

EPIDEMIOLOGY AND SUBTYPES OF HAEMATOLOGICAL NEOPLASMS, AND DIAGNOSTIC CHALLENGES IN NIGERIA

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Abstract-

Background: Information on the epidemiology and subtypes of Haematological Neoplasms (HNs) in a region are imperative for decisions on effective and efficient patients' care and health policy formulation on HNs. Little was known about the epidemiology and subtypes of HNs in the Federal Capital Territory (FCT), Abuja. Hence, this study determined the epidemiology and subtypes of HNs at University of Abuja Teaching Hospital (UATH), Gwagwalada, FCT.

Methods: A retrospective descriptive study of all haematological malignancies diagnosed at UATH from January 2005 - December 2020. The data abstracted from patients' medical register at the Department of Haematology and Blood Transfusion included morphologic/histologic types and subtypes of HNs, sex, age, state of origin, occupation, education, place of residence, marital status, co-morbidity at diagnosis, stage at diagnosis and socioeconomic status. The data were analysed using Statistical Package for Social Sciences (SPSS) version 26 and Microsoft Excel version 16 software.

Result: A total of 328 HNs were diagnosed, with male predominance, 63.4% of the HNs, while females constituted (36.6%), with the male to female ratio of 1.8:1, and overall median age at diagnosis of 44.5 years \pm 21.30, 75% of the HNs cases presented in late stage (III & IV) disease. The distribution of HNs by subtypes showed that Small lymphocytic lymphoma, non-Hodgkin lymphoma (SLL, NHL); Mixed cellularity Hodgkin's lymphoma (MCHL); Chronic lymphocytic leukaemia (CLL); Acute lymphoblastic leukaemia (ALL), FAB L2; and Multiple myeloma (MM), were the most common lymphoid HN subtypes, while Diffuse mixed small and large cell NHL; Lymphocyte depleted Hodgkin's lymphoma (LDHL); Chronic lymphocytic/prolymphocytic leukaemia (CLL/PLL), ALL FAB L3; MGUS and WM were the least common subtypes. Granulocytic Leukaemia Philadelphia chromosome positive (Ph+); Acute myeloid leukaemia (AML) FAB M4; Polycythaemia Vera (PV), and Refractory Anaemia (RA) were the most prevalent myeloid HNs observed, while Chronic neutrophilic leukaemia (CNL); AML, FAB M3 and FAB M5; Essential thrombocythaemia and Myelofibrosis were the less common subtypes seen. **Conclusion:** The most common HNs subtypes in this study were SLL, MCHL, CLL, FAB L2. MM, CML Ph+, FAB M4, PV and RA. HNs occurred at a younger age, with median age at diagnosis of 44.4 years \pm 21.30 years, in contrast to the older age in the Western countries where median age at diagnosis was 67Years. 75% of the Patients presented with advanced stage disease (III & IV). Our findings agreed with similar reports within and outside Nigeria. We highlighted the diagnostic challenges and advocate for provision of essential ancillary diagnostic facilities that are imperative for standard clinical care and better management outcome.

Keywords: Haematological Neoplasms, Epidemiology, Types, Subtypes, Diagnostic Challenges Resource poor setting.

I.INTRODUCTION:

Haematological neoplasms (HNs) are heterogeneous groups of clonal neoplasms of myeloid and lymphoid tissues, which show greater variation than most other malignancies, with remarkable differences in epidemiology, types, subtypes and prognostic features in different populations and geographic regions due to ethnic, environmental, socio-economic background and life-style variation^{1,2,3,4,5,6}. Recent reports showed that Non-Hodgkin's Lymphoma (NHL) is the most common HN type with diffuse large B cell lymphoma (DLBCL) being the commonest subtype globally^{4,7,8,9,10}. NHL have been reported to be the sixth commonest cancer in SSA¹¹; and one of the top five cancers in Nigeria, while leukaemia was among the top ten cancers in the Federal Capital Territory¹². Worldwide, HNs are generally more prevalent in males than females, with male to female ratio ranging from 1.2 to 2.2 : 1, in contrast to non-haematological malignancies which show female predominance in developing countries^{13,14,15,16}. Several studies also revealed that HNs affect younger population in developing countries, with the mean and median ages at diagnosis generally lower (36.2 – 54 years)^{17,18,19,20,21} than that of the Western countries (65 -72 years)^{5,22,23}. Reports from studies conducted in Nigeria and other parts of the world revealed disparities in the types and subtypes of HNs. The most common subtypes of Malignant Lymphomas (NHL and HL) reported from the six regions in Nigeria were: Small lymphocytic lymphoma (SLL), 47.9% of NHL and nodular lymphocyte predominant HL, 63.6%, (Akpan et al, South-South Nigeria)²⁴; diffused mixed small cleaved and large cells – NHL, 26.47%, and nodular sclerosis Hodgkin's lymphoma (NSHL), 49.2%, (Kagu et al, North East Nigeria)²⁵; while DLBCL, 26.3%, was the commonest NHL in multi-centre study in South-Eastern and South-South regions of Nigeria (Madu et al)²⁶. A study from South-Western Nigeria (Oluwasola AO et al), found diffuse small non-cleaved cells (Burkitt's lymphoma), 29.9% and NSHL 5%, being the commonest NHL and HL²⁷ respectively; Burkitt's lymphoma was the most frequent NHL in Zaria (Samaila et al, North-West Nigeria)²⁸. DLBCL was shown to be the most dominant NHL, 55% of adults NHL in Sub-Saharan Africa (SSA)²⁷. Recent report showed that DLBCL, which constituted 31% of adult NHL, was the commonest

