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Socio-economic class distribution of the prognostic variants of lymphoproliferative cancers in Nigerians

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Summary

One hundred and twenty Nigerians with various lymphoproliferative cancers were grouped according to socio-economic class and the prognosis of their disease. The best prognostic variant of acute lymphoblastic leukaemia occurred mainly in the highest socio-economic class and the worst variant mostly in the low socio-economic class. Chronic lymphocytic leukaemia, a low grade malignancy, and the high grade Burkitt's type of Non-Hodgkin's lymphoma occurred predominantly in the low class. The relationship between prognosis and socio-economic class was not so remarkable in patients with Hodgkin's disease and multiple myeloma. The precise mechanisms by which socio-economic strata influence development of the different prognostic variants of individual lymphoproliferative cancers are not certain.

Résumé

Cent vingt Nigeriens avec les cancers lymphoïde divers étaient groupés selon les classes socio-économiques et les résultats (prognostic) de leurs maladies. La qualité avec le pronostic meilleur de leucémie lymphoblastique aiguë est arrivée surtout dans la classe socio-économique basse.

Leucémie lymphocytaire chronique et la qualité de lymphome Non-Hodgkin (lymphome de Burkitt) sont arrivés à prédominer dans la classe socio-économique basse. La parenté entre le résultat pronostic et les classes socio-économiques n'était pas très remarquable dans les patients avec leucémie de Hodgkin et myélome multiple.

Les modalités précises que les qualités pronostic des cancers, lymphoïde étaient influencées par les classes socio-économiques ne sont pas claires.

Introduction

Factors exogenous to the patient are thought to play aetiological roles in various cancers. Such factors include cigarette smoking in lung cancer[1], ionising radiation in leukaemias[2], hepatitis B virus in hepatocellular carcinoma[3], and Epstein - Barr virus as well as the malaria parasite

in endemic (African) Burkitt's lymphoma[4]. Ramot and Magrath put forward the hypothesis that the environment is a major determinant of the immunological subtype of lymphoma and acute leukaemia in children[5]. Results of previous studies in this environment suggest that, environmental factors play a role in the pathogenesis of acute lymphoblastic leukaemia (ALL), chronic lymphocytic leukaemia (CLL) and Burkitt's lymphoma (BL) as disease entities, since CLL and BL, but not ALL, occurred predominantly in the low socio-economic class[6,7]. This communication compares the socio-economic class distribution of the normal population in this environment with that of patients with the different prognostic variants of individual lymphoproliferative cancers.

Patients and methods

During the three and half years from December 1986 to May 1990, one hundred and twenty newly diagnosed patients with lymphoproliferative malignancies seen at the University College Hospital, Ibadan, Nigeria were admitted into this study. Leukaemias were diagnosed from clinical features, blood and bone marrow cell counts, cytology and cytochemistry. Acute lymphoblastic leukaemia (ALL) was classified into the French - American - British (FAB) morphological types as L1 (good prognosis), L2 (bad prognosis) and L3 (very bad prognosis)[2,8]. Lymphomas were diagnosed from biopsy of enlarged lymph nodes or involved tissues, and classified according to the WHO Working Formulation by a panel of pathologist[9]. Burkitt's lymphoma (BL), a small non-cleaved cell type, was separated from other high grade Non-Hodgkin's lymphomas (NHL) because it is relatively common in this environment and occurs almost exclusively in children[4]. Chronic lymphocytic leukaemia (CLL) was regarded as analogous to NHL of the diffuse well differentiated lymphocytic type and therefore a low grade malignancy[10]. On the other hand, multiple myeloma (MM) was uniformly classified as a high grade malignancy. All patients with myelomatosis had at least 2 of the 3 major diagnostic criteria: bone marrow plasmacytosis > 10%, generalized osteolytic lesions and monoclonal immunoglobulin

