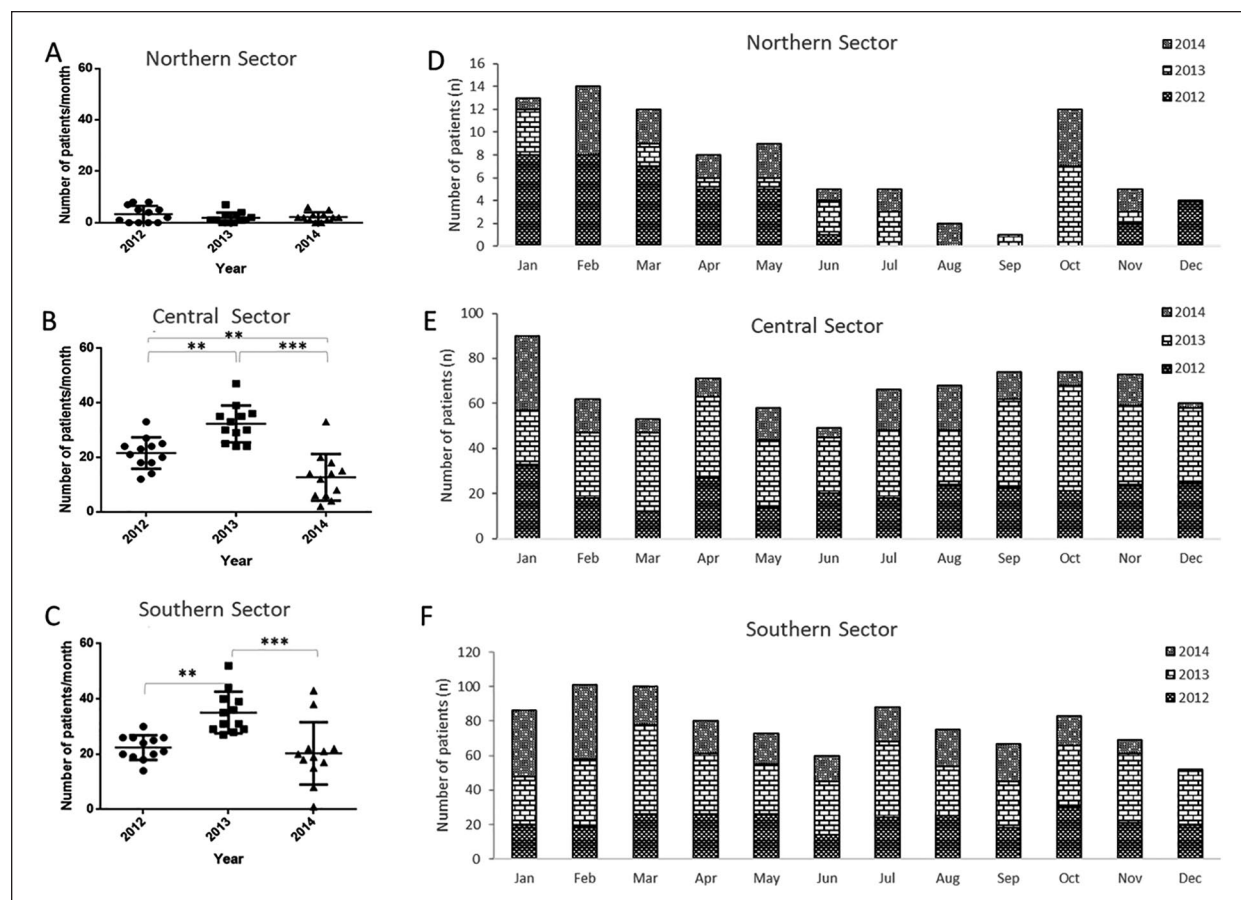
**Figure 3.** Pattern of reported gastroenteritis diagnosis in the Volta Region: the variation in the annual diagnosis of gastroenteritis in the Northern (A), Central (B), and Southern (C) sectors were analyzed using 1-way analysis of variance. The monthly patterns of gastroenteritis diagnoses from 2012 to 2014 are represented in stacked bar graphs (D) Northern, (E) Central, and (F) Southern sectors.