HNL in most Western nations⁷; DLBCL was also the commonest NHL subtype in Latin America, 49.1¹ and Japan, 45.3%⁸ respectively; DLBCL, 50%, MCHL, 63.6%, and FAB M0, 11.1%, were the most common subtypes of NHL, HL and AML respectively in Chile²⁸; similarly, DLBCL and MCHL, were the most common NHL and HL subtypes, in Iran 37.8% and 50%¹⁰; Yemen 41.6% and 49.2%²⁹ respectively; while FAB L2, 75% and M2, 33%, were the most prevalent ALL and AML subtypes in Western region of Nepal³⁰.

These studies revealed that HNs show greater variation in epidemiology, types, and subtypes than most other neoplasms, thus, local data are needed to aid decisions on patient care and health policy formulation. Little was known about the epidemiology and subtypes of HNs diagnosed in FCT. Hence, this study determined the epidemiology types, and subtypes of HNs that were seen at UATH, Gwagwalada, FCT, North-central Nigeria during the sixteen-year study period and compared our finding with reports from similar studies, we also highlighted the paucity of ancillary diagnostic facilities in resource limited setting like ours.

II. MATERIALS AND METHOD:

This was a retrospective descriptive analysis of all cases of haematological neoplasms diagnosed at the University of Abuja Teaching Hospital UATH), Gwagwalada, FCT, Abuja, Nigeria from 1st, January 2005 to 31st, December 2020. The hospital is a 500 bedded public tertiary health care institution that serves as a referral hospital for patients from the FCT (with its cosmopolitan population of people from all the states in Nigeria and non-Nigerians), and the neighbouring states. Data on HNs were abstracted from patients' medical records at the Department of Haematology and Blood Transfusion, UATH, Gwagwalada. The data abstracted included morphologic/histologic type and subtype, date of diagnosis, clinical stage at diagnosis of HNs; and socio-demographic variables: sex, age, state of origin, occupation, level of education, place of residence, marital status, and socio-economic status. We used Microsoft Excel version 16 and Statistical Package for Social Sciences (SPSS) version 26 software for data abstraction and analysis. The descriptive statistics were presented by tables and graphic charts, Chi-square test was used for comparison of frequency, a P-value of < 0.05 and 95% confidence interval CI) considered statistically significant.

HNs were primarily diagnosed based on patients' Clinical features, Full Blood Count and Bone Marrow Aspirate morphological examination and differential counts, Bone Marrow, Lymph Node, and other involved tissues biopsy histological examination. Imaging studies (such as X-ray, ultrasound scan and computerized tomography (CT) scan), for the secondary diagnosis and staging. Due to lack of essential ancillary diagnostic facilities, only the patients diagnosed with plasma cell/lymphoplasmacytic neoplasms, lymphoma and myeloproliferative neoplasms who could afford had confirmatory evaluation (serum protein electrophoresis, immunofixation, serum Ig free light chain, β_2 -microglobulin, immunohistochemistry and cytogenetic and/or molecular analysis), conducted from private laboratories. Acute Leukaemia subtypes were based on French-American-British (FAB) cooperative group morphological classification of leukaemias, while lymphomas were based on working formulation and World Health Organization (WHO) 2016 Classification respectively. Ethical approval for this study was obtained from the UATH Health Research Ethics Committee.

