

# Diagnostic Challenges in Hematological Malignancies in Nigeria and Their Impact on Treatment Outcome: The experience of a tertiary health institution in South South Nigeria

## ABSTRACT

Haematological malignance constitutes a major public health disease burden globally due to the degree of mortality and morbidity they cause.

**Aim:** This review was aimed at exploring and reporting some of the difficulties that hinder early/accurate diagnosis and management of haematological malignancies in Nigeria emphasizing a single centre experience and to further highlight how they affect treatment outcome.

**Methodology:** Google scholar, Pubmed and African Journals online sites were explored in July 2024. Relevant articles were selected. The most senior consultant haematologist in the single centre in South South Nigeria being studied was interviewed and account was documented.

**Results:** The difficulties encountered in the prompt/proper diagnosis and management of haematological malignancies reported by the studies and the clinician interviewed include, visiting orthopaedic and other specialists as well as herbalists and spiritualists for several months before reporting to the haematology clinic, mis – and/or missed diagnosis due to inadequate diagnostic equipment and techniques like use of morphological studies alone for Rowmanawsky stained blood picture examination and histological diagnosis without cytogenetics, immunophenotyping, polymerase chain reaction fluorescent insitu hybridization, poverty, cultural and religious beliefs. Poor treatment outcome as a result of these challenges were also reported.

**Conclusion:** Enlightenment campaigns on the benefits of early diagnosis and prompt presentation to the hospital should be encouraged. Provision of up-to-date advanced technologies for early/accurate diagnosis and sub classification of haematological malignancies should be made in main health facilities across the country. Diagnosis and treatment of haematological malignancies should be built into the National Health Insurance scheme to strengthen the system in this regard.

*Keywords: Difficulties, treatment outcome, Diagnosis, Haematological Malignancies, Leukaemia, Lymphoma.*

## 1. INTRODUCTION

Haematological malignancies are a group of cancers that affect the blood, bone marrow, and lymphatic system because of malignant transformation of cells stemming from disruption of normal hematopoietic function [1,2]. These malignancies can be grouped based on immunologic, cytogenetic and molecular genetic methods into myeloid or lymphoid, depending on the cell lineage affected, and into acute and chronic depending on the progression of the disease and stage of maturation of cells being affected [3]. Haematological malignancies include but not limited to leukaemias, lymphomas and myeloma [4,5].

The incidence of haematological malignancies depends on some factors such as age, gender, geographical region, as well as histological subtypes, It was reported that haematological malignancies represent about 6.5% of all cancers globally in 2012 [5]. A recent review on the global burden of haematological malignancies and evolution patterns over the past 30 years revealed that the global incident cases of hematologic malignancies have increased over the decades reaching 1343.85 thousand in 2019, nonetheless, the age-standardized death rate (ASDR) for all types of hematologic malignancies has been declining [2]. Furthermore, the ASDR for leukaemia, non-Hodgkin lymphoma, Hodgkin lymphoma and multiple myeloma were 4.26, 3.19, 0.34 and 1.42 per 100,000 population in 2019, respectively, with Hodgkin lymphoma showing the most significant decline. It is noteworthy that the trend varies by gender, age, region, and the country's economic situation with the burden generally higher in men compared to women [2]. These malignancies are the fourth most frequently diagnosed malignancies in both men and women in developed countries of the world, with leukaemia accounting for 3.1% of mortality globally in 2020 [6].

Leukaemia, the most common haematological malignancy is the 11th leading cause of cancer related death worldwide, with a prevalence of 32.26% in 2017. The 2020 World Health Organisation Global Cancer Observatory report highlights that the burden of leukemia in Nigeria is a significant public health concern with 3,378 new cases reported and leukemia ranking 6th among all malignancies, accounting for 2.7% of the total cancer cases in the country. Leukemia-related mortality is also substantial, with 2,504 recorded deaths, placing it at the identical rank of 6th among cancer-related mortality, translating to a concerning percentage death rate of 3.2%, emphasizing the need for comprehensive strategies to address the disparities in disease occurrence and outcomes in Nigeria [7].

