# Clinical and epidemiological characterisation of Burkitt's lymphoma: an eight-year case study at Komfo Anokye Teaching Hospital, Ghana

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**ABSTRACT**

Endemic Burkitt's lymphoma (BL) is a juvenile malignant neoplasm of B-lymphocyte origin, markedly affected by climate, vegetation and geographical location. This real country-based, cross-sectional, retrospective study reviews all out-patient clinical records of patients histologically and/or clinically diagnosed with BL from January, 2000 to December, 2007 at the Komfo Anokye Teaching Hospital, Ghana, a country within the malaria and lymphoma belts of the world. The aim of the study is to clinically and epidemiologically characterise all cases of BL over an eight-year period to ascertain the most common form of BL demographically prevalent. A mean age of 6.9±2.7 (range: 1–16) was observed. Males generally dominated in incidence (M:F=1.43:1, $P< 0.001$) and significantly with facial presentation ($P<0.05$). Females weakly dominated in abdominal tumour presentation ($P>0.05$). The age range 4–8 years was the high risk range ($P< 0.001$) for both sexes. Males were affected early in life (4–7 years) compared to their female counterparts (6–11 years). Of the 551 cases reviewed, 48.3%, 32.7%, 15.8% and 3.3% involved the face, abdomen, combined facial and abdominal and either facial or abdominal with central nervous system (CNS) involvement (usually paraplegia), respectively. An intriguing observation was evident between facial and combined facial and abdominal cases which exhibited reversed trends in incidence. Three regions within the forest zone showed significantly higher ($P< 0.001$) incidences compared to the seven cohorts from the coastal and savannah agro-ecological zones of Ghana. No region was explicitly associated with any particular clinical presentation. The study has shown that although BL can present with demographic patterns in prevalence within a given geographical location, no clinical characterisation is associated with such patterns.

KEY WORDS: Burkitt's lymphoma. Neoplasms.

## Introduction

Burkitt's lymphoma (BL), described exactly six decades ago by Dennis Burkitt in Uganda,[1] is a malignant neoplasm of monoclonal B-lymphocyte origin which harbours a hallmark genetic mutation (translocation).[2] This tumour was the first to have a proposed viral aetiology[3] as well as the potential for being treated with chemotherapy alone;[4] however, its pathogenesis remains obscure.

The endemic subtype of BL, thought to be the form originally described by Burkitt, predominates in tropical regions of the world, especially in Africa and Papua New Guinea.[5] In Europe and the USA, BL is estimated to represent only 3% of all childhood malignant neoplasms, compared to 50–95% in Africa.[4,6] In equatorial Africa, endemic BL (eBL) is the most frequent childhood malignancy among all paediatric and adolescent lymphomas,[7] such that its pattern of incidence and mortality can be compared to that of non-Hodgkin's lymphoma (NHL) in general.[8]

*Plasmodium falciparum* malaria is intimately implicated in eBL.[9–14] Sporadic (sBL) and human immunodeficiency virus (HIV)-related BL are the other subtypes described,[2,15–18] and they exhibit different characteristics, even in terms of responsiveness to chemotherapy.[4]

Ghana is a sub-Saharan country which falls within the world's lymphoma and malaria belt.[20] There are 10 regions in Ghana that have varied climatic conditions and vegetation, even though the country generally experiences two climatic seasons, dry and rainy. The country's two main treatment centres for BL are Korle-Bu Teaching Hospital, situated in the southern part of the country, and Komfo Anokye Teaching Hospital (KATH), situated in the middle zone of the country.

The paucity of literature on BL in Ghana, coupled with the subtle but important differences reported[6,21,22] on the clinical and epidemiological characteristics of paediatric neoplasms, motivated the current work. Therefore, this study aims to investigate BL inter-regionally using data from KATH over an eight-year period to give a real country-based insight into the disease.