III. RESULTS:

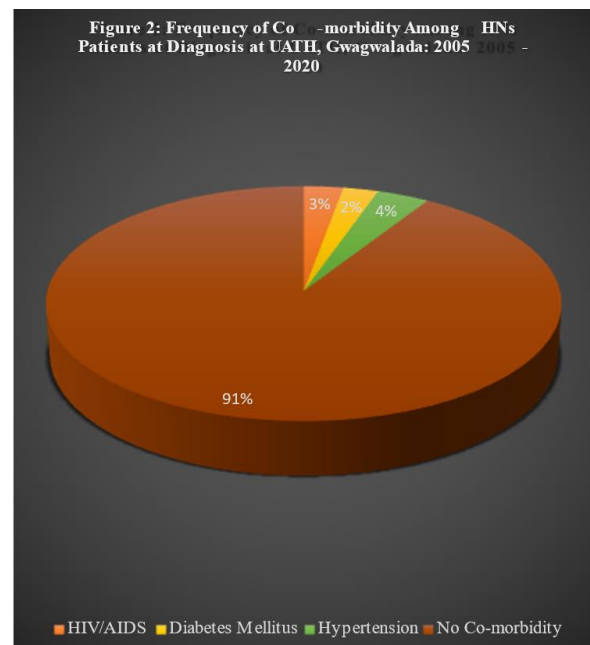
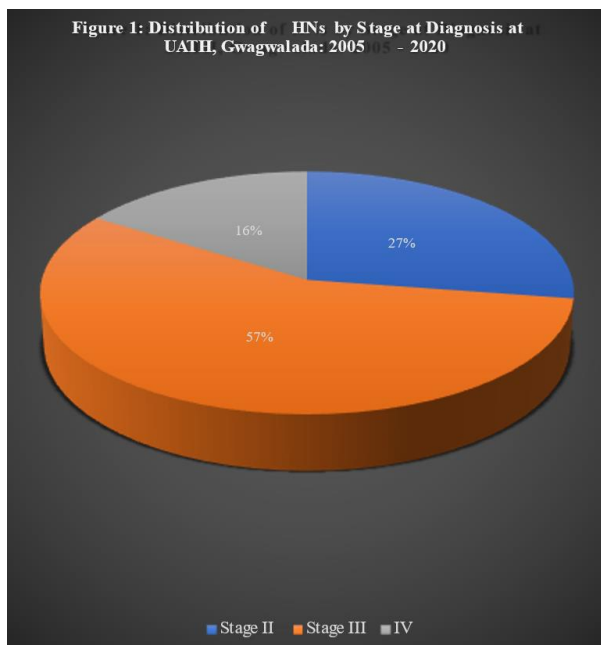
A total of the three hundred twenty-eight (328) HNs were diagnosed during the sixteen-year study period (January 2005 – December 2020), with male predominance of 63.4%, while females constituted (36.6%), with a male to female (M: F) ratio of 1.8: 1. The overall median age at diagnosis was 44.5 years \pm 21.3. The distribution of these patients by their geographic region of origin revealed that 32% of the patients were from North-Central (the FCT included); 25% from South-East; 13%.

HNs	Frequency (N)	Percent (%)	Median Age at Years	Std. deviation	Gender:		M:F Ratio	
					Male.	Female		
Total	328	100.0%	44.5	21.304	63.4% (N=208)	36.6% (N=120)	1.8 : 1	
Geographic Regions	Frequency (N)	Percent (%)	Occupation	Frequency (N)	Percent (%)	Residential Place	Frequency (N)	Percent (%)
North-Central	105	32%	Farmer	40	12.0%	Rural /Semi-Urban	228	70.0%
North-East	30	9.0%	Other Self Employed	85	26.0%	Urban	100	30.0%
North-West	44	13.0%	Public Servants	87	27.0%	Total	328	100.0%
South-East	81	25.0%	Retired	17	5.0%	Socio-Economic Status	Frequency (N)	Percent (%)
South-South	38	12.0%	Unemployed	99	30.0%	High	9	3.0%
South-West	30	9.0%	Total	328	100.0%	Medium	67	20.0%
Total	328	100.0%	Marital Status	Frequency (N)	Percent (%)	Low	252	77.0%

