

Burkitt lymphoma: Trends in children below 15 years reveal priority areas for early diagnosis activities in north-west Cameroon

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Background: Burkitt lymphoma is one of the most common childhood cancers in Cameroon. Incidence rates of 5.9/100 000 and 2.58 per 100 000 have been reported in two studies in 2005 and 2012 amongst children below 15 years in the North-West Region.

Aim: This study seeks to examine how Burkitt lymphoma incidence has varied between the various health districts of north-west Cameroon from 2003 to 2015.

Setting: North-West region of Cameroon.

Method: Ethics approval was obtained from the relevant university and Health Services Institutional Review Board. Population data was obtained from the regional delegation of public health. The Paediatric Oncology Networked Database registry from two hospitals and two pathology-based registries were reviewed for cases per year from the various districts. Age-standardised incidence rates were computed for all districts by year using the World Health Organization world standard populations.

Results: A total of 317 cases were registered. Overall age-standardised incidence rate was 3.07 per 100 000. Annual incidence ranged from 0.09 in 2003 to 6.12 in 2010. The districts with the highest incidence rates for the entire study period include Nwa with 10.54; Ndop with 5.63; Benakuma with 5.48; Ako with 4.97; and Nkambe with 4.73.

Conclusion: Clustering of Burkitt lymphoma is seen in the region, with the highest incidence in Nwa, Ndop, Benakuma, Ako and Nkambe. These districts should be prioritised for awareness creation campaigns. There is need for a population-based childhood cancer registry in the region, which will use both active and passive surveillance methods to record all childhood cancer cases.

Introduction

Burkitt lymphoma (BL) is a malignant neoplasm of lymphoid tissue, affecting the B-lymphocytes.¹ It mostly affects children between 2 and 15 years of age and is known to affect more boys than girls in the ratio of 1.5:1.² Burkitt lymphoma is a clinically aggressive and rapidly growing tumour with a reported tumour doubling time of less than 3 days.³ Burkitt lymphoma development has been linked to Epstein-Barr virus infection and malaria,⁴ and higher incidence rates have been reported amongst populations with higher burden of malaria, Epstein-Barr virus (EBV) and human immunodeficiency virus (HIV).^{5,6,7} The most common sites of presentation of the disease as seen in Cameroon include the following: abdomen (76%), face (50%), spleen (36%), liver (20%), kidney (18%), paraspinal (9%), bone marrow (9%), external lymph nodes (7%), chest wall (4%), cerebrospinal fluid (4%), cranial nerves (3%), femur (2%) and testis (2%).⁸ Diagnosis of BL is confirmed by histological and immunocytological demonstration of BL cells in tissue specimens.³ Cytological examination of cerebrospinal fluid and bone marrow specimens is essential to ascertain metastasis and facilitate staging.⁸

Burkitt lymphoma makes up about 30%–50% of all childhood cancers recorded in tropical Africa.^{1,9} Burkitt lymphoma treatment is available in a few treatment centres operating independently in different regions of Cameroon. A population-based cancer registry in the capital city Yaoundé reported an age-standardised incidence rate (ASIR) of 46.8 per million person years.¹⁰ Hospital-based paediatric cancer registries exist in two centres in the North-West Region centres, including Banso and Mbingo Baptist Hospitals. Pathology laboratories also each keep a pathology-based cancer registry, including the pathology laboratories at Mezam Polyclinic Bamenda and Mbingo Baptist Hospital, both in the North-West Region.

Two earlier studies have described the epidemiology of BL in north-west Cameroon. Wright et al.¹¹ reported an incidence of 5.9/100 000 in 2005, while Lewis et al.¹² revealed an average incidence of 2.58 per 100 000 children under 15 years. As paediatric oncology care develops in the North-West Region of Cameroon, this study seeks to examine how the trends of BL incidence have varied between the various health districts of the region from 2003 to 2015, with the goal of identifying hot spots of the disease, which would be priority areas for awareness creation and early diagnosis initiatives.