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## Materials and methods

A retrospective review was undertaken of all records of patients seen at the paediatric oncology unit at KATH. All BL cases diagnosed clinically and/or histologically from January

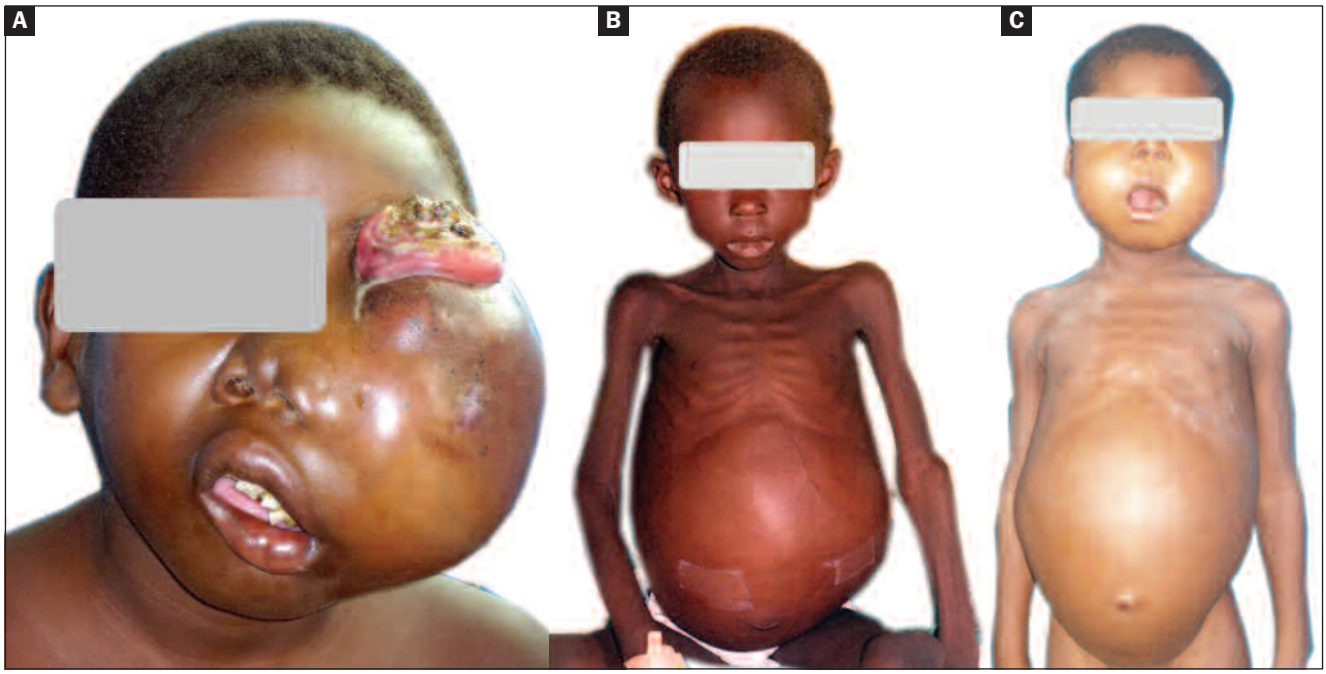


**Fig. 1.** Common sites of clinical presentation of BL in Ghana. A) facial (with eye infiltration), B) abdominal and C) combined facial and abdominal.

2000 to December 2007 were included in the study. Detailed information on region of origin, age, gender and primary site of clinical presentation were extracted from the hospital's local registry, coded and entered into a database. All computations were performed using SPSS version 16 (SPSS, Chicago, IL, USA) and Epi Info version 3.4.1 (CDC, Atlanta, GA, USA) statistical packages. Distribution of variables is expressed as mean±SD. Statistical significance for differences in categorical variables was analysed using the $\chi^2$ test. Statistical significance was set at $P<0.05$. The study was approved by the Committee on Human Research and Ethical Publications of the School of Medical Sciences, Kwame Nkrumah University of Science and Technology (KNUST) and Komfo Anokye Teaching Hospital (KATH).