Educational Status	Frequency (N)	Percent (%)	Married	182	55.0%	Total	328	100.0%
Illiterate	83	25.0%	Single	96	29.0%			
Primary	45	14.0%	Divorced	25	8.0%			
Secondary	99	30.0%	Widowed	25	8.0%			
Tertiary	101	31.0%	Total	328	100.0%			
Total	328	100.0%						

from North-West; 12% from South-South; and 9% each from North-East and South-West regions of Nigeria respectively, the observed difference between the proportion of patients with HNs from the various geographic regions of origin was due to the location and is statistically significant ($p < 0.05$) Out of the 328 HNs cases in this study, 31% of them had tertiary education, 30% had secondary education, while 14% and 25%, had primary education and no formal education respectively. With regards to occupation, 38% of the patients with HNs were self-employed (12% farmers and 26% other self-employed business), 30% were unemployed (this included children, students, and unemployed adults, such as fulltime housewives and applicants); 27% were public servants, while 5% were retired. 55% of patients with HNs were married, 29% were single (included children and students) and 8% each were divorced and widowed. 70% of all HN patients reside in rural and semi-urban areas, while 30% reside in urban areas; Socio-economy wise, 77% of patients in this study were of low socio-economic status, while 20% and 3% were of medium and high socio-economic status respectively as depicted in table 1.

Figures 1 and 2 showed the pie charts distribution of clinical stages and comorbidity at presentation: 27% of the HN cases presented with stage II disease at diagnosis; 57%, stage III, and 16% stage IV, this finding was highly statistically significant ($P < 0.001$). Co-existing comorbidities showed that 4% of study population had Hypertension, 3% had HIV/AIDS, and 2% had Diabetes Mellitus, prior to HN diagnosis. The frequency distribution of lymphoid haematological neoplasms subtypes as shown in table 2 revealed that Small lymphocytic lymphoma (SLL), 38%, was the predominant Non-Hodgkin’s Lymphoma subtype; followed by follicular mixed small and large cleaved cells, 22%; Small non-cleaved cells (Burkitt’s lymphoma), 16%; Lymphoblastic lymphoma, 13%; Diffuse Large cells lymphoma, 12%; and Diffuse mixed small and large cells, 9%. MCHL subtype was the most predominant (40%) HL; followed by NSHL 35%; lymphocyte rich Hodgkin’s lymphoma (LRHL), 15% and LDHL, 10%. There was no incidence of nodular lymphocyte predominant HL recorded within the study period. The most frequent chronic lymphoid leukaemia was CLL, 93%, while CLL/PLL 7% was the least common. In the acute lymphoblastic leukaemia group, FAB L2, which accounted for 57% of ALL cases was the commonest ALL subtype observed in this study; followed by FAB L1, 34% and FAB L3, 9%. The most frequent plasma cell/ lymphoplasmacytic dyscrasia subtype, was MM, 94%; MGUS and WM 3% each respectively were less common.



Subtypes of NHL (Working Formulation)			Subtypes of Acute Lymphoblastic Leukaemia (ALL)		
Low grade	Frequency	Percent	ALL Subtypes	Frequency	Percent
Small lymphocytic lymphoma	19	28.0%	ALL 1 (small, monomorphic cells)	15	34.0%

Follicular small cleaved and large cells	15	22.0%	ALL 2 (small and large heterogeneous)	25	57.0%
Intermediate grade			ALL 3 (Burkitt-cell type)	4	9.0%
Diffused mixed small and large cells	6	9.0%	Total	44	100.0%
Diffused large cell	8	12.0%	Subtypes of Chronic Lymphoid Leukaemia (CLL)		
High grade			CLL Subtypes	Frequency	Percent
Lymphoblastic	9	13.0%	CLL	43	93%
Small non-cleaved cells (BL)	11	16.0%	CLL/PLL	3	7%
Total	68	100	Total	46	100.0%
Subtypes of HL (WHO Classification of HL)			Types Plasma Cell & Lymphoplasmacytic Neoplasms		
Classic HL	Frequency	Percent	Types	Frequency	Percent
Lymphocyte rich (LRHL)	3	15.0%	MM	30	93.8%
Lymphocyte depleted LDHL)	2	10.0%	MGUS	1	3.1%
Mixed cellularity (MCHL)	8	40.0%	WM	1	3.1%
Nodular Sclerosis (NSHL)	7	35.0%	Total	32	100.0%
Total	20	100.0%			