Haematologic malignancies constitute a major burden to affected subjects and their families in terms of their health, finance and psychological state [5]. These diseases require precise and timely diagnosis as well as accurate classification to enable effective treatment, the available traditional methods like morphology and cytogenetics fail to differentiate specific subtypes of these malignancies and identify clinically significant genetic abnormalities [6]. Disturbingly, these have not been effectively achieved in Nigeria due to some difficulties faced by the healthcare system which include, inadequate diagnostic infrastructure, insufficient training and retraining of healthcare professionals, delays in referral, economic constraints, and significant urban-rural healthcare disparities [5,9]. These challenges contribute to delays in diagnosis, misdiagnosis, missed diagnosis and suboptimal treatment outcomes, exacerbating the burden of these diseases on patients and the healthcare system. Other factors that contribute to delayed diagnosis and poor treatment outcomes in Nigeria include poverty, ignorance, apathy to seek medical attention; 34 self-medication with over-the-counter drugs; visiting spiritual healers and herbalists for herbal medication which may cause renal and/or hepatic injury, 36 religion and cultural beliefs. and in extreme cases superstitious belief by laying blames on witches, ancestors or enemies [10].

According to studies, a lack of knowledge about hematological malignancies among medical professionals at all levels of treatment may be additional factor contributing to delayed presentations [11,12]. A review in 2020 of eight earlier reports based on scientific investigations and case reports revealed that wrong/ delayed diagnosis due to poor diagnostic facility such as use of only morphology for histological diagnosis without immunohistochemistry, immunophenotyping etc, poorly equipped health facilities to manage haematological malignancies, late presentation of patients in advanced stage of disease, inability to pay for investigations and treatment due to financial constraint were the major challenges of diagnosis and management of haematological malignancies in Nigeria [5]. The effect of these factors culminates in poor outcome. It has been reported that cure rates can vary according to region and may be impacted by prompt and accurate diagnosis, treatment

availability and access to care [13,14]. This study aims to explore the experience of a health institution in South South Nigeria on the difficulties encountered in the diagnosis of haematological malignancies as well as review what in literature in this regard.

## **2. MATERIALS AND METHODS**

### **2.1 Description of Study Area**

The study site for this work was Federal Medical Centre Asaba (FMC). FMC, Asaba is situated in the central Area of Asaba metropolis, the capital city of Delta State. The hospital is a tertiary health institution, a research and referral centre serving the entire state capital territory and neighboring towns like Ibusa, Iseleukwu, Ogwashiuku, Onicha – Ugbo, Onicha – Olona, Agbor etc. It also serves the neighboring states like Edo and Anambra states including Onitsha, the largest commercial city of the South-Eastern Nigeria. Federal Medical Centre Asaba is in the South-South Geo-political zone of Nigeria. The hospital was established on 12th August 1998 because of the Federal Government of Nigeria policy to setup a Federal Medical Centre in states where a Federal Teaching Hospital is non-existent.

### **2.2 Methodology**

Surveys and interviews with healthcare professionals, including haematologists, pathologists and laboratory scientists were conducted to gather firsthand information on diagnostic practices and challenges. The most senior consultant haematologist in the single centre in South South Nigeria being studied was interviewed and account was documented. Google scholar and African Journals online sites were explored in July 2024. Studies conducted in Nigeria addressing the difficulties in the diagnosis of haematological malignancies written in the English language were selected for review whereas studies that didn't meet these criteria were excluded. The google scholar search gave rise to 3870 results whereas African journals online search produced 253 results. The studies that met the inclusion criteria for the study from google scholar and African journals online were therefore selected and reviewed for this work.

