Original Article

The Economic Burden of Malignant and Premalignant Hematological Diseases in Southern Nigeria

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Abstract

Background: Hematological malignancies are a significant cause of morbidity and mortality. They constitute an economic burden for the patients, their relatives, and the society because of the cost associated with their management, which is usually long term. We aimed to determine the total direct cost of managing patients with premalignant hematological disorders (PMHDs) and malignant hematological disorders (MHDs). **Materials and Methods:** A hospital-based retrospective study was carried out between 1997 and 2015. Data were retrieved from the case notes of adult patients diagnosed with either PMHD or MHD. The total cost of medical care was calculated as the sum of in-patient and out-patient direct cost associated with their management. Data were analyzed using Statistical Package for Social Sciences. **Results:** There was a total of 129 patients; 74 (57.4%) males and 55 (42.6%) females with mean age of 45.7 ± 16.3 years and the majority (n = 76, 58.9%) being employed. Males were more affected than the females except in chronic lymphocytic leukemia, myelodysplastic syndrome, and paroxysmal nocturnal hemoglobinuria. The commonest MHD was chronic myeloid leukemia with 37 (28.7%) patients. Full blood count was the commonest investigation done, whereas free light chains were the least (n = 2; 1.6%). The total cost of care for the 129 patients was N30,041,900.00 ($82,306.58) with an average total cost of care per patient of N232,882.95 ($638.04). Patients with non-Hodgkin lymphoma had the highest mean cost of care per patient (N373,196.30; $1,022.46). The average monthly expenditure per patient was about N70,000 ($190). **Conclusion:** In our setting, management of CHDs constitutes an economic burden.

Keywords: *Cost of care, economic burden, hematological malignancies*

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Introduction

Hematological malignancies are a group of malignant clonal disorders that primarily affect the blood and blood producing tissues. According to the World Health Organization, the hematological malignancies are broadly classified into the myeloid and lymphoid malignancies. The myeloid malignancies include acute myeloid leukemia (AML), chronic myeloid leukemia (CML), polycythemia vera (PV), essential thrombocytemia (ET), myelofibrosis (MF), myelodysplastic syndromes (MDS), and myelodysplastic syndrome/myeloproliferative neoplasms (MDS/MPNs);[1] whereas the lymphoid malignancies include acute lymphoblastic leukemia (ALL) and the mature B-cell, T-cell, or NK-cell neoplasms including chronic lymphocytic leukemia (CLL), plasma cell neoplasms (PCNs), and Hodgkin's lymphoma (HL).[2] Premalignant hematological disorders (PMHDs), although benign, have the propensity to progress or transform to malignant hematological disorders (MHD) (especially to AML). They include aplastic anemia (AA) and paroxysmal nocturnal hemoglobinuria (PNH). These PMHDs are also clonal in origin.[3,4] For the purpose of this study, the MHDs will be grouped into the acute and chronic

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leukemias, HL, Non-Hodgkin lymphoma (NHL), PCN, MPNs, whereas the PMHD will consist of MDS, AA, and PNH.

Hematological malignancies are a significant cause of morbidity and mortality and constitute about 17.4%–18.05% of all cancers in Nigeria.[5,6] The lymphomas have the highest prevalence;[5] whereas among the leukemias, chronic leukemias are more common (70.3%) than the acute leukemias (29.7%) with CML being the most common type of chronic leukemia.[7] These diseases constitute an economic burden for the patients, their relatives, and the society at large because of the cost associated with their diagnosis and management, which is usually long term. The cost of managing these disorders is the sum of those incurred by patients and their families emanating directly through payment of hospital bills, procurement of blood, and drugs as well as indirectly through lost work time by way of absenteeism, disability or premature death, and unpaid care rendered by family members.[8] This study is aimed at identifying the total direct cost of managing patients with HMDs and PMHDs and to determine the economic burden it has in our environment.