Out of the 39 cases of acute myeloblastic leukaemia (AML) diagnosed in this study, AML, FAB M4 subtype, 49%, was the most prevalent; followed by AML, FAB M2, 36%; AML, FAB M1, M3 and M5 subtypes, 5% each, respectively. 94.6% of chronic myeloid leukaemia cases had chronic granulocytic leukaemia Ph+ ABL-BCR 1 subtype, while only 3.6% cases had chronic eosinophilic leukaemia (CEN) and chronic neutrophilic leukaemia (CNL), 1.8%, (Ph - subtype). The most common classical Philadelphia negative (Ph-) myeloproliferative neoplasm was polycythaemia vera (PV), 44.4%; while essential thrombocythaemia (ET) and primary myelofibrosis (PMF) accounted for 27.8% each; refractory anaemia (RA) subtype 100%, was the only myelodysplastic syndrome observed in this study (table 3).

FAB Classification of AML			MPN Subtypes		
AML SUBTYPES	Frequency	Percent	Classical Ph - MPN Subtypes:	Frequency	Percent
M1 (AML without maturation)	2	5.00%	PV	8	44.4%
M2 (AML with maturation)	14	36.00%	ET	5	27.8%
M3 (Promyelocytic AML)	2	5.00%	PMF	5	27.8%
M4 (Acute Myelomonocytic leukaemia)	19	49.00%	TOTAL	18	100.0%
M5 (Acute monoblastic leukaemia)	2	5.00%	MDS Subtypes		
Total	39	100.00%	MDS Subtype	Frequency	Percent
MPN Types: CML	Frequency	Percent	RA/MDS-SLD	6	100.0%
CGL Ph + (BCR-ABL 1)	52	94.60%			
CEL	2	3.60%			
CNL	1	1.80%			
Toal	55	100.00%			

FAB =French-American-British classification, **AML** = Acute myeloid leukaemia, **MPN** = Myeloproliferative neoplasm, **CML** = Chronic myeloid leukaemia, **CGL** = Chronic granulocytic leukaemia, **CEL** = chronic eosinophilic leukaemia, **CNL** = Chronic neutrophilic leukaemia, **PV**= Polycythaemia Vera, **ET** = Essential Thrombocythaemia **PMF** = Primary Myelofibrosis, **Ph** = Philadelphia chromosome, **MDS** = Myelodysplastic Syndrome, **RA** = Refractory anaemia, **MDS-SLD** MDS with single lineage dysplasia.

IV. DISCUSSION:

This study showed that the ethnic region of most, 32% of the 328 HN cases, was North-Central (FCT included) Nigeria; followed by 25%, South-East; 13%, North-West; 12%, South-South; and 9% each, North-East and South-West regions of Nigeria respectively. The observed statistically significant ($p < 0.05$) difference between the proportion of patients with HNs from the various geographic regions of origin could be attributed to the cosmopolitan nature of FCT and location of the hospital, and concord with findings reported in similar studies^{14, 17}. This study revealed that 75% of these patients were literate, while the remaining 25%, had no formal education. With regards to occupation, we noted that 65% of the patients with HNs were gainfully employed (27% were public servants, 26% self-employed in various business and 12% farmers); 30% were unemployed (this included children, students, and unemployed adults, such as fulltime housewives and applicants); while 5% were retired. 55% of patients with HNs were married, while 45% were single (included divorced, widowed, students and children). The study also revealed that 70% of the patients with HNs reside in rural and semi-urban areas, while only 30% reside in urban areas with a great number of them diagnosed in advanced stage disease, 57%, stage III and 16%, stage IV, while only 27% were diagnosed in stage II. These findings could be related to the observed high proportion (77%) of patients in the low socio-economic class, which invariably leads to late presentation to health facilities and lack of access to the highly costly ancillary laboratory tests required for prompt and accurate diagnosis, staging, prognostication and treatment that are imperative for better management outcome. Our study also showed that 9% of the 328 HN cases had co-morbidities (hypertension 4%, HIV/AIDS 3% and diabetes mellitus 2%), prior to HN diagnosis. These findings on socio-demographic characteristics in our study were consistent with published reports from similar studies^{14, 17, 19, 21, 31}.