## Results

A total of 551 cases were retrieved from the registry and the mean age of the patients was 6.9±2.7 years (age range: 1–16 years) (Fig. 2). Although the disease was fairly evenly distributed among both sexes, males dominated (324/551, $P<0.001$) giving a male:female ratio of 1.43:1. The common sites of primary clinical presentation were facial ($n=266$, Fig. 1A), abdominal ($n=180$, Fig. 1B), combined facial and abdominal ($n=87$, M:F= 1.29:1, Fig. 1C) and either facial or abdominal with central nervous system (CNS) involvement (usually paraplegia) ($n=18$, M:F= 2:1, Fig. 3). The lowest incidence of the disease was observed in the age ranges 1–3 and 13–16 years (Fig. 4) with general male dominance in all except the range of 9–11 years during which female dominance emerged ($P=0.725$).

In general, a significant relationship ($P=0.0005$) was found between site of tumour and gender. Most males presented with facial involvement (55.2%, M:F=2.21:1) while abdominal involvement dominated among the female

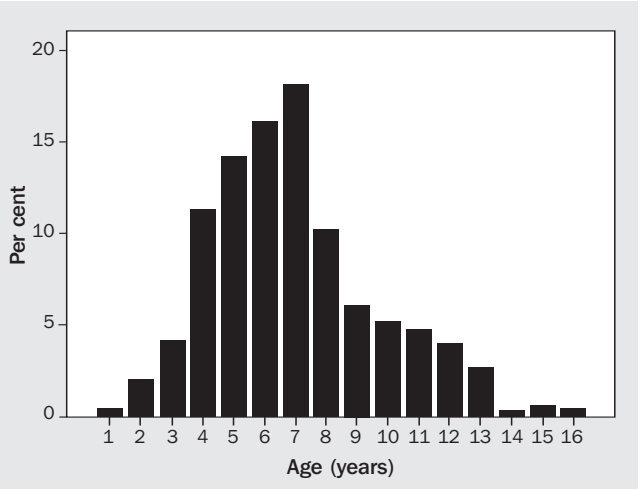


**Fig. 2.** Overall age distribution of Burkitt's lymphoma patients (KATH, 2000–2007).

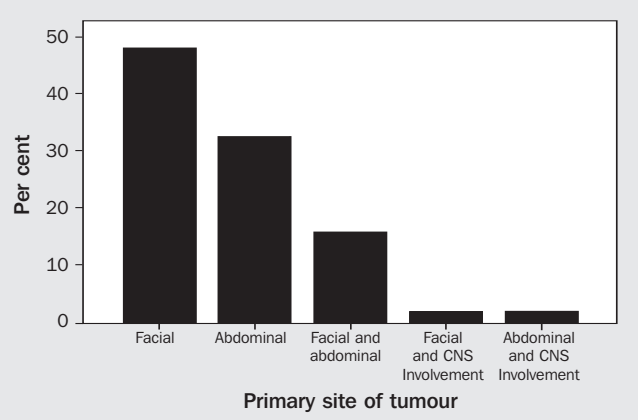


**Fig. 3.** Common sites of primary tumour presentation.

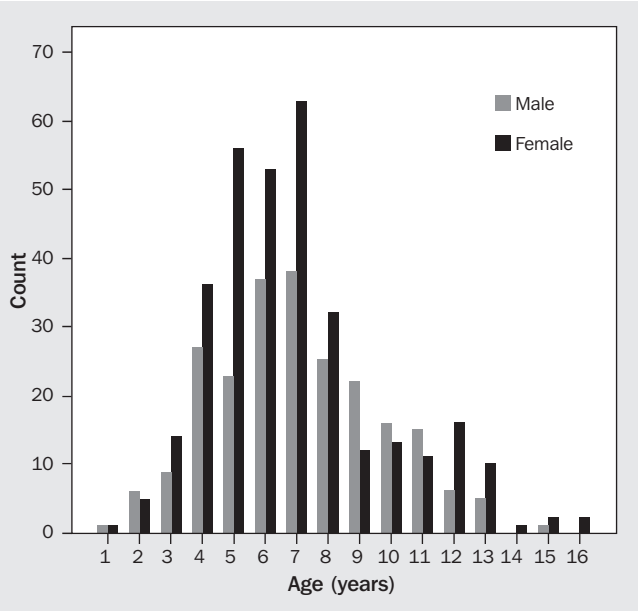


**Fig. 4.** Age and gender distribution of cases.

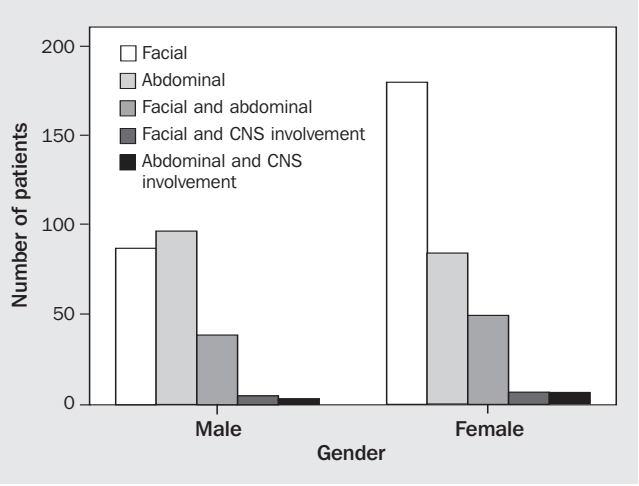


**Fig. 5.** Site(s) of primary tumour presentation by gender.

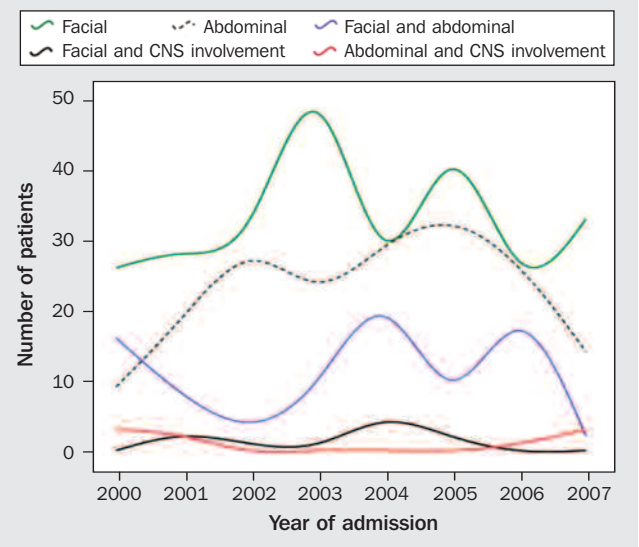


**Fig. 6.** Trend of sites of primary tumour presentations (2000–2007).

cohort (42.1%, M:F=1:1.14). The other anatomical sites of primary involvement demonstrated varied percentages (Fig. 5).