Materials and Methods

The study was hospital-based retrospective, utilizing data from patients' case notes retrieved from the Department of Haematology and Blood Transfusion and the Medical Records Department. These patients were diagnosed with MHDs or PMHDs at the University of Port Harcourt Teaching Hospital (UPTH) between the period of September 1994 and August 2015. The case notes included in the study were those who had confirmed diagnoses made via morphology/histology with or without immunophenotyping, cytogenetics, or molecular methods and were at least 18 years at the time of diagnosis. Case notes were excluded if there were incomplete data or if a definitive diagnosis was not made. Data collected from the notes included sociodemographics, presenting complaints, date of diagnosis, method of diagnosis, investigations done, number of days on admissions (if any), number of blood transfusions, and all drugs or therapeutic interventions received.

The total cost of medical care was calculated as the sum of in-patient and out-patient direct cost associated with diagnosis and treatment of MHD or PMHD, excluding out-of-hospital cost as well as costs of treatments and admissions unrelated to the malignancy. The cost was calculated to reflect the present-day cost of care. Prices over the years were adjusted to specific prices of investigations, drugs, supportive care, and procedures as of August 2015. The currencies used were the Nigerian Naira and United States Dollar (USD). The exchange rate at the time of writing in August 2017 was three hundred and sixty-five Naira (N365) to one USD. Data collected were recorded into excel spreadsheets and analyzed using the Statistical Package for Social Sciences (SPSS) version 20. With a 95% confidence interval, a P value ≤0.05 was considered as statistically significant.

Results

In total, 129 patients met the inclusion criteria of which there were 74 (57.4%) males and 55 (42.6%) females giving a male to female ratio of 1.3:1. The age of the patients ranged from 18 to 80 years (mean age ± SD: 45.7 ± 16.3 years). The majority (n = 76, 58.9%) were employed, 26 (20.2%) were unemployed, while 19 (14.7%) were students and 8 patients were retired (6.2%). The distribution of patients' age, sex, and time to diagnosis (time from first presentation at hematology to the time a definitive diagnosis was made) and days on admission for the various disorders are shown in Table 1. Males were generally more affected than the females except in CLL, MDS, and PNH, where the male to female ratios were reversed. The commonest clonal hematological disorder was CML, which occurred in 37 (28.7%) patients with a mean age of 38.8 ± 15.1 years, whereas there was only one patient with PNH, which occurred at age 28 years. About a quarter of the patients (n = 32, 24.8%) were hospitalized with an average hospital stay of 23.3 days. No patient with MPN was hospitalized.

The most common investigations were full blood count (100%), uric acid (90.7%), electrolytes, urea, and creatinine (87.6%), liver functions tests (81.4%), and viral screening for HIV and hepatitis B and C (70.5%). Clotting profile and immunophenotyping were the least common investigations (3.1%). The mean duration of therapy was 8.8 ± 16.0 months for all patients, whereas patients with CML had the longest duration of therapy with a mean duration of 22 months.

The summary of monthly cost of care per patient by type of diagnosis is also given in Table 2. Fourteen 14 (11%) patient did not receive any form of supportive or definitive therapy due to early mortality after diagnosis or refusal of medical care, whereas 33 (25.6%) received supportive care but no definitive therapy for their disorder. The majority of the patients (n = 96, 74.4%) received chemotherapy as definitive therapy. No patient received hematopoietic stem cell transplantation as part of his/her treatment.

The total cost of care for the 129 patients was N30, 041,900.00 ($82,306.58). This included N11,278,300.00

Table 1: Distribution of patients' characteristics according to the type of diagnosis