world, the global burden of child mortality and morbidity remains a global concern.<sup>20</sup> Effective prevention and control of diseases rely on data on the disease trends, factors responsible for these trends, and how the disease trends vary across different regions.<sup>21</sup> However, the lack of common methods for data collection makes it difficult to evaluate disease burden.<sup>22</sup> Comprehensive reports on disease patterns and frequency are important in the control of diseases, as well as the decision-making and planning processes of health sectors of countries.<sup>12</sup> As such, our study sought to evaluate the pattern of frequently diagnosed morbidities responsible for pediatric hospitalization in the Volta Region of Ghana.

The data showed that the Southern sector of the Volta Region had a higher number of pediatric hospitalizations compared with the Central and Northern sectors of the region. The high number of hospitalizations in the Southern sector could be due to higher population density<sup>23</sup> and the presence of a greater number of hospitals compared with the other 2 sectors (Table S1).<sup>24</sup> In

addition, there are less rural dwellers in the Southern sector compared with the Central and Northern sectors, which reflected in the smaller rural to urban ratio recorded in the South.<sup>23</sup> The health care-seeking behavior of Ghanaians has been found to be tightly shaped by the level of education of individuals.<sup>25</sup> This implies that urban dwellers of the Southern sector are likely to report to hospitals more frequently than their rural counterparts of the Central and Northern sectors, who tend to resort to traditional medicine. This is in line with a study that found that low-income households as well as individuals with low level of education often adopt alternative medicine to cater for their health needs.<sup>26</sup>

From our analysis, the number of hospitalizations decreased with increasing age, with children aged 1 year having the highest number of hospitalizations compared with other age groups. The low number of hospitalizations in children below the age of 1 year could be due to passive immunity conferred on them by their mothers, and children aged more than 1 year gradually develops



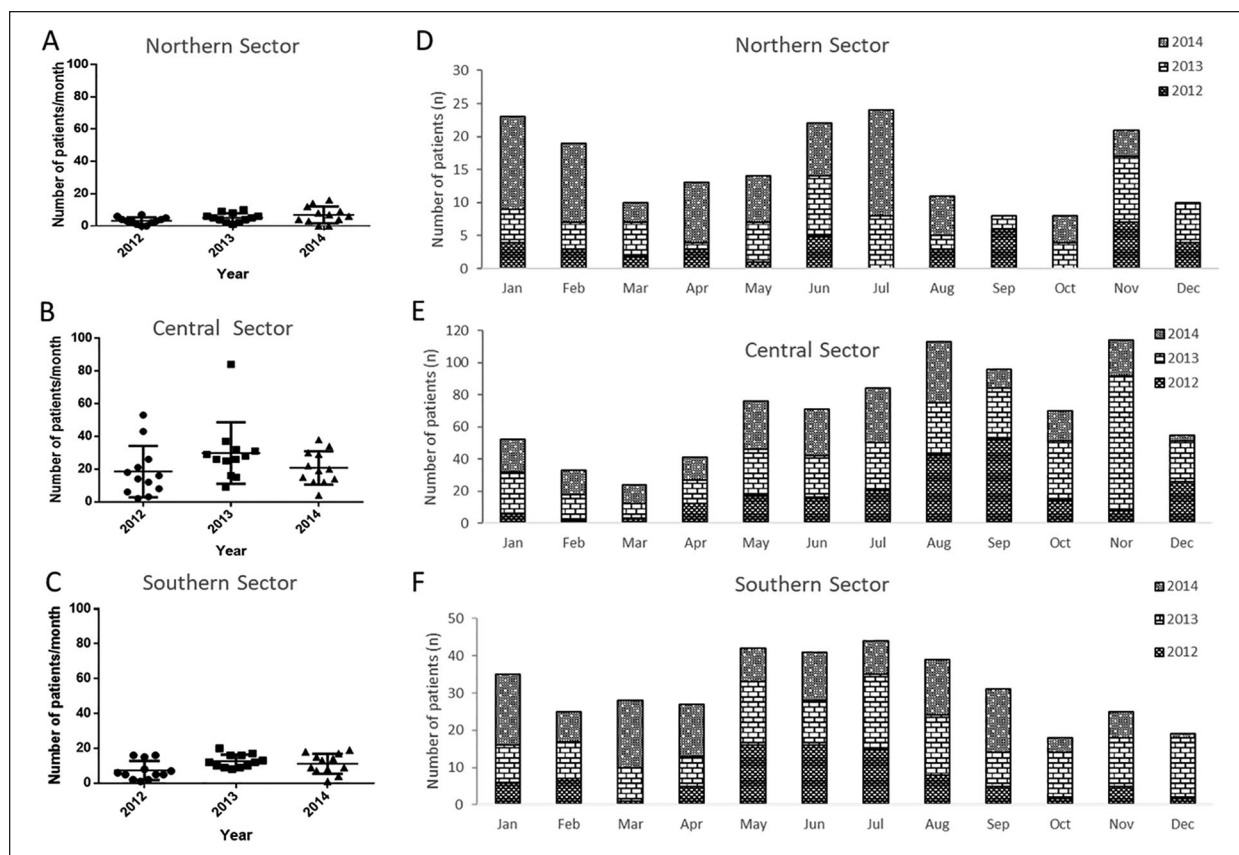
**Figure 4.** Pattern of reported systemic infections in the Volta Region: the variation in the annual diagnosis of systemic infections in the Northern (A), Central (B), and Southern (C) sectors were analyzed using 1-way analysis of variance. The significance levels are represented as  $* < .5$ ,  $** < .1$ ,  $*** < .01$ , respectively. The monthly patterns of systemic infections diagnoses from 2012 to 2014 are represented in stacked bar graphs: (D) Northern, (E) Central, and (F) Southern sectors.