Facial involvement was the most frequently observed clinical presentation, with the highest incidence occurring in 2003 and 2005. The lowest incidence of facial presentation was seen in 2006. Interestingly, as the incidence of facial involvement changed, combined facial and abdominal presentation demonstrated a direct opposite response (Fig. 6). Although facial and abdominal presentations increased in 2005, the latter showed a downward trend after 2006. Facial cases from 2006 demonstrated an upward trend and cases involving the CNS remained steady.

The frequency of facial involvement was low among patients of eight years old and above (Fig. 7). Abdominal cases and combined facial and abdominal presentations demonstrated their highest incidence (11.5% and 7% rise, respectively) from an average of 13 cases at around age six years. Figures 8 and 9 show the clinical presentation of the disease related to gender and age. On average, BL cases that involved the face predominantly affected younger children (age: 6.6±2.7 years), of which 67.3% were males. Abdominal cases appeared to be frequent among children of 7.3±2.6 years, with equal presentation among the sexes. Cases that involved combined facial and abdominal sites were more common in the intermediate age range (6.9±2.5 years) compared to that for facial and abdominal presentations. Additionally, females were generally affected later in life (age: 7.7±2.8 years) than their male counterparts (6.2±2.2 years). Cases involving the CNS and other anatomical sites were less common but could not be ignored altogether. Males were most commonly affected (66.67%) cumulatively and at an early age (Table 1).