Diagnosis	Number of patients (%)	Age (years)±SD	Number of patients admitted, *n* (%)	Average number of days on hospital admission	Sex Male:female	Time to diagnosis (days) Mean±SD
Aplastic anemia	6 (4.6)	34.8±15.4	2 (33.3)	27.5	5:1	10.6±4.0
Acute leukemia	4 (3.1)	45.5±19.4	4 (100)	35.2	3:1	13.5±2.1
CLL	16 (12.4)	56.5±14.8	4 (25)	16.0	1:3	30.7±55.3
CML	37 (26.7)	38.8±15.1	6 (16.2)	13.3	1.5:1	14.4±12.9
HL	8 (6.2)	33.3±15.6	2 (25)	23.5	1:1	39.3±40.5
NHL	27 (20.9)	49.6±16.3	4 (14.8)	28.3	2.4:1	16.8±13.6
MDS	2 (1.5)	61.5±5.00	1 (50)	4	0:2	86.0±89.1
MM	20 (15.5)	50.4±13.3	8 (40)	30.6	1.5:1	18.5±24.0
MPN	8 (6.2)	49.4±11.5	0 (0)	0	1.7:1	13.4±11.4
PNH	1 (0.8)	28.0±0.0	1 (100)	26	0:1	0.0±0.0
Total	129 (100)	45.7±16.3	32 (24.8)	23.2	1.3:1	20.4±30.3

SD=Standard deviation; AA=Aplastic anemia; PNH=Paroxysmal nocturnal hemoglobinuria; MDS=Myelodysplastic syndrome; AL=Acute leukemia; CLL=Chronic lymphocytic leukemia; CML=Chronic myelocytic leukemia; HL=Hodgkin's lymphoma; NHL=Non-Hodgkin's lymphoma; MM=Multiple myeloma; MPN=Myeloproliferative neoplasm

Table 2: Summary of monthly cost of care per patient by type of diagnosis

Diagnosis	Number of patients	Number - *n* (%) with number Rx	Specific chemo regimen used	Specific chemo regimen; number (frequency %)	Mean duration of care in month±SD	Mean total monthly cost per patient±SD in NGN	Mean total monthly cost per patient±SD in USD
AA	6	5 (83.3)	Oxy-methalone	1 (16.7)	1.7±1.2	97,720.83±54,364.19	267.73±148.94
AL	4	0 (0)	COAP	2 (50)	3.0±1.8	66,679.38±23,563.41	182.68±64.56
			DA	2 (50)			
CLL	16	3 (18.8)	CP	10 (62.5)	3.1±2.3	45,630.34±31,960.61	125.02±87.56
			CVP	2 (12.5)			
			FCP	1 (6.25)			
CML	37	0 (0)	Interferon	1 (2.7)	22.2±25.1	23,594.48±29,963.13	64.64±82.09
			Busulphan	1 (2.7)			
			HU	35 (94.6)			
HL	8	1 (12.5)	ABVD	6 (75.0)	5.4±3.1	55,448.52±17,976.85	151.91±49.25
			COPP	1 (12.5)			
NHL	27	12 (44.4)	R-CHOP	2 (7.4)	3.2±2.9	134,235.67±149,145.09	367.77±408.62
			CVP	3 (11.1)			
			CHOP	10 (37.0)			
MDS	2	2 (100)	-	0 (0)	1.5±0.7	88,837.50±37,565.05	243.39±102.92
MM	20	5 (25)	VMP	3 (15)	4.6±4.2	85,704.28±48,785.29	234.81±133.66
			VRD	2 (10)			
			MP	8 (40)			
			CVAP	2 (10)			
MPN	8	4 (50%)	HU	4 (50)	2.5±1.7	53,518.85±39,923.41	146.63±109.38
PNH	1	1 (100)	—	0 (0)	1.0±0.0	98,450.00±0.00	269.73±0.00
Total	129	33 (25.6)		96 (74.4)	8.8±16.0	69,321.21±84,686.43	189.92±232.02

Rx=Treatment; SD=Standard deviation; NGN=Nigerian Naira; USD=United States Dollar, AA=Aplastic anemia; AL=Acute leukemias; PNH=Paroxysmal nocturnal hemoglobinuria; MDS=Myelodysplastic syndrome; AL=Acute leukemia; CLL=Chronic lymphocytic leukemia; CML=Chronic myelocytic leukemia; HL=Hodgkin's lymphoma; NHL=Non-Hodgkin's lymphoma; MM=Multiple myeloma; MPN=Myeloproliferative neoplasm; HU=Hydroxyurea