acquired immunity to infections, and this could account for the reduction in the number of hospitalizations with increasing age.<sup>27</sup>

Malaria was the most diagnosed disease among children hospitalized in the hospitals used in this study between 2012 and 2014, and this observation was consistent with recent reports on the burden of the disease.<sup>28</sup> Among children less than 5 years globally, malaria mortality has reduced from 14.4% to 0.6% between the years 2000 and 2012.<sup>29</sup> In Ghana, there has been a general reduction in malaria reported cases for all ages from about 50% in 2012 to 20.4% in 2016<sup>28,30</sup>; however, the pediatric diagnoses in the Volta Region of Ghana, which is reported in this study, suggest otherwise. Although there was no significant difference in the yearly malaria cases recorded from 2012 to 2014 in Northern and Central parts of the Volta Region, there was a statistically significant increase in the number of malaria cases within the same period in the Southern sector of the

Region. There are 2 major malaria transmission seasons in Ghana, high and low, which corresponds to the rainy and dry seasons, respectively.<sup>31</sup> In our current study, however, the Northern sector, which has savanna vegetation,<sup>32</sup> reported higher number of malaria cases in dry seasons compared with raining seasons. A different trend was, however, observed in the Central and Southern sectors<sup>32</sup> where higher malaria cases were reported in the raining seasons.

Gastroenteritis was the second most common cause of hospitalization among children from the Volta Region. This corroborates with a study that indicated that diarrheal diseases constitute a large proportion of the childhood morbidity and mortality in resource-poor areas.<sup>33</sup> There was, however, no statistically significant difference between the yearly gastroenteritis cases record from 2012 to 2014, although analysis of the monthly distribution revealed an increase in reported cases during the dry seasons. Similar findings of increased gastroenteritis in



**Figure 5.** Pattern of anemia diagnosis in the Volta Region: the variation in the annual diagnosis of anemia in the Northern (A), Central (B), and Southern (C) sectors were analyzed using 1-way analysis of variance. The monthly patterns of anemia diagnoses from 2012 to 2014 are represented in stacked bar graphs: (D) Northern, (E) Central, and (F) Southern sectors.

the dry season have been reported in Navrongo, Ghana,<sup>34</sup> and Ouagadougou, Burkina Faso.<sup>35</sup> The increase in the number of gastroenteritis diagnosed during the dry seasons is probably due to rotavirus infection, which have been shown to peak in the dry season.<sup>35,36</sup>