Climate, vegetation and geographical location have long been associated with BL incidence, and therefore the origins of all the recorded cases were analysed using the regional boundaries within Ghana as grouping determinants. Among the 10 regions of Ghana, Ashanti, Brong-Ahafo and Western (all within the forest zone) were the regions that showed the highest incidences of BL (Fig. 10). The general trends are shown in Figure 11. It can be inferred from these data that all sites of tumour presentation are common in all the regions of Ghana ($P$=0.821).

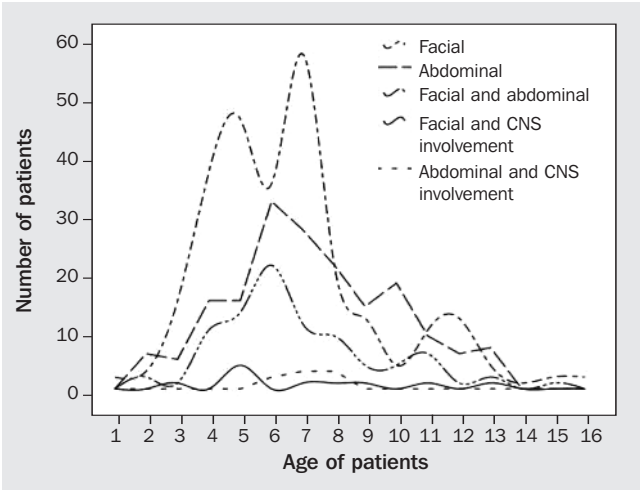


**Fig. 7.** Overall trend of site(s) of primary tumour presentation(s) in relation to age of patients.

## Discussion

Burkitt's lymphoma is regarded as 'endemic' in Africa because it stands out as the predominant childhood malignancy.[7,8] Scanty information is available on this important juvenile neoplasm in local and international literature on Ghana, which has one of the highest incidences of this condition.[23] According to GLOBACON 2002, Uganda is the country with the highest BL incidence in Africa, recording approximately 20 cases per year.[8] This misinformation has been made possible largely because of the unavailability of a cancer registry in Ghana.

Nkrumah and Olweny[23] reported an annual BL incidence of approximately 40 cases over an 11-year study conducted in Accra, Ghana. The data presented here show an incidence of approximately 75 cases annually at KATH. However, this may be an underestimate because of the limited number of treatment centres to which people could report easily. The overall gender (M:F) ratio found in the present study is comparable to those reported elsewhere in Africa (e.g., 1.5:1 in Uganda,[8] 1.8:1 in Nigeria[24] and 1.7:1 in a 1985 Ghanaian report).[23] In contrast, Algeria, Brazil and Europe[25–27] exhibit higher male predominance in the few cases observed. The reason why most Western countries exhibit higher male predominance is unclear but this has been well documented by Sandlund and colleagues.[6]

Although an overall mean age of approximately 6.9 years was observed, which is comparable with international literature reports,[6,8,14,23,28] there was an intriguing observation as to the relationship between specific age ranges (within 95% CI) and the primary site of tumour presentation. The overall age range for this study was 1–16 years, which is comparable with the study by Parkins and colleagues in Ghana,[29] whose cohort had an age range of 2–14 years. Thus, one can speculate that BL is rare among children less than a year old in this country. Although NHL is said to have no clear age-related incidence,[30] the present study identified Ghanaian children of age 4–8 years to be at high risk of BL.

The general trend is that facial cases manifest at an early age, with male dominance, while females show the highest number of abdominal presentations. which tend to appear at a later age. Boerma and colleagues[31] reported age and gender as strong predictors of BL occurrence. It is also worth noting that malaria incidence and mortality among Ghanaian children have been reported to assume an age-gender pattern whereby males exhibit higher susceptibility until puberty, when there is a reversal in incidence.[32] In light of this, the susceptibility of children to protracted *P. falciparum* malaria cannot be over-emphasised as an important factor in BL pathogenesis.