## **3. RESULTS**

From the interviews conducted in the single centre in south south Nigeria, it was gathered that diagnosis of haematological malignancies most times is based on morphology alone. This is because most patients are unable to afford the cost of immunocytochemistry due to financial constraint which is a major setback in diagnosis. Even when morphology could be used, sometimes, the power supply is epileptic making it difficult to use the microscope. It was revealed that in cases of lymphomas, sometimes, samples are taken, and it takes a long time before the results are made available because the number of pathologists to assess the tissue is limited. Additionally, the subtypes of lymphoma are not assessed due to the lack of necessary equipment. In some cases, the stains available degenerate and expire with numerous artifacts and the actual morphology of the cells are marred. Few times, malignant lymphoma have been mis-diagnosed as reactive "lymphoid cells". Additionally, ignorance on the part of the patients contributes to these difficulties and delays as some of them resort to spiritual and herbal consultations before showing up in the hospital with end-stage disease. Also, most cases are commonly erroneously diagnosed as typhoid fever and malaria before they get to the haematologist in advanced stages. In the case of Multiple Myeloma, the patients would have been seeing orthopedic surgeons and other clinicians in smaller hospitals before sending to the haematology experts. Even when the patient has the money for further investigation, transporting the sample material to laboratories where advanced testing can be performed becomes a challenge due to distance, the tissue degenerates or denatures due to

bad handling on the part of the ignorant “transportation agency”. It was also pointed out that there is limited Haematology Consultant manpower in the centre and other centres in Nigeria.

Interestingly, these experiences outlined by the single centre under review are in line with those retrieved from literature. The studies selected to have met the study inclusion criteria used for this review revealed late presentation of patients in advanced stage of disease, missed/misdiagnosis due to use of only morphology for histological diagnosis without immunohistochemistry, immunophenotyping and polymerase chain reaction, inability to pay for investigations due to financial constraint associated with poverty as leading challenges in the diagnosis of haematological malignancies in Nigeria.

#### **4. DISCUSSION**

Nigeria Global cancer statistics in Nigeria has shown an estimated increasing cancer occurrence per year with many unreported cases. WHO predicts that the number of blood-related malignancy cases will increase by approximately 48% in less developed countries by the year 2030 [15]. These reports provide the need for urgent attention in this area of medical science. The difficulties in the diagnosis of haematological malignancies and their impact on patients' survival rate in Nigeria has been widely studied across different regions of the country and the report from this single centre study is not different from that of other centres across the nation. In 2016, a cross sectional study carried out in Lagos state Nigeria revealed that out of 116 cases of lymphomas, only 32 (27.6%) were correctly diagnosed and subtyped by morphology alone, 53 (46%) were diagnosed to be lymphomas but could not be subtyped by morphology, 19 (16.4%) were wrongly subtyped while five cases of reactive lesions were wrongly diagnosed as malignant lymphoma [16]. These challenges of inaccurate diagnosis and classification of lymphomas were apparently due to use of only morphology without further investigation such as immunohistochemistry. This pitfall in the diagnosis and subtyping of lymphoma ultimately leads to wrong therapeutic options and poorer outcomes.

Another group of researchers shared the view of difficulties in the diagnosis of haematological malignancies in a case report of a previously transfused 36-year-old tailor who presented at the accident and emergency unit of a hospital in North Central Nigeria with fever, epistaxis, severe anaemia, thrombocytopenia, eosinophilic leukocytosis and menorrhagia as well as myeloid hyperplasia with eosinophilic myeloblasts on bone marrow aspiration cytology. The case was later diagnosed to be acute eosinophilic leukaemia. They researchers postulated that diagnosis of certain subtypes of leukaemia is rarely made in Nigeria and that descriptions in the literature are scantily found. Furthermore, they concluded that rare forms of leukaemia when seen in developing nations are faced with management limitations [17]. Contrary to what is obtainable in developed countries, the burden of haematological malignancies in Africa often culminates in poorer patient outcome owing to different factors including restricted access to healthcare facilities, shortage of trained haematologists and most importantly, unavailability of modern diagnostic techniques [18]. All these setbacks put together lead to delays in diagnosis and militate against optimal treatment strategies [8].