Methods

This is a descriptive cross-sectional study. This study involved children under the age of 15 years living in the North-West Region of Cameroon between 2003 and 2015. Cameroon is classified by the World Bank as a lower middle income country in central Africa and holds a total population of 24 million inhabitants, of which 43% are younger than 15 years.¹³ The North-West Region of Cameroon has a total population of about 1 950 000 people¹⁴ divided into 19 health districts, namely Ako, Bafut, Bali, Bamenda, Batibo, Benakuma, Fundong, Kumbo East, Kumbo West, Mbengwi, Oku, Njikwa, Nkambe, Ndup, Ndu, Nwa, Santa, Tubah and Wum.¹⁵

The population data for the various years of the study was obtained from the regional delegation of public health. This is updated as per the 2007 national population census, and it is the population figures used for healthcare planning in the region. The population for the age group 0–14 years was calculated as 42.47% of the total population for each district, as suggested in the National Demographic Health Survey.¹⁶ The World Health Organization (WHO) world standard populations were used to calculate ASIRs.¹⁷

Two hospital-based children's cancer registries were reviewed for extraction of data for BL in the age group 0–14 years from 2003 to 2015. These are the registries of Bansa Baptist Hospital and Mbingo Baptist Hospital, all using the Paediatric Oncology Networked Database (POND) – an online paediatric cancer registration platform developed by St Jude's Children's Hospital in the USA.¹⁸ In these hospitals children clinically suspected of having BL are subjected to a fine needle tumour aspirate, bone marrow and cerebrospinal fluid cytopathology and an abdominal ultrasound to confirm the diagnosis. Two pathology-based registries in the region were also explored. Patient names and medical record numbers were cross-checked to avoid duplication of cases during data extraction from the various registries.

Data analyses

Data extracted from the hospital-based and pathology registries included demographics (age, sex, district of residence), diagnosis information (disease name, method of diagnosis, date of diagnosis) and tumour site. Data were collected in Microsoft Excel 2016 and analysed using SPSS version 25. Calculations of ASIR using WHO standard populations were done by inserting formulas into the Excel spreadsheets. Means and standard deviations were

used to describe continuous variables. Age-standardised incidence rates were computed for all districts by year.

Ethical considerations

This study used secondary data form. Ethics approval was obtained from the relevant Health Services Institutional Review Board (ethical clearance number: IRB2016-28). Permission was obtained from the administrators of all the health units and laboratories from which data were obtained.

Results

Clinical profile of cases

From 2003 to 2015, there were 317 registered children with BL in the North-West Region of Cameroon. A total of 279 cases were registered in the two hospital-based registries; while 38 more were only recorded in the pathology-based registries. There were 136 (42.9%) females and 181 (57.1%) males, making a female:male ratio of 1:1.3. The age at diagnosis ranged from 1 to 14 years, with a mean of 8.02 years (standard deviation[SD] = 2.76).

Of all cases, 252 (79.5%) had cytological confirmation of BL while 57 (18%) were diagnosed only on a clinical basis, mostly with the use of ultrasound scan. One hundred and seventy one (54%) of the cases had only abdominal disease, 95 (30%) had facial disease, while 45 (14%) had both abdominal and facial tumours.

Burkitt lymphoma distribution by year and district

The overall ASIR was 3.07 per 100 000 for children below 15 years in the region in the study period from 2003 to 2015. Annual incidence ranged from 0.09 to 6.12. Age-standardised incidence rates generally increased over the study period, with a peak ASIR of 6.12 per 100 000 in 2010. From 2010 the BL incidence rate dropped steeply and has been fairly constant between 2.57 and 3.17 per 100 000 from 2013 to 2015 (Figure 1).

The average ASIR in individual districts of the region for the entire study period ranged from 0/100 000 in Bali and Njikwa health districts to 10.54/100 000 in Nwa health