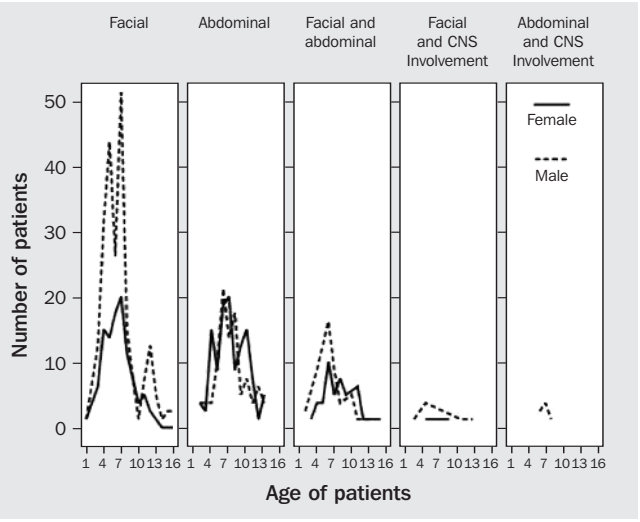


**Fig. 8.** Distribution of BL with respect to gender and age stratified by site of tumour presentation.

Approximately 3.3% of the patients had CNS involvement, which suggests that the nervous system is not a common site of primary involvement compared to the significantly higher ($P<0.05$) levels of facial or abdominal presentation among Ghanaian children (Fig. 3, Table 1). The observation that facial and combined facial and abdominal presentation exhibit directly opposite incidences (Fig. 6) requires validation from other BL registries. Once verified, clinical presentation prediction models could be developed to anticipate the predominant form in a given year.

Ever since it was shown that certain climatic conditions, especially moisture and warmth, characterise endemic BL regions,[33] the search has continued to identify direct aetiological factor(s) for this tumour. Ghana is divided into three agro-ecological zones: savannah, forest and coastal. All three regions within the forest zone showed a significant BL incidence compared to their cohorts (Fig. 11). As originally noted by Burkitt,[34] the tumour is rarely seen in areas with a yearly mean temperature below 15.5°C, annual rainfall less than 50 cm, and high altitude. The annual mean rainfall and temperature for the three regions within the forest zone are 125 cm and 26°C, respectively, with humidity of 70–80%.[35]

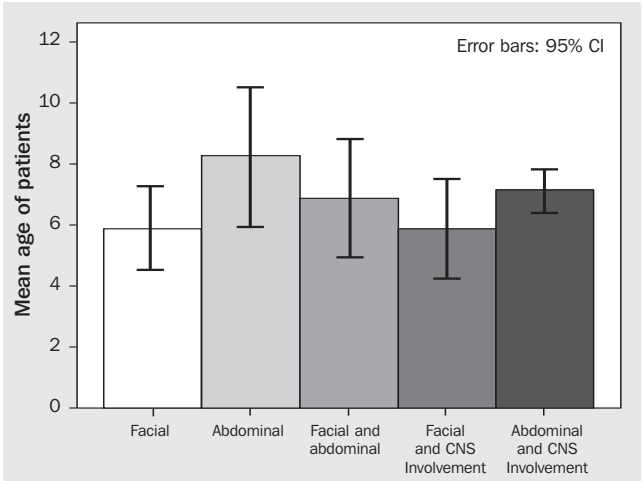


**Fig. 9.** Mean age distribution of BL cases.

**Table 1.** Mean age (SD) and gender characteristics of BL cases involving either the face or abdomen with the CNS (usually paraplegia).

| | Facial plus CNS (*n*) | Abdominal plus CNS (*n*) |
|---|---|---|
| Overall | 7.1±3.1 (10) | 7.1±0.8 (8) |
| Male | 7±4 (6) | 6.8±0.8 (6) |
| Female | 7.3±1.7 (4) | 8 (2) |

CNS: central nervous system.