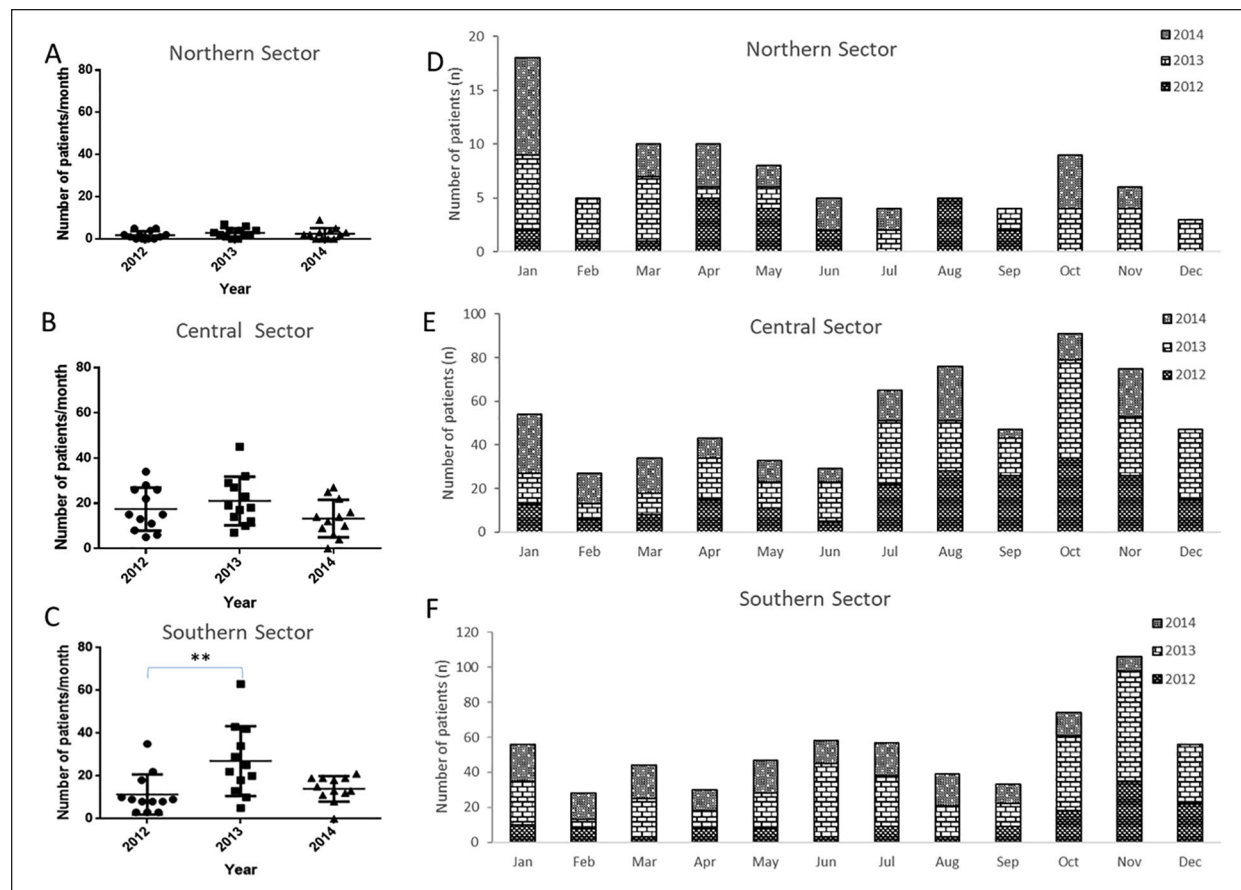
A significantly higher number of systemic infections were recorded in the Central and Southern parts of the Volta Region in 2013 compared with 2012 and 2014. Majority of the systemic infections were diagnosed as sepsis, bacteremia, shigellosis, and salmonella infections. In a study that was conducted in Ghana, *Staphylococcus epidermidis* was identified as the most common isolate in culture-proven sepsis, with a prevalence of 17.3%.<sup>37</sup> In other studies, however, nontyphoid salmonellae were identified as the most frequent systemic infections followed by *Streptococcus aureus* and *Streptococcus pneumoniae*.<sup>38,39</sup> The high number of systemic infection cases during the dry seasons compared with wet seasons may be due to frequent exposure of children to pathogens during dry seasons.<sup>40,41</sup>