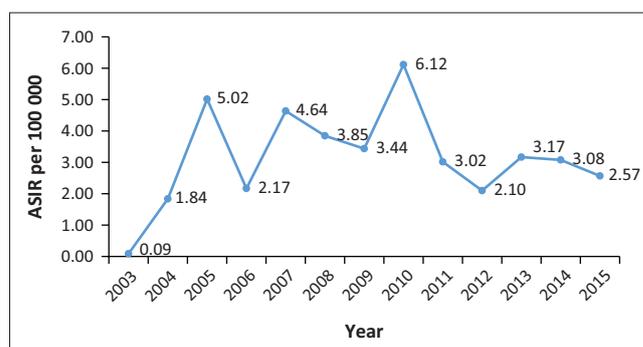
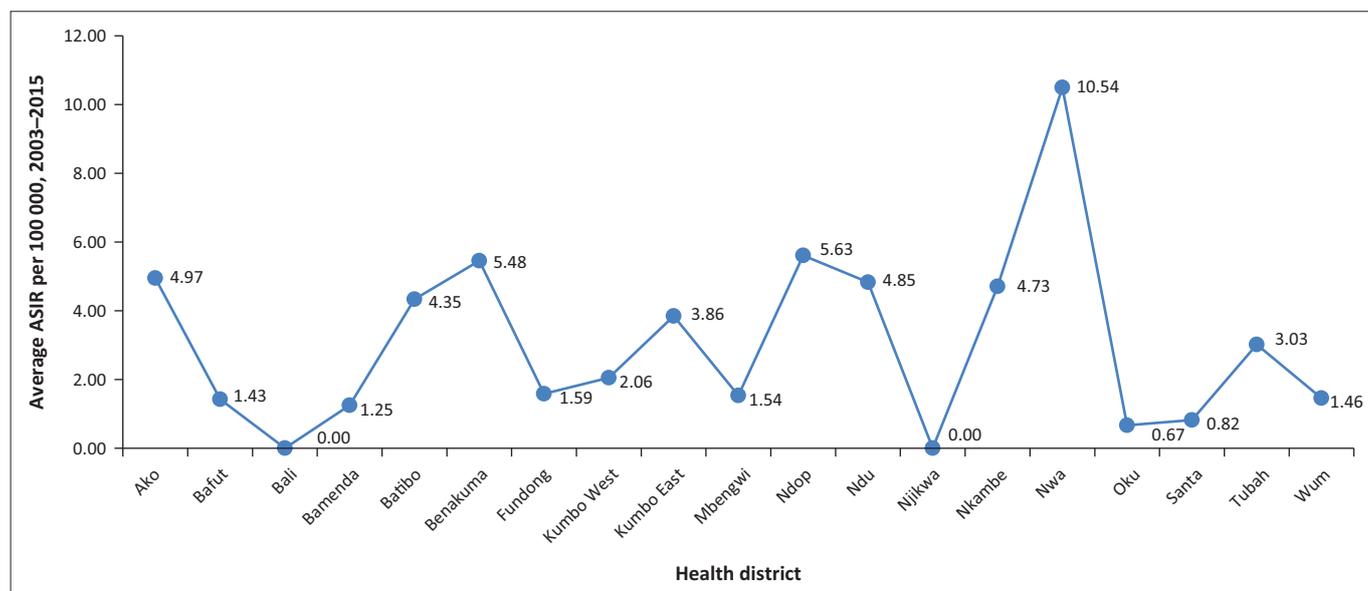


FIGURE 1: Trend of age-standardised incidence for Burkitt lymphoma in the North-West Region, 2003–2015, for children aged 0–14 years.

TABLE 1: Annual age-standardised incidence (0–15 years) of Burkitt lymphoma in various districts of the North-West Region, 2003–2015.