($30,899.45) spent on investigations and N18,763,600.00 ($51,407.12) for treatment [Table 3]. The minimum expenditure of N1,800 ($4.93) was for a patient who had only a full blood count done, whereas the maximum expenditure of N3,891,950 ($10,662.88) was for a patient with a CD20 positive NHL who received Rituximab-based chemotherapy regimen. The average total cost of care per patient was N232,882.95 ($638.04) with an estimated mean monthly expenditure of N69,321.21 ± N84,686.43 ($189.92± $232.02). Patients

Table 3: Summary of total cost by type of diagnosis

Diagnosis (total number of cases)	Number of patients	Total cost of investigations in NGN (USD)	Total cost of treatment in NGN (USD)	Total cost of care in NGN (USD)	Total cost of care per patient in NGN (USD)
AA	6	398,150.0 (1090.82)	610,000.00 (1671.23)	1,008,150.00 (2762.06)	168,025.00 (460.34)
AL	4	366,700.0 (1004.66)	427,800.00 (1172.06)	794,500.00 (2176.71)	198,625.00 (544.18)
CLL	16	1,161,050.0 (3180.96)	668,300.00 (1830.96)	1,829,350.00 (5011.92)	114,334.38 (313.25)
CML	37	2,403,350.0 (6584.52)	3,251,600.00 (8908.49)	5,654,950.00 (15,493.01)	152,836.49 (418.73)
HL	8	652,400.0 (1787.40)	1,583,800.00 (4339.18)	2,236,200.00 (6126.58)	279,525.00 (765.82)
NHL	27	3,276,100.0 (8,975.62)	6,800,200.00 (18,630.69)	10.076,300.00 (27,606.30)	373,196.30 (1022.46)
MDS	2	148,450.0 (406.71)	91,500.00 (250.69)	239,950.00 (657.40)	119,975.00 (328.70)
MM	20	2,235,800.0 (6125.48)	5,072,000.00 (13,895.89)	7,307,800.00 (20,021.37)	365,390.00 (1001.07)
MPN	8	561,850.0 (1539.32)	234,400.00 (642.19)	796,250.00 (2181.51)	99,531.25 (272.688)
PNH	1	74,450.0 (203.98)	24,000.00 (65.75)	98,450.00 (269.73)	98,450.000 (269.73)
Total	129	11,278,300.0 (30,899.45)	18,763,600.00 (51,407.12)	30,041,900.00 (82,306.58)	232,882.95 (638.04)

NGN=Nigerian naira; USD=United States Dollar; AA=Aplastic anemia; PNH=Paroxysmal nocturnal hemoglobinuria; MDS=Myelodysplastic syndrome; AL=Acute leukemia; CLL=Chronic lymphocytic leukemia; CML=Chronic myelocytic leukemia; HL=Hodgkin's lymphoma; NHL=Non-Hodgkin's lymphoma; MM=Multiple myeloma; MPN=Myeloproliferative neoplasm

Table 4: Comparison of cost of care for different diagnoses by gender and employment status

Diagnosis	Cost of care (NGN) by gender		*t*	*P*	Cost of care (NGN) by employment status		*t*	*P*
	Male	Female			Unemployed	Employed		
	Mean±SD	Mean±SD			Mean±SD	Mean±SD		
AA	80,600.00±38,676.00	183,325.00±0.00	2.43	0.07	97,720.83±54,364.19	-	-	-
AL	77,668.33±10,407.14	33,712.50±0.00	3.66	0.07	89,330.00±0.00	33,712.50±0.00	1.181	0.359
CLL	27,981.25±19,829.35	51,513.37±33,684.80	1.31	0.21	51,167.86±41,683.87	41,323.38±23,757.49	0.598	0.559
CML	21,535.61±31,164.05	26,614.16±28,902.81	0.5	0.62	28,591.42±34,736.45	19,787.30±25,997.30	0.883	0.383
HL	46,794.27±5,578.41	64102.78±22,873.90	1.47	0.19	54,016.15±7,323.75	56,880.90±26,361.87	0.209	0.841
NHL	155,041.36±165,654.48	84,822.14±89,958.04	1.12	0.27	96,728.47±95,998.75	152,989.27±169,016.70	0.921	0.366
MDS	—	88,837.50±37,565.04	—	—	62,275.00±0.00	115,400.00±0.00	—	—
MM	90,719.34±59,710.88	78,181.68±27,376.42	0.55	0.57	107,485.71±64,043.76	73,975.81±35,941.16	1.514	0.147
MPN	49,053.50±26144.92	60,961.11±63,863.38	0.38	0.72	39,650.00±22,203.15	58,141.81±45,058.29	0.538	0.610
PNH	-	98,450.00±0.0	—	—	—	98,450.00±0.0	—	—
Total	76,872.65±102,479.80	59,161.10±51,178.35	1.18	0.24	65,507.33±61,286.40	71980.90±98,072.60	0.426	0.671