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bulin naemia[11]. Lymphocyte predominant and lymphocyte depleted types of Hodgkin's Disease (HD) are respectively known to have the best and worst prognosis, with the mixed cellularity and nodular sclerosis types having intermediate prognosis[12]. The socio-economic class (SEC) of the patients (or their parents in case of children) were determined according to criteria defined by Williams[6]. In this study SEC 1 and 2 were regarded as high class, SEC 3 as middle class, and SEC 4 and 5 as low class. The socio-economic stratification in this environment has been published by the Nigerian Institute for Social and Economic Research[13]. About 10-15% of the populace belong to SEC I and 2, 10 -15% to SEC 3, and 70 - 80% to SEC 4 and 5[7]. Taking this socio-economic class distribution of the normal population as the control, the goodness of fit test was used to compare the SEC distribution of patients who had different prognostic variants of the lymphoproliferative cancers with the expected frequency distribution if these variants were to occur randomly among the populace.

Results

There were 81 males and 39 females among the 120 patients. Their ages ranged from 10 months to 77 years, with a mean of 33.7 years. Children aged 16 years or below were 43 in number, the predominant malignancies among them were Burkitt's lymphoma(25 patients) and acute lymphoblastic leukaemia (14 patients). HD and lymphoblastic NHL (other than BL) each occurred in 2 children. Table 1 shows the distribution of the patients with each malignancy according to prognostic variants and socio-economic classes.

Slightly more than half of the patients with ALL had L1 and L2 morphology, belong to the high SEC. Nobody from the high SEC had the L3 variant with the worst prognosis. The observed distribution of the L1, L2 and L3 variants of ALL differed significantly from the expected frequencies shown in parentheses ($X^2 = 63.5$, $P < 0.001$, critical value of X^2 at $V = 4$ is 18.5). The L1 and L2 variants occurred more frequently than expected in the high and middle SEC.

Table 1 Socio-economic class and prognostic type distribution of Nigerians with lymphoproliferative malignancies

Malignancy	Prognostic Type	Socio-economic Class			
		High	Middle	Low	
ALL (n=27)	L1	6(1)	2(1)	1(7)	
	L2	9(2)	3(2)	2(10)	
	L3	0(0.5)	1(0.5)	3(3)	
HD (n=9)	Lymphocyte predominant	0(0)	0(0)	1(1)	
	(Mixed cellularity and nodular sclerosis)	1(1)	5(1)	1(5)	
	Lymphocyte depleted	0(0)	1(0)	0(1)	
NHL (n=53)	High grade				
	BL	0(4)	4(4)	25(17)	
	Others	2(2)	12(2)	3(13)	
	Intermediate grade	0(0)	1(0)	2(3)	
Multiple Myeloma (n=14)	Low grade	2(0.5)	1(0.5)	1(3)	
	All high grade	4(2)	3(2)	7(10)	
CLL (n=17)	All low grade	0(2)	1(2)	16(12)	
Totals		120	24	34	62

*Expected frequencies in parentheses ().

Seven of the 9 patients with HD presented with nodular sclerosis and mixed cellularity (intermediate prognosis), with 5 of the 7 coming from the middle class. The SEC distribution of the various prognostic variants of NHL was significantly different from the expected pattern ($X^2=26.5$ $P < 0.001$). Burkitt's lymphoma occurred predominantly in the low SEC, but the other high grade Non-Hodgkin's lymphomas were encountered mainly in the middle class. Chronic lymphocytic leukaemia, though a low grade malignancy, was diagnosed almost exclusively in the low SEC individuals. Half of the patients with myelomatosis came from the low SEC, with the other half almost equally distributed among the middle and high social classes.

In Table 2, the patients with cancers which have morphologically distinct prognostic variants (ALL, HD & NHL) are pooled together and put into prognostic groups irrespective of the particular neoplasm each had. Statistically, the difference between the observed and expected distribution of the prognostic variants was highly significant ($X^2=98.3$, $P < 0.001$). The good and intermediate prognostic variants occurred more frequently in the high and middle SEC, and less frequently in the low SEC, than would be expected.