Lymphomas:

Non-Hodgkin's Lymphoma (NHL): Although studies have revealed great differences in the prevalence of the various types and subtypes of HNs in different populations and geographic regions due to ethnic, environmental and life-style variation^{1, 2, 3, 4, 5, 6}; NHL, have been shown to be the most common HN globally^{4, 7, 8, 9}, and within Nigeria^{12, 13, 14, 25, 32}. Remarkable disparity in subtypes of NHL, were reported from studies conducted in various regions of Nigeria^{24, 25, 26, 33, 34}, and outside Nigeria^{1, 7, 8, 27}. Small lymphocytic lymphoma (SLL) was the predominant NHL subtype noted in this study, it accounted for 28% of NHL cases; the second most frequent subtype was follicular mixed small and large cleaved cells, 22%; small non-cleaved cells (Burkitt's lymphoma); lymphoblastic lymphoma; diffuse large cells; and diffuse mixed small and large cells subtypes, accounted for 16%, 13%, 12% and 9% of the NHL cases respectively. Our finding was consistent with report from studies by Akpan et al, (South-South region of Nigeria) and Sant et al (Europe), where SLL, 47.9%, was the most frequent NHL subtype²⁴ and small (B-cell lymphocytic lymphoma) SBLL/CLL was the most frequent NHL subtype²². In contrast, diffuse mixed small cleaved and large cells, 26.4%, was the most prevalent NHL subtypes seen in North-Eastern Nigeria (Kagu et al)²⁵; while, diffuse small non-cleaved cells (Burkitt's lymphoma) was the commonest subtype reported by Oluwasola AO et al³³ and Samaila MO³⁴ in South Western and North Western Nigeria respectively. Diffuse large B-cell lymphoma (DLBCL) 26.3%, was the commonest NHL reported in multi-centre study in South-Eastern and South-South regions of Nigeria (Madu et al)²⁶, DLBCL was also the commonest NHL subtype 55% (adult NHL) in SSA²⁷, and 31% of adult NHL, in most Western nations⁷; in Latin America, 49.1¹; Japan, 45.3%⁸; 50%, in Chile²⁸, and 41.6%, in Yemen²⁹ respectively. HIV/AIDS have been associated with aggressive NHL subtypes^{7, 33, 35, 36}; in this study, we found statistically significant association between diffuse large cell lymphoma, lymphoblastic lymphoma NHL subtypes and HIV/AIDS, $P < 0.0001$; five diffuse large cell, three lymphoblastic lymphoma and one BL cases were positive for HIV/AIDS infection at diagnosis, this was higher than the report by Madu et al, where 1 in every 10 cases of NHL was found to be infected with HIV²⁶.

Hodgkin's lymphoma (HL): Globally, reports have shown that classic HL, accounted for 95% of all HL, while nodular lymphocyte predominant HL (NLPHL) constituted 5%. NSHL was the most common subtype in western nations, while MCHL subtype was the most prevalent in most Asian countries^{10, 37, 38}. MCHL subtype 40%, was the most prevalent HL in this study, followed by NSHL 35%; while LRHL, and LDHL, accounted for 15% and 10% of HL respectively, no case of nodular lymphocyte predominant HL (NLPHL) was observed in this study. Our observation agreed with the reports by Hamid GA and Mozaheb et al, where MCHL subtype was the most prevalent and accounted for 49.2% and 51% of HL in their studies^{29, 38}, but, at variance with the findings in studies reported by Akpan et al, Kagu et al, Mustafa Yildirim et al and Alshemmari et al which showed that the most common HL subtypes were NLPHL, 63.6%²⁴; NSHL, 49.2%²⁵, 52.7%³⁹, and 58.9%⁴⁰.

Leukaemias:

Chronic myeloid leukaemias (CML): CML accounts for 15% - 20% of adult leukaemias, with median age at diagnosis of 65 years and male preponderance, it is rare in children^{2, 22, 41, 42}. Studies from Nigeria and Asia revealed younger median age at diagnosis (37 - 55 years)^{32, 43, 44, 45}; Cytogenetic studies have showed that about 95% of CML cases are Philadelphia chromosome (Ph) positive (BCR-ABL 1+), and > 98% BCR-ABL1+ by molecular analysis⁴⁶. We found that chronic granulocytic leukaemia Philadelphia chromosome positive (Ph+) BCR-ABL 1+ subtype, 94.6%, was the commonest CML in this study, while chronic eosinophilic leukaemia (CEL) and chronic neutrophilic leukaemia (CNL) accounted for 3.6% and 1.8% of all CML cases respectively. Our finding was consistent with reports in the literature⁴⁶.