Additionally, the findings of a review of literature on research carried out in different parts of Nigeria showed that there was poor outcome of haematological malignancies due to challenges in diagnosis and management. They researchers further argued that inadequate number of research relevant to haematological malignancies has been undertaken in Nigeria claiming that this may probably be due to less attention given to haematological cancers in Nigeria [5].

A critical factor contributing to late, mis- or missed diagnosis of haematological malignancies as revealed by a study carried out in Southern Nigeria is limitation on the number of

investigations done to aid diagnosis as only 3.1% of 129 patients studied were able to do immunophenotyping due to high cost [19]. Delayed diagnosis because of late presentation was reported to be a critical concern militating against prompt therapeutic intervention and proper management of multiple myeloma in Nigeria. This is because most multiple myeloma patients first present to Orthopaedic clinic due to bone pain. A study carried out in Rivers State, Southern Nigeria showed that 84.6% of the patients studied presented with bone pain first at the Orthopaedic clinic resulting to 61.5% and 30.8% of them being diagnosed with Multiple myeloma late stage III and II Durie and Salmon clinical staging system respectively. Only 7.7% are presented in stage I [20].

Another significant contributing factor to low survival and compliance is the high cost of treating hematological cancers. Two case reports of a 9-year old in Ile – Ife, South Western Nigeria with primary cardiac lymphoma and 5-year-old girl with lymphoblastic lymphoma in Bida, North Central Nigeria respectively both had poor treatment outcome, and even early fatality due to financial constraint, socio-cultural, financial for both investigative and therapeutic interventions), inadequate resources and facilities [21,22]. A study conducted in Calabar, Southern Nigeria showed that 50% of 41 children with Burkitt Lymphoma presented in late stage of the disease, 25% of them could not afford confirmatory test while 20% of the patients did not receive chemotherapy because of inability of their parents to pay. Additionally, 31.7% of parents withdrew their children against medical advice due to financial constraint. Again, 26.8% of the subjects were reported to have consulted traditional or spiritual healers while 31.7% sought treatment from unorthodox practitioners and patent medicine dealers before presenting to the hospital [23].

Quite frankly, the problem of late presentation is not unique to Nigeria but also a challenge in other developing countries. In a study conducted among 169 patients with multiple myeloma in Ghana, it was reported that one third of the patients waited for over one year after onset of symptoms before presenting to the health facility while 51.3% of the patients were diagnosed in stage III of International Staging System (ISS) [24]. Similarly, in a study conducted among cancer patients in Ethiopia, it was reported that 41.7%, 59% and 42.6% of female patients with cervical, breast and ovarian cancers respectively presented in advanced stage of disease. Again, among males, 46.7% and 29% of patients with prostate and colorectal cancers respectively presented in advanced stages at the time of diagnosis [25]. In Mali, it was reported that diagnosis was most often delayed, owing to financial constraints, the lack of a multidisciplinary approach and the unavailability of adequate facilities and equipment for diagnosis, follow-up and treatment [26]. They further recommended that strategies geared towards improving survival must be put in place, particularly by enhancing supportive care, optimizing the treatment protocol and reducing delay in diagnosis.

Undeniably, this is contrary to what is obtained in developed countries where presentation is mostly at early stage [25]. In a study conducted among patients with haematological cancers in England, it was found that only 16% of the patients waited for more than three months after onset of symptoms before seeking [27].