Discussion

In this environment, a patient with ALL or NHL from the high socio-economic class is more likely to have good or intermediate prognostic variant of the disease than one from the low SEC. Chronic lymphocytic leukaemia occurs almost exclusively in low SEC individuals though it is considered a low grade malignancy. This epidemiological feature of CLL has been observed in previous studies in this environment [6,7]. The relatively low prevalence of poor prognostic variants in the high social class is most exemplified by Non-Hodgkin's lymphoma of the Burkitt's type and the rare L3 morphological type of ALL.

It is not clear how socio-economic class influences the prognostic type of these haematological cancers in an individual. Undernutrition with attendant immunodeficiency, malaria which causes immunosuppression, Epstein-Barr virus infection, all thought to be most prevalent and severe in the low SEC, have been used to explain the preponderance of the high grade Burkitt's type NHL in the low SEC [4,14-16]. However, the precise pathogenetic mechanisms by which these factors operate have not been clearly elucidated.

The absence of the L3 variant of ALL and Burkitt's type NHL in the high SEC is interesting because they have other features in common.

Table 2 Socio-economic class and prognostic group distribution of Nigerians with ALL, HD and NHL

Prognostic Group	Socio-economic Class			Totals
	High	Middle	Low	
Good prognosis	8(2)	4(2)	2(10)	14
Intermediate prognosis	10(3)	9(3)	5(18)	24
Poor prognosis	2(6)	18(6)	31(39)	51
Total	20	31	38	89

*Expected frequencies in parentheses ()

The chromosomal translocations t(8,14), t(8,22) and t(2,8) occur in the two malignancies[17]. They are neoplasia of mature B-lymphocytes because the malignant cells bear surface membrane immunoglobulin in both conditions[10]. Morphologically, the tumour cells in both entities appear as large lymphoblasts with deeply basophilic, vacuolated cytoplasm[10]. Loosening of the tooth and loss of lamina dura were observed in two of the patients with L3 type ALL. These features are known to occur in Burkitt's lymphoma[18]. Finally as mentioned earlier, both entities are high grade malignancies. It will be illuminating to find out why the low socio-economic class is associated with these variants of ALL and NHL.

The concept of lymphoma-leukaemia which views solid lymphoid tumours and lymphoid leukaemia as belonging to the same disease spectrum of lymphoproliferative disorders, could explain the similarities which Burkitt's type NHL and L3 type ALL have in their cytogenetics, immunology, morphology, clinical features and epidemiology. If the lymphoma-leukaemia concept is correct, the two entities may be essentially the same neoplasm in which most of the malignant cells form solid tumours in some patients, whereas in other patients a considerable number of the malignant cells invade the blood stream. That malignant cells have been detected in the peripheral blood of patients with Burkitt's type NHL lends support to this views[10]. Therefore it may not be surprising that L3 type ALL and Burkitt's type NHL occur predominantly in the low socio-economic class, because the same environmental factors operate in that SEC.

Table 1 shows that most patients with L1 and L2 variants of ALL came from the high SEC. However, when the high SEC patients were separated into SEC 1 (highly educated professionals and top business executives) an SEC 2 (post-secondary individuals), SEC 1 was found to contain mainly patients with L1 morphology whereas SEC 2 contained most of those with the L2 variants. It can also be seen from Table 1 that 67% of the patients with L1 came from the high SEC, 22% from the middle class and 11% from the low SEC. In contrast 75% of the patients with L3 came from the low SEC and none from the high social class. The distribution of the prognostic types of ALL thus appears to be such that the variant which has the best prognosis occurs mostly in the highest SEC, whereas that with the worst prognosis occurs mainly in the low SEC.

Although the middle SEC contained 71% of the patients with intermediate prognostic types of Hodgkin's disease, and the low SEC contained 50% of patients with the highly malignant myelomatosis and prognosis in HD and MM is not as striking as is found with Burkitt's type NHL, acute lymphoblastic leukaemia and chronic lymphocytic leukaemia.

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