Chronic lymphoid leukaemias: Studies have shown that chronic lymphoid leukaemias' incidence ranked first among all leukaemias, accounts for about 30% of adult leukaemias in Western countries, with median age at diagnosis of 65 - 72 years with male preponderance, and lower among Asians, with the least incidence in Indian^{1, 42, 47}. Chronic lymphocytic leukaemia (CLL) subtype, accounted for 93% of the chronic lymphoid leukaemias, while chronic lymphocytic leukaemia/lymphocytic leukaemia (CLL/PLL) subtype, constituted 7% in this study. Our observation was higher than the 2% reported by Onoja AM et al⁴⁸ but lower the > 12% reported by D. Oscier et al⁴⁹.

Acute lymphoblastic leukaemia (ALL): ALL is the commonest diagnosed leukaemia in patients ≤ 20 years, accounts for 80% of childhood and about 15% of adult leukaemias in developed countries^{3, 42, 50}. ALL, FAB L2, 57%, was the most prevalent ALL subtype in our centre, followed by FAB L1, 34%; with the least frequent being ALL, FAB L3 subtype, 9%. Our finding was

consistent with findings reported by, Olaniyi JA et al and, Ahmed S. and I. E. Okpala (South Western Nigeria)^{51, 52}; Errahhali et al (Eastern Morocco)²⁰ and D. Ghartimagar et al (Nepal)³⁰ who found FAB L2 as the most prevalent ALL in their studies. Contrary to our finding, ALL, FAB L1 subtype 81% was the most common ALL reported by A. Nayyar, S. Ahmed (Pakistan)⁵³.

Acute myeloid leukaemia (AML): AML accounts for 23.1% of all leukaemias Worldwide in 2017, it affects all age groups, most common in adults than children and adolescents, with the highest incidence in Europe and US^{22, 42}. AML is not uncommon in our environment, the most frequent AML subtype seen in this centre was AML, FAB M4, 49%; followed by AML, FAB M2, 36%; AML, FAB M1, M3 and M5 were rare, accounted for 5% each respectively. This is in contrast to the reports Nigeria by Olaniyi et al, Okpala et al and SG Ahmed, BA Umar, where AML, FAB M2 was the most common AML subtype in their studies^{51, 52, 54}; AML, M2 was also shown to be the most prevalent AML subtype in Morocco, 46%, Errahhali et al²⁰ and Nairobi 29.5%, B. Kabera et al⁵⁵.

The differences in prevalence of acute leukaemia subtypes highlights the limitations of morphology as the sole means of diagnosis and thus, underscores the need for updated diagnostic methods.

Plasma Cell and Lymphoplasmacytic Neoplasms:

Multiple Myeloma (MM): Globally, MM is the most prevalent plasma cell neoplasm, constitutes about 10% - 13% of haematological neoplasms with a median age of diagnosis of 65 years – 70 years, affecting more males than female, male to female ratio of 1.5 :1, and higher incidence in Blacks than Whites and Asians^{3, 56, 57}; Our study revealed that MM accounted for 9.4% of all the plasma cell neoplasms (9.1% of all HNs), with lower median age at diagnosis of 57.5 years and male predominance (M:F ratio of 1.5:1). This finding was close to the findings from various parts of Nigeria which have reported MM prevalence of 10% - 12.3%, with median age at presentation of 54 years – 62 years and male preponderance (M :F ratio, 1.2 : 1 – 2.1 :1)^{13, 58, 48}. Our finding was higher than the 3.3% and 7.6% of HNs reported by Egesie OJ et al (North Central Nigeria)¹⁹ and C. Omoti et al (South- South, Nigeria)⁵⁹ but lower than the 19.3%, 20% and 29.5% of HNs reported by Refeno V et al (Madagascar)⁶⁰, Steven Alan Leak et al (Moshi, Tanzania)²¹ and Tietsche V et al (Latin America)¹. **Monoclonal Gammopathy of Undetermined Significance (MGUS) and Waldenstrom's Macroglobulinaemia (WM)** subtypes, constituted 0.3% each of all the HMs (3% of all the plasma cell dyscrasias); the median age at diagnosis MGUS and WM were 69years and 52 years respectively. MGUS has been reported to affect about 3.5% of individuals older than 50 years in Western countries, with 1% of this progressing to MM per annum, the low prevalence of MGUS observed in this study could be attributed to the fact that routine medical check-ups through which MGUS is diagnosed in developed countries is rarely done in resource limited setting like ours, due to low universal health insurance coverage.