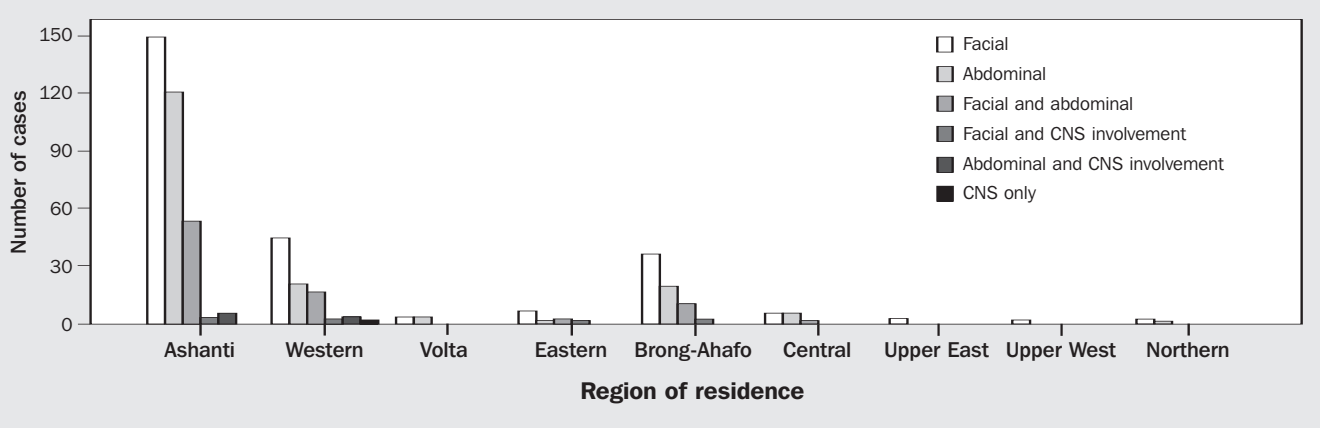


**Fig. 10.** Incidence of BL in the 10 regions of Ghana (KATH 2000–2007).

The other zones exhibit one or two of the necessary conditions but high fluctuations exist compared to the relatively stable conditions of the forest zone.[34]

Of the more than 3.5 million malaria cases recorded in 2003 nationwide, 40% were children under five years old. The Ashanti region showed the highest incidence (22%), followed by Brong-Ahafo region (16%), with the Western region contributing 6% to the total incidence.[36] These conditions clearly satisfy the characteristics defined by Burkitt, and hence explain the significant BL incidence observed in this zone.

In conclusion, all clinical presentations of Burkitt's lymphoma are fairly common among Ghanaian children under the age of 17 years. This small study has demonstrated that geographical assessment within endemic countries is necessary to establish demographic maps of BL incidence, management and monitoring. This study has confirmed previous findings of ecological importance in BL pathogenesis. However, it is imperative that similar investigations are carried out at other treatment centres in Ghana and in other countries with a high incidence of BL. □

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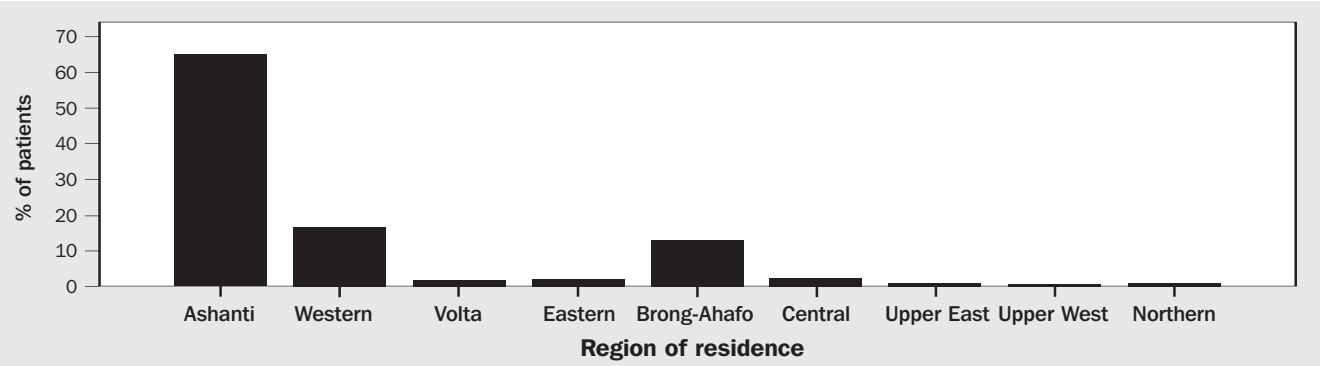


**Fig. 11.** Regional BL presentation in the 10 regions of Ghana.

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