SD=Standard deviation; NGN=Nigerian Naira; AA=Aplastic anemia; AL=Acute leukemia; PNH=Paroxysmal nocturnal hemoglobinuria; MDS=Myelodysplastic syndrome; AL=Acute leukemia; CLL=Chronic lymphocytic leukemia; CML=Chronic myelocytic leukemia; HL=Hodgkin's lymphoma; NHL=Non-Hodgkin's lymphoma; MM=Multiple myeloma; MPN=Myeloproliferative neoplasm; HU=Hydroxyurea

with NHL had the highest mean cost of care per patient (N373,196.30; $1,022.46) followed by those with MM (N365,390.00; $1,001.07). On the other hand, PNH and MPN patients had the least mean total cost of care per patient-N98,450.00 ($269.73) and N99,531.25 ($272.69), respectively [Table 3]. Although males had a higher mean cost of care (N76,872 ± 102,479.80; $210.61 ± 280.77) compared with the females (N59,161.10 ± 51,178.35; $162.09 ± 140.21), this was not statistically significant (t = 1.177; P value = 0.242) [Table 3]. The employment status also did not significantly affect expenditure, although the mean cost of care was higher for those who were employed compared with those who were unemployed-N71,980.90 ± 98,072.60 ($197.2 ± 268.69) and N65,507.33 ± 61,286.40 ($179.47 ± 167.91), respectively (t = 0.43; P = 0.67) [Table 4].

Discussion

In this study, males were more commonly affected than the females in most of the clonal hematological disorders except in CLL, MDS, and PNH; however, this was a hospital-based study and therefore may not reflect the sex distribution in the community. Worldwide, CLL appears to be more common in males,[9] but a similar finding of females being more affected than males was also noted by Salawu *et al*. in Nigeria.[10] Studies have shown that CLL runs a more benign course in females than in males[11] and there is a higher overall survival in the females than in the males,[12] supporting our finding. This was also the case with MDS.[13,14] On the other hand, PNH is more common in the females in Europe, but more common in the males in Asia.[15] There was only one case of PNH in our study which happened to be a female.

Patients with CML had the longest median follow-up time although this was not the disorder with the highest expenditure probably because patients diagnosed with CML at our center were referred to another tertiary institution where they received Imatinib gratis (which is the treatment of choice for CML).[16] In the United States, the annual cost of care for CML is about $90,000 per patient.[17] Standard of care in CLL has drastically improved in recent years due to emergence of various new drugs such as rituximab, bendamustine, fludarabine, ibrutinib, venetoclax, idelasib, ofatumumab, and obinutuzumab.[18,19] The majority of our patients were only able to receive chlorambucil, prednisolone, and occasionally, fludarabine; and diagnostic methods using immunophenotyping, cytogenetics, or molecular methods were unavailable. This may, in large part, explain the large disparity in cost of care for CLL in our patients compared with the estimated cost of treatment in Russia (€13,580 or $16,342), Ukraine (€7,453 or $8,968), or the United States ($147,000).[20,21] All patients with acute leukemia were treated with chemotherapy alone because of unavailability of transplantation facilities. The total cost of care per patient at N198,625 ($544.2) was remarkably lower than is estimated for acute leukemia patients who do not undergo transplant where cost ranges from about $49,000-$280,000.[22,23] The average number of days on hospital admission by our patients was also shorter compared with an average of 52 days for nontransplant AML patients.[23]