Anemia in children continue to be a major public health disease<sup>42</sup>; and from this study, it is the fourth most

commonly diagnosed condition in childhood hospitalization in the Volta Region of Ghana, occurring all year round in the Northern sector but seasonal in the Central and Southern sectors. A major cause of anemia in Ghana is poor nutrition,<sup>43</sup> and the Northern sector of the Volta Region is inhabited by poor rural dwellers who often have nutritional problems,<sup>23</sup> and hence the all year round report of anemia in this sector. The seasonality observed in the diagnoses of anemia in the Central and Southern sectors might be due to malaria cases reported during the 2 different malaria transmission seasons (high and low) in Ghana. Malaria has been shown to strongly correlate with the burden of anemia<sup>44</sup> and supports the patterns of malaria and anemia in the Central and Southern sectors in our study.

Pneumonia and RTI have previously been reported as leading causes of under-5 mortality and morbidity globally<sup>45</sup> and in Ghana,<sup>46</sup> which is in line with findings of this study. Majority of the 2 diseases were diagnosed in the first and second quarters of the year in the Northern part of the Region, whereas majority of the cases were diagnosed in the third and fourth quarters of the year in





**Figure 6.** Pattern of reported pneumonia diagnosis in the Volta Region: the variation in the annual diagnosis of pneumonia in the Northern (A), Central (B), and Southern (C) sectors were analyzed using 1-way analysis of variance. The significance levels are represented as  $* < .5$ ,  $** < .1$ ,  $*** < .01$ , respectively. The monthly patterns of pneumonia diagnoses from 2012 to 2014 are represented in stacked bar graphs: (D) Northern, (E) Central, and (F) Southern sectors.

the Central and Southern parts of the Volta Region. Similar to the Central and Southern parts of the Volta Region, the Greater Accra Region (found at the coastal belt of Ghana) had higher RTI reported cases during the mid-wet season (June to December), which appears to be the period of seasonal circulation of human respiratory syncytial virus.<sup>47</sup>