## **5. CONCLUSION**

It is difficult to escape the conclusion that diagnosis, management and outcome of haematological malignancies in Nigeria is poor. Morbidities and mortality from haematological malignancies are as a result of difficulties and delay in diagnosing, classifying and treating hematological malignancies owing to inadequate diagnostic facilities, late presentation in advanced stage of the disease, ignorance, poverty, cultural, religious beliefs etc. Addressing the diagnostic challenges of hematological malignancies in Nigeria is crucial for improving patient outcomes and reducing mortality rates. There is urgent need for training

and retraining of health care professionals at all levels in this regard, provision of basic and advanced facilities for diagnosis and treatment of these cancers as well as public enlightenment to create awareness of haematological malignancies in order to reduce significant morbidity and mortality.

## REFERENCES

1. Arber D. A. Hemopoietic-lymphoid neoplasms: Principles of pathologic diagnosis. In: Greer JP, Arber D. A, Glader B, List A. F, Means R. T, Paraskevas F, editors. *Wintrob's Clinical Haematology*. 13th ed. Philadelphia: Lippincott Williams and Wilkins, 2014; 1391–8.
2. Zhang, N., Wu, J., Wang, Q., Liang, Y., Li, X., Chen, G., Ma, I., Liu, X., & Zhou, F. Global burden of hematologic malignancies and evolution patterns over the past 30 years. *Blood Cancer Journal*, 2023; 13(1): 82-5.
3. Durosinmi M. A. A design handbook of Haematooncology chemotherapy for medical students and doctors. 3rd ed. Lagos Nigeria: Amkra and allied services Ltd, 2013; 3.
4. Hoffbrand A. V, Moss P. A. H. *Essential Haematology*. 6th ed. UK: Wiley-Blackwell, 2011; 151–5.
5. Ugwu, N. I., & Nwannadi, I. A. Haematological malignancies in Nigeria: Challenges in diagnosis and management—A systematic review. *J Biomed Res Clin Pract*, 2020; 3: 282-92.
6. Obeagu, E. I., Omar, D. M., & Omar, U. Leukaemia burden in Africa. *Int. J. Curr. Res. Biol. Med*, 2023; 1: 17-22.
7. Batubo, N. P., Ogbu, O. S., & Victor, D. D. Hematological, histopathological and oxidative stress responses to n-hexane extract of *Terminalia catappa* nuts in leukemia-induced Wistar rats. *International Journal of Research in Medical Sciences*, 2024; 12(1): 61-5.
8. Samson, E. O., Adamu, I., Mba, I., Emmanuel, A., & Amarachi, B. J. Diagnostic approach to Haematologic Malignancies in Resource-Limited Settings-A Review. *Sokoto Journal of Medical Laboratory Science*, 2024; 9(2).
9. Chukwu BF, Ezenwosu OU, Ikefuna AN, Emodi IJ. Diagnostic Delay in Pediatric Cancer in Enugu, Nigeria: A Prospective Study. *Pediatric Hematology and Oncology*, 2015; 32(2): 164–71.
10. Rafii F, Tehrani FJ, Saeedi M. Spiritual healing from Iranian cancer patients' viewpoints: A hybrid concept analysis. *J Edu Health promot*, 2020; 9: 32.
11. Bolarinwa RA, Olowookere SA, Owojuyigbe TO, Origbo TC, Durosinmi MA. Challenges to Care and Medication Adherence of Patients With Chronic Myeloid Leukemia in a Resource Limited Setting: A Qualitative Study. *Journal of Patient Experience*, 2018; 5(3): 196-200.