Health district	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Average
Ako	-	-	-	0.00	8.63	0.00	0.00	11.52	16.82	6.31	0.00	5.39	6.00	4.97
Bafut	0.00	0.00	6.77	0.00	6.03	0.00	0.00	4.01	0.00	0.00	3.14	0.00	0.00	1.43
Bali	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Bamenda	0.00	0.96	1.81	0.00	4.76	1.06	2.74	1.82	0.71	2.37	0.00	0.68	0.57	1.25
Batibo	0.00	6.22	5.20	2.53	12.41	7.47	0.00	8.06	3.15	7.00	0.00	2.46	6.48	4.35
Benakuma	-	-	-	-	-	13.90	12.79	0.00	4.63	3.80	0.00	0.00	14.79	4.86
Fundong	0.00	0.00	0.00	0.00	1.35	0.00	1.17	10.07	5.96	0.00	3.70	0.00	0.00	1.59
Kumbo West	1.31	0.00	5.81	2.98	3.24	5.34	8.67	1.42	0.00	0.00	0.00	0.00	0.00	2.06
Kumbo East	0.00	7.88	7.81	2.96	9.20	4.19	2.72	2.70	9.09	0.00	4.43	0.00	3.06	3.86
Mbengwi	0.00	0.00	3.51	0.00	2.45	0.00	2.77	0.00	0.00	0.00	0.00	8.62	4.25	1.54
Ndop	0.00	7.37	21.37	6.00	3.33	5.67	7.74	12.70	5.00	2.56	5.90	1.17	0.00	5.63
Ndu	0.00	0.00	8.53	1.38	2.19	2.13	0.00	17.52	6.59	0.00	26.38	0.00	3.14	4.85
Njikwa	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Nkambe	0.00	3.34	3.00	8.70	9.47	1.13	3.40	7.38	0.00	7.73	7.87	10.33	3.90	4.73
Nwa	-	-	-	-	0.00	17.30	23.89	17.48	4.31	13.83	2.81	15.13	10.65	10.54
Oku	-	-	-	-	-	-	-	-	0.00	0.00	1.38	0.00	2.66	0.67
Santa	0.00	0.00	0.00	2.43	2.03	0.00	0.00	3.61	0.00	0.00	0.00	0.00	3.35	0.82
Tubah	-	-	-	4.69	4.55	12.28	0.00	7.30	0.00	0.00	4.55	0.00	0.00	3.03
Wum	0.00	0.00	6.48	3.11	0.00	0.00	8.83	0.00	2.03	0.00	0.00	0.00	0.00	1.46
Average	0.09	1.84	5.02	2.17	4.64	3.85	3.44	6.12	3.02	2.10	3.17	3.08	2.57	3.07



ASIR, age-standardised incidence rate.

FIGURE 2: Variation of Burkitt lymphoma incidence across health districts.

district (Table 1). Spatial clustering of BL cases was noticed within the region. The districts that recorded the highest incidence rates for the entire study period include Nwa with 10.54/100 000; Ndop with 5.63 per 100 000; Benakuma with 5.48 per 100 000; Ako with 4.97 per 100 000; and Nkambe with 4.73 per 100 000. Despite fluctuations in ASIR over the years, with a remarkable drop from 2010, these districts consistently have higher incidence rates (Figure 2).

Discussion

The 317 patients included in this study were all the patients diagnosed and registered within the two pathology laboratories, two childhood cancer units in the North-West Region. It is likely that patients who travelled to other provinces for treatment were not recorded. The male

predominance in Burkitt lymphoma amongst children under 15 years has been reported in other population studies across Africa.^{4,5,19,20} The ratio of 1.3:1 in this study is the same as that reported by Lewis et al. in the North-West Region of Cameroon¹² and not much lower than the ratio of 1.8 reported by Enow-Orock and colleagues in Yaoundé, Cameroon.²¹ Pierce and Parker report a larger number of boys than girls for all childhood cancers put together.²² They suggest that this might be because of a prioritisation of the health of males over females amongst poor populations. The modal age group of 5–9 with mean of 8 years corresponds to expert suggestions and what has been reported in Yaoundé,²¹ and in other population studies.^{4,19}

All the cytological diagnoses were done by use of fine needle aspiration cytology. This method has been shown to be safe,

cheap and fast²³ and has been recommended for use in the diagnosis of BL in developing countries, where there is a limited number of surgeons and pathologists.²⁴ In the absence of pathology, clinical diagnosis is accepted if the patient responds to BL treatment and if there is no contrary pathology diagnosis.²⁴ Ultrasound scan has been shown to be helpful in the diagnosis of BL, by describing the nature of the tumours, which are typically hypoechoic.²⁵ This is also useful for staging the disease.²⁴

The dominance of abdominal involvement in this study supports what has been reported previously in Cameroon^{12,21,25} and in Nigeria.¹⁹ Historically, facial presentation has been described as most common in BL in sub-Saharan Africa,²⁶ but with advancement in imaging technology and increasing availability of ultrasound, early abdominal involvement is now detectable, which would otherwise be missed on clinical evaluation.²⁵ As more developing countries use ultrasound as a routine clinical investigation for BL patients, there is increasing predominance of abdominal presentation of BL over facial presentation.²⁷

