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Clinical Presentation of Splenomegaly at Kigali University Teaching Hospital, Rwanda - A Retrospective Descriptive Study

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ABSTRACT

INTRODUCTION: Splenomegaly is a common condition in malaria endemic region and is frequently associated with cytopenias. Splenomegaly is usually a clinical finding, but imaging studies have helped to assess for or confirm it. Evaluating the clinico-hematological presentation of splenomegaly at the biggest referral hospital in Rwanda would bring important information to the clinicians.

METHODS: This was a retrospective descriptive study conducted at Kigali University Teaching Hospital, medical department, for a period of one year. We reviewed patients' charts admitted with the conditions known to be associated with splenomegaly referring to the available literature, and were enrolled if found to have it. Demographic, clinical, hematological and radiological information was extracted, then descriptive analyses were performed.

RESULTS: A total of 1950 patients' files were examined, and 117 (6%) patients had splenomegaly. The mean age was 39 years, and women were predominant (55.5%). Many cases of splenomegaly were detected on admission (49.6%), at stages II (33.3%) and III (23.1%). Many patients had no symptoms of splenomegaly (30.7%), others had features of anaemia (22.2%), and infection (25.6%). Abdominal ultrasound was the imaging of choice to evaluate the spleen size, and has discovered splenomegaly in 28.2% of cases after clinical examination was unremarkable. The main causes of splenomegaly were Hyper-reactive Malarial Splenomegaly (21.4%) and portal hypertension (19.6%).

CONCLUSION: Splenomegaly is a frequent condition and more prevalent in the eastern province, it was detected on admission at a moderate stage and associated with hemolysis in many cases.

Keywords: Splenomegaly, Anemia, Stage, Ultrasonography

INTRODUCTION

The human spleen is a dark purple bean-shaped, largest lymphoid organ, located in the left hypochondrium of the abdomen, underlying left ribs 9, 10 and 11, on the posterior to the mid-axillary line. The size is about (12 X 7 X 4 cm) and weighs (130–150 g) [1, 2]. The major functions of the spleen are: sequestration and phagocytosis of red blood cells and platelets, extramedullary hemopoiesis, blood pooling, production of humoral antibodies, production and maturation of B and T cells and plasma cells [1]. Splenomegaly is defined as enlargement of the spleen measured by size or weight [2]. The spleen has to increase in size threefold before it becomes palpable [3]. Causes of splenomegaly are varied and include: infection (among them septic shock, infective endocarditis, typhoid, infectious mononucleosis, tuberculosis, brucellosis, malaria, kala-azar, schistosomiasis), inflammation (rheumatoid arthritis, sarcoidosis),haematological disorders (haemolytic anaemia, haemoglobinopathies, leukaemia, lymphomas

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and myeloproliferative disorders), portal hypertension and congestion (chronic liver diseases, congestive heart failure),storage diseases, amyloidosis, the lymphoid and myeloid neoplasms, tropical splenomegaly syndrome [6, 7]. Massive splenomegaly is seen in myelofibrosis, chronic myeloid leukaemia (CML), chronic malaria, kala-azar or, Gaucher's disease [8, 9].

Splenomegaly is usually associated with increased workload (hypersplenism), leading to cytopenia(s) from haemolysis and a compensatory bone marrow proliferative response [10, 11]. There are many ways to classify and evaluate the magnitude of splenomegaly. Hackett's classification is the most frequently used in cross-sectional studies; it classifies splenomegaly in five classes: from a non-palpable spleen (class I) to a huge spleen with the lowest point in the right iliac fossa (class V) [4].

In some cases, there are no symptoms of splenomegaly, while some patients complain of mild, vague, abdominal discomfort, pain which is referred to the left shoulder, early satiety from gastric displacement, or symptoms and signs that are related to the underlying disorder [20-22]. In the past, splenomegaly was a clinical finding, but in recent years, imaging studies have also helped to assess for or confirm mild splenomegaly [5].