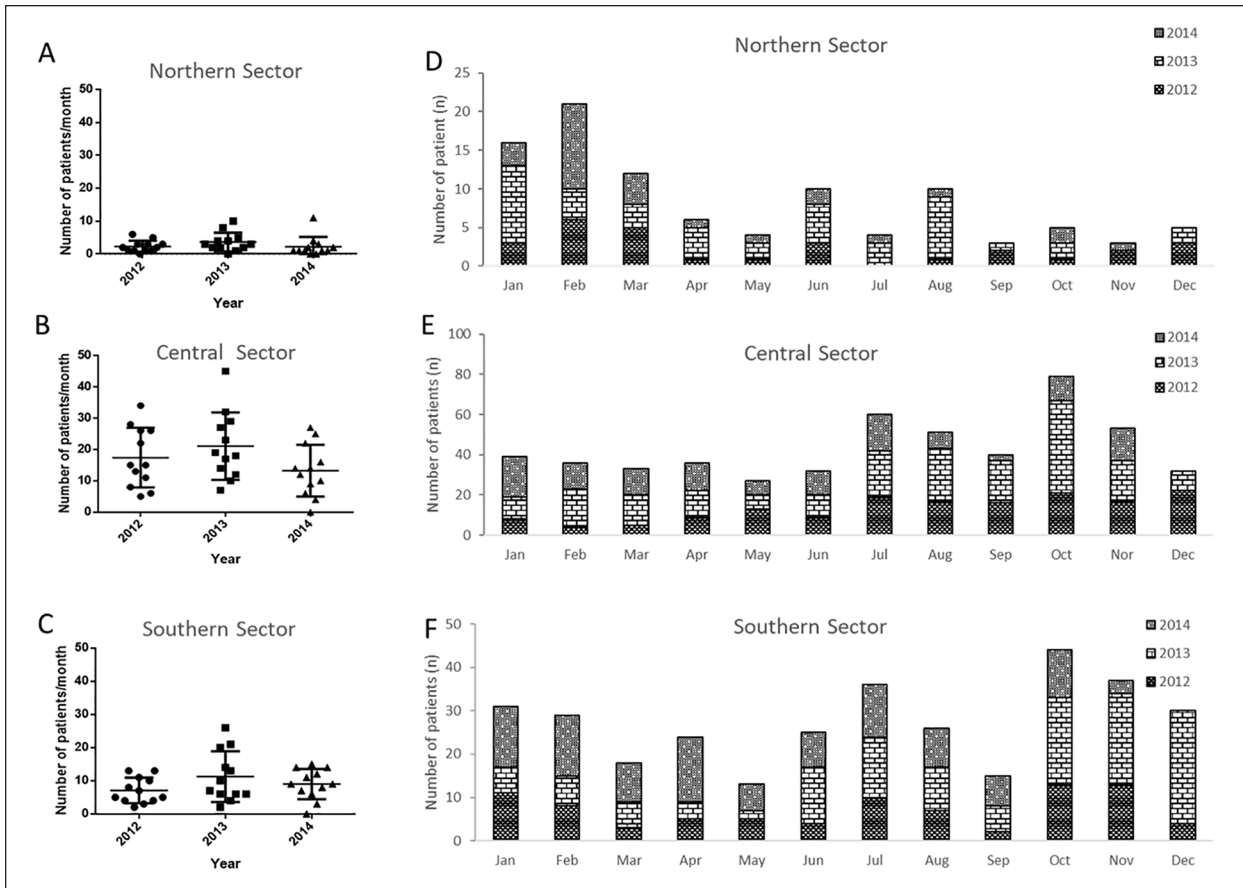
Although the management and treatment of pediatric diseases in Ghana is largely effective, there are still modest efforts by the Ministry of Health to improve the quality of health care delivery in the country.<sup>48,49</sup> It is encouraging to note that the two most frequently diagnosed pediatric diseases, malaria and gastroenteritis, had the lowest percentage mortality.

## Conclusion

In summary, the frequently diagnosed pediatric disease in the Volta Region of Ghana were identified as malaria,

gastroenteritis, systemic infection, anemia, pneumonia, and RTI. There was an increase in the number of malaria-diagnosed cases from 2012 to 2014 in the Southern sector of the Volta Region, which was contrary to what has been observed globally. A seasonal pattern of gastroenteritis hospitalization was found in the Region, with majority of the cases recorded in the dry seasons. In the year 2013, there was a significant increase in the number of systemic infections in the Central and Southern Volta compared with 2012 and 2014 with the highest number of hospitalizations recorded in the dry season.

The study results indicated that most children are hospitalized during the dry season and suggesting seasonal trends that can be exploited to fight pediatric morbidity and mortality. The pattern of pediatric hospitalizations in the Northern sector of the Volta Region were different from the patterns observed in the Central and Southern sectors of the Region. The data from this study suggest that even though there may be general global or national



**Figure 7.** Pattern of reported respiratory tract infection (RTI) diagnoses in the Volta Region: the variation in the annual diagnosis of RTI in the Northern (A), Central (B), and Southern (C) sectors were analyzed using 1-way analysis of variance. The monthly patterns of RTI diagnoses from 2012 to 2014 are represented in stacked bar graphs: (D) Northern, (E) Central, and (F) Southern sectors.

trends in diseases that cause childhood mortality, peculiar disease information within smaller geographical locations are needed for the implementation of specific interventions.

### Author Contributions

SMA: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

RA: Contributed to acquisition and analysis; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

SL: Contributed to analysis and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

DQ: Contributed to acquisition and analysis; drafted manuscript; critically revised manuscript; gave final approval; agrees

to be accountable for all aspects of work ensuring integrity and accuracy.

OQ: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

### Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

### ORCID iD

Osbourne Quaye  <https://orcid.org/0000-0002-0621-876X>

## Supplemental Material

Supplemental material for this article is available online.

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