The average BL incidence rate of 3.07/100 000 over the 13-year period was a little higher than the rate of 2.58/100 000 reported by Lewis et al. in the North-West Region of Cameroon¹² but lower than the 4.68/100 000 reported from the Yaoundé Cancer Registry.¹⁰ The case ascertainment in this study and the study by Lewis and colleagues is likely to be less complete than that of Enow-Orock et al. because the data was extracted from hospital-based registries, while the Yaoundé Cancer Registry is a population-based registry, which is more complete in nature. Higher incidence rates have been reported elsewhere, with rates as high as 8.4/100 000 children below 15 years in Ibadan, Nigeria.²⁸ Reported rates elsewhere in Africa include 2.15/100 000 in Kenya¹⁴; 5.7/100 000 in Tanzania²⁹; and 4.3/100 000 in Uganda.³⁰

The drop in ASIR for the region from 2010 raises a question on whether there is a challenge with identifying and referring cases to the treatment centres or whether there is indeed a drop in the incidence rate of childhood cancer. One major issue surrounding childhood cancer care in Cameroon in general is the low level of community awareness about cancers in children and the availability of care.³¹ With the creation of the childhood cancer centre in the region in 2003 at Bansa Baptist Hospital, followed by another centre at Mbingo Baptist Hospital in 2006, childhood cancer care team members embarked on community sensitisation, leading to increased childhood cancer awareness in the region. This could arguably explain why BL diagnosis increased with a steep gradient between 2003 and 2005 and remained fairly high until 2010. However, the drop in registered number of BL patients below 15 years from 2010 despite continuous and intensified community sensitisation remains unexplained. A decline in BL incidence has been shown in Ibadan, Nigeria, a neighbouring country, by two different researchers, with incidence consistently decreasing with time.^{20,32} Babatunde et al. warn that the decreased number of registered BL cases

might be because of economic crisis, as many children are left to die at home with disease without being brought to the hospital.²⁰

We identified the districts with the highest incidence rates of BL to include Nwa, Ndop, Benakuma, Ako and Nkambe. Clustering, which refers to the concentration of cases in particular areas, in the region has been reported in the past.^{11,12} Previous studies highlight only the Ndop District as a cluster zone for BL in the region, with an incidence rate as high as 21.5 per 100 000 reported from 2003 to 2005¹¹ and 10.3 per 100 000 for the period from 2003 to 2010,¹² in contrast to this study, which found an incidence rate of 5.63 per 100 000 in Ndop. This study did not investigate the disease stage for cases nor the delay from onset of disease to diagnosis, but Hesselting et al. report a predominance of late stage disease in this population with 72% Stage III and 12% Stage IV at diagnosis.⁸ This indicates a change in the high-risk areas for BL in the region and calls for refocusing of awareness creation and early diagnosis trainings to the new areas of high incidence to ensure that all patients are promptly diagnosed and referred for treatment. Clustering was also noticed in western Kenya⁵ and has been reported to be associated to malaria endemicity.^{4,5,6,7} The two districts with the highest ASIR of BL are also the districts of highest malaria incidence in 2015.³³ Investigating the association of BL with malaria in this region might provide some explanation for the observed clustering. Earlier studies in Kenya^{5,34} and Malawi⁷ have reported an association between BL and malaria incidence.

Limitations

Cancer registration in Cameroon is not well developed. Until now BL registration in north-west Cameroon has only been in the form of hospital-based childhood cancer registries and pathology-based cancer registries. It is purported that many children with cancer in developing countries like Cameroon go unrecorded for several reasons including paucity of cancer registries.³⁵ In addition, there is the issue of non-identification of paediatric cancer patients, because of low paediatric cancer awareness in communities.³¹

Conclusion

This study has provided information about the trends in incidence rate of BL in children below 15 years between 2003 and 2015. We have identified districts with high ASIR for BL, which should be targeted for awareness creation and early diagnosis trainings. The authors observe the possibility of incomplete case ascertainment in this study, which relied only on data from hospital-based and pathology registries. There is therefore need for a population-based childhood cancer registry in the region, which will use both active and passive surveillance methods to capture all the cases in the region. Further research is required to establish reasons why the ASIR is higher for some districts than others, as well as reasons for the drop in BL incidence in the region.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

G.M.A. designed the study, collected and analysed data and wrote the manuscript. P.B.H. established the hospital-based registries, provided supervision to the principal investigator and contributed to the study design, data analysis and writing of the manuscript. P.A. contributed pathology registry data and contributed to the writing of the manuscript. R.B. contributed pathology registry data and contributed to the writing of the manuscript. K.F. contributed to data collection and writing of the manuscript.

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