12. McShane CM, Murphy B, Santin O, Anderson LA. Low knowledge and awareness of monoclonal gammopathy of undetermined significance (MGUS) among general practitioners. *BMC Family Practice*, 2019; 20: 61.
13. Okocha E.C., Aneke J. C., Ulasi T. O., Ezendu C. E., Umeh E. O., Ebubedike U. R. Pattern of childhood and adolescent malignancies at a tertiary institution in South-East Nigeria: A ten-year study. *Niger J Paediatr*, 2015; 42:111-5.
14. Kagu MB, Ahmed SG, Bukar AA, Mohammed AA, Mayun AA, Musa AB. Spectrum of Haematologic Malignancies and Survival Outcomes of Adult Lymphomas in Maiduguri, North Eastern Nigeria—a Fourteen Year Review. *Afr J Med Med Sci*, 2013; 42(1): 5-14.
15. Egesie, O. J., Jatau, E. D., Damulak, O. D., Zakari, A., Jasini, J., Akinola, O., Dahiru, A. M. C., Nasiru Raheem, N. & Egesie, U. G. Prevalence and type of haematological malignancies among adults in a tertiary hospital in Jos-Nigeria: A sixteen-year retrospective analysis. *Highland Medical Research Journal*, 2017; 17(2): 92-6.
16. Akinde OR, Anunobi CC, Osunkalu OV, Philips AA, Afolayan OM. The challenges of lymphoma diagnosis in a Tertiary Hospital in Lagos, Nigeria. *J Clin Sci*, 2016; 13: 58–71.
17. Damulak Obadiah Dapus, Egesie J Ochaka and Jatau E Danjuma. Acute Eosinophilic Leukemia: The Challenges of Management in a Resource Poor Setting. *International Journal of Biomedical Investigation*, 2021; 2(1): 1–7.
18. Taofeek, I. D. B. E. O., Kwaifa, O. Y. A. I. K., Isaac, F. O. A. B. I., & Oluwasayo, Z. B. A. H. B. Challenges associated with living with haematological malignancies in sub-Saharan Africa. *Sokoto Journal of Medical Laboratory Science*, 2023; 8(3).
19. Korubo KI, Okoye HC, Efobi CC. The economic burden of malignant and premalignant hematological diseases in Southern Nigeria. *Nig J Clin Pract* 2018; 21:1396 – 1402.
20. Nwabuko OC, Anazodo NM, Igbigbi EE, Okoh DA. Plasma cell myeloma: Challenges in Diagnosis in Sub-Saharan Africa. *Jokull Journal*, 2015; 65(1): 254–66.
21. Adefehinti O, Onakpoya UU, Komolafe AO, Adeodu OO, Durosinmi MA. Treatment challenges and outcome of Intra-cardiac Lymphoma in a resource-limited setting: A case report. *Annals of Health Research*, 2015; 1(2): 86–91.
22. Amiwero C, Okuku G, Adeboye N, Aina O. 5 yea rold girl with malignant lymphoblastic lymphoma: Challenges of managing haematological malignancies in a developing country. *Africa Health Sciences*, 2011; 11(2): 290–95.
23. Mmeremikwu M. M., Ehiri J. E., Nkanga D. G., Udoh E. E., Ikpat O. F. & Alaje E. O. Socioeconomic constraints to effective management of Burkitt's lymphoma in South-eastern Nigeria. *Tropical Medicine and International Health*, 2005; 10(1): 92-8.
24. Acquah ME, Hsing AW, McGuire V, Wang S, Birmann B, Dei-Adomakoh Y. Presentation and survival of multiple myeloma patients in Ghana: a review of 169 cases. *Ghana Med J*, 2019; 53(1): 52-8.

25. Samrawit S, Wudeneh M. Diagnosis and Risk Factors of Advanced Cancers in Ethiopia. *J Cancer Prev*, 2019; 24: 163-72.
26. Doumbia, A. K., Konaré, H., Simaga, T., Togo, P., Kouma, O. N., Diall, H. G., Coulibaly, O., Dembélé, A., Cissé, M.E., Sacko, K. & Togo, B. Management of Acute Myeloblastic Leukaemia (AML) Treated with Intensive Chemotherapy: Experience in a Single Centre. *Open Journal of Pediatrics*, 2024; 14(2): 401-11.
27. Howell DA, Warburton F, Ramirez A, Roman E, Smith AG, Forbes LJL. Risk factors and time to symptomatic presentation in leukaemia, lymphoma and myeloma. *British Journal of Cancer*, 2015; 113: 1114-20.

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