There was a wide variability for the cost of care for NHLs. Combining HL with NHL, about a third of our patients did not receive any form of chemotherapy due to financial constraints, early mortality or being lost to follow up. Diagnostic pattern varied as a few patients had bone marrow biopsy, lymph node biopsy, immunohistochemistry, and imaging techniques, whereas others had only lymph node biopsy for their diagnosis. Treatment cost also varied as most patients of NHL were treated with cyclophosphamide, hydroxodaunorubicin, oncovin, and prednisolone (CHOP) regimen, whereas two patients could afford novel therapy with rituximab–CHOP. The mean cost of care per patient for NHL was N373,196.30; ($1,022.46). This is much lower than what was reported by Herald *et al*.[24] Unlike CLL and the NHLs, about a quarter of the myeloma patients were exposed to novel therapy involving bortezomib or lenalidomide. Although the mean monthly cost of treatment with these novel drugs was higher (N102,000–N167,000; $279.5–$457.5) than it was for those who received melphalan and prednisolone regimen (N18,000; $49.3), the cost of care with the novel therapy was still remarkably lower than the estimated in the western world to be between $133,000 and 150,000 per annum.[25] The fact that these novel drugs may have been prescribed differently[26] and the drugs used by our patients were generics (not the branded forms) may be contributory.

Treatment of the PMHDs (AA and PNH) and MDS in our patients basically comprised of supportive care. The definitive treatment of AA using drugs such as cyclosporine-A and anti-thymocyte globulin were not achieved in our patients. These drugs are expensive and are not readily available in the country. The singular patient diagnosed with PNH was lost to follow up. The two patients with MDS received only supportive care and had a short mean duration of therapy of about 1.5 months. The cost of care per patient with MPN was relatively low compared with some of the other MHDs. Factors influencing this may include the use of phlebotomy as therapeutic options for patients with PV and none of the patients were hospitalized. Also, the MPN patients who required drug therapy were placed on hydroxyurea and this is inexpensive and widely available.

Unemployment did not significantly affect cost of care in our patients. This may be due to a strong family support system, as it is common practice in our environment for family members to assist financially when a family member is ill. The healthcare system in Nigeria is divided into the public (or government) and private sectors. The public sector owns 66% of the health facilities in Nigeria and has three levels of care. The primary level is more in rural areas and funded by state governments, and the secondary and tertiary levels are more in urban areas, with funding from state and federal governments, respectively. The World Health Organization in 2010 recommended universal health coverage with the aim of individuals having access to healthcare irrespective of financial status. This can be achieved via health insurance. Presently only about 4%–5% of Nigerians have some form of government funded or private insurance.[27,28] None of our patients had health insurance; therefore, all expenditure by them were out-of-pocket. Treatment of MHDs constitutes an economic burden.[29] These CHDs are generally uncommon disorders, yet only 129 patients spent over N30,000,000 (>$80,000) for their hematological care. This cost does not reflect transportation to and fro the hospital or treatment of comorbidities. It is also worth noting that absence from work during their time of illness may also affect income especially for those who were self-employed. The average monthly expenditure per patient even in this low socioeconomic setting was high (about N70,000; $190), given that >60% of Nigerians live on

less than $1.25/day.[30,31] This is compounded by the fact that there is poor government funding for health and about 95% of patients pay for their medical bills out-of-pocket.[27,28]

Conclusion

Worldwide, the management of MHDs and PMHDs constitutes an economic burden. However, this burden is more in developing nations. Widespread coverage of healthcare insurance is essential to reduce out-of-pocket expenditure for people who develop hematological disorders. Improved government funding of the health sector, including provision of better diagnostic facilities at affordable rates, and novel drugs for treatment will aid better management of these disorders in our environment.

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Conflicts of interest

There are no conflicts of interest.

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