Classical Ph- Myeloproliferative Neoplasms (MPNs):

In this study, Polycythaemia Vera subtype was the most common MPN, accounted for 44.4% of MPNs, the median age at presentation of PV was 62, which was consistent with reports from literature⁶¹ and higher than the 46.7 years reported from Togo⁶². Essential Thrombocythaemia (ET) and Primary Myelofibrosis (PMF) constituted 1.5% of all the HNs and 27.8% of MPNs each, with the median age at presentation of 56 years and 52 years respectively. The low prevalence of MPNs observed in our study was comparable to the reported low prevalence rates of MPNs among HNs by other similar studies^{1, 5, 11, 13}. We found highly statistically significant male predominance among the MPNs, with the M : F ratio of 7 : 1 for PV and 4 : 1 each for ET and PMF respectively, Although generally, HNs have been shown to be more in males, our study revealed higher male predominance than those reported in literature (within and outside Nigeria)^{14, 23, 25, 28}. Our report was in contrast to finding from a study by Haematology Malignancy Research Network (HMRN), which showed no apparent gender difference in sex incidence of MPN⁵.

Myelodysplastic Syndrome (MDS):

MDS have been shown to be more prevalent among elderly, with about 86% of MDS incident cases aged 60 years or more at presentation with a median age at diagnosis of 71 - 76 years, more common in Whites than other ethnic groups and male preponderance⁶³. The most prevalent MDS subtype in this study was myelodysplastic syndrome with single lineage dysplasia (MDS-SLD / RA), which accounted for 100% of the MDS cases, our observation contrasted with the study from Ile-Ife by L. Salawu, M. Durosinni, which showed that the commonest MDS, 70%, was myelodysplastic syndrome with multilineage dysplasia⁶⁴. Our study established that MDS accounted for 1.8% of the overall HNs with the median age at diagnosis of 55 years and both genders equally affected, a male : female ratio of 1: 1. This finding was similar to the report by Kingsley et al in which MDS constituted 1.45% of the HNs, though with male predominance and older median age at presentation¹³, but higher than the 0.4% reported by Kagu et al²⁵ and much lower than the 3% of overall HNs with M:F of 0.7; 11.5% of overall HNs reported by M. Errahhali et al²⁰ and AM. Onoja et al⁴⁸.

V. CONCLUSION:

Knowledge of epidemiology and timely accurate diagnoses of the types and subtypes of HNs are vital for creating awareness and policy formulation for prevention/control as well as prognostication and therapeutic decision making on standard clinical care for better management outcome. We determined for the first time, the epidemiology, and subtypes of HNs in FCT, Nigeria. This study showed that SLL, Mixed Cellularity, CLL, FAB L2 and MM were the most prevalent lymphoid HN subtypes, while CML Ph+, FAB M4, PV and RA were the most common myeloid HN subtypes seen at UATH. We also established that HNs occur at a younger age, with median age at diagnosis of 44.4 years ± 21.30 years and noted that 75% of the Patients presented with advanced disease stages (III & IV). In contrast to the older age in the Western countries where the median age at diagnosis was 67 years and early presentation. Our findings agreed with similar reports from resource poor settings within and outside Sub-Saharan Africa. Studies have shown great differences in the prevalence of the various types and subtypes of HNs in different populations and geographic regions due to ethnic, environmental, and life-style variation, the findings in this study also revealed the need for further

collaborative prospective studies to accurately classify HNs based on the latest revised WHO classification of HNs, in Nigeria. Evaluation of blood parameters and genomic studies for novel disease biomarkers in HNs that could have great impact on early detection, management, and cancer control and prevention in this era of targeted and personalized therapies.

Limitation:

Majority of the diagnosed 328 HN cases in this study were not confirmed through the required ancillary analyses such as serum immunochemistry, cytochemistry, immunophenotyping, immunohistochemistry, cytogenetic and molecular studies, hence, the WHO 2016 classification of HNs was supplemented with FAB for acute leukaemias and working formulation for the lymphomas.

Recommendations:

This study provided information on HNs and highlighted the diagnostic challenges encountered due to paucity of ancillary diagnostic facilities in Nigeria. We advocate for collaboration with international and nation HNs clinical trials / research groups (both government and non-governmental organizations / institutions) for prospective studies. Provision of essential ancillary diagnostic facilities for accurate and prompt diagnosis, classification, and prognostication of HNs that are imperative for standard clinical care and better management outcome. And for nationwide universal health insurance coverage to make health care accessible to people in need.

Authors' contribution:

T. I. OTU conceptualized and designed the study, was involved in data extraction, data curation and analysis; and wrote the manuscript. U. G. EJKEME contributed to the data extraction. Both authors read and approved the final manuscript.

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