Chronic splenomegaly is a common condition in tropical Africa, and it is only in about 25% that the aetiology is found [6]. In malaria endemic area, approximately 50-80% of its residents have splenomegaly, and Hyper-reactive Malarial Splenomegaly is the main cause [7]. In the United States, one large series reported a palpable spleen in 2% of patients and another in 5.6% of patients [8].

Referring to a study done in Kenya; where aetiologies of chronic splenomegaly were investigated in131 Kenyan patients, the major causes were hyper-reactive malarial splenomegaly (31%), hepatosplenic schistosomiasis (18%), visceral leishmaniasis (5%), non-schistosomal forms of portal hypertension (20%), while no diagnosis could be established in 12% [9]. One study conducted in the Eastern Province of Rwanda found that the prevalence of hyper reactive malarial splenomegaly in healthy pupils from the selected primary schools was 6.2% (13 out of 210 participants) [10].

Rationale and study objectives

To the best of our knowledge, there are no data about the prevalence of splenomegaly and associated etiologies in the Rwandan population although our preliminary data from the hospital's statistics department show that a significant number of patients admitted in the medical department had splenomegaly. Only one study, without comparator, has evaluated splenomegaly in Butare, focusing only on the therapeutic aspects of HMS [11].

A wide variety of diseases can lead to splenomegaly, and the predominant causes vary with geographical distribution of diseases prevalent in the region. With this study, we hope to bring an important information to the clinicians and researchers about the diseases that are commonly associated with splenomegaly in Rwanda which is not yet known.

In the majority of cases, splenomegaly can be detected clinically by the treating clinician during physical examination, however, there is still a good number of splenomegaly that are discovered by imaging studies, which were sometimes ordered for other purposes ; we want to formally assess this discrepancy and provide preliminary data that can guide policy makers for appropriate quality improvement projects.

Splenomegaly is a subject of considerable clinical concern and warrants thorough clinical and laboratory evaluation; we anticipated that assessing the demography, common clinical presentations and hematological characteristics of patients with splenomegaly referred to the biggest national referral hospital receiving patients from all over the country could bring important information to clinicians and health decision makers that will contribute to improve the clinical assessment of patients with splenomegaly.

This study aims to assess the demographic data, clinical presentation, diagnostic aspects and hematological profile of patients with splenomegaly. In addition, we also l document different conditions associated with splenomegaly among hospitalized medical patients at Kigali University Teaching Hospital, observed during the year 2018.

METHODS

Patients and settings: This was a retrospective descriptive study conducted at Kigali University Teaching Hospital (CHUK), Department of Internal Medicine from January 1, 2018 to December 31, 2018. CHUK is a tertiary referral hospital and main public health institution in Rwanda. It is located in the center of Kigali city and receive patients from all the corners of the country via District hospitals. It has a 560 beds capacity.

The study included patients that were admitted in internal medicine to either ward 3 (male), ward 4 (female) ward 6 (Isolation ward) and PCK (prison ward). We did not include patients admitted from the other departments as the most causes of splenomegaly are medical conditions and not directly surgical or obstetrics diseases. Patients' files with various systemic diseases and hematological conditions, where splenomegaly was not present were not enrolled.

Sample size: The estimated sample size was calculated using the following formula [12,13]

$$\frac{N= Z^2.P.(1-P)}{E^2}$$

N: Sample size **P**: Expected Prevalence in the study population E: Absolute standard error (precision), **E**= 0.01

Z is the statistic corresponding to level of confidence, **Z**=1.96 and the level of confidence aimed for is 95%

Given the lack of prior local data in the study population, the prevalence of splenomegaly in hospitalized medical patients was estimated based on figures from California in United States where the prevalence of splenomegaly was 5.6% [8]. Based on a large eligible population of hospitalized medical patients and assuming the estimated prevalence of splenomegaly of 5%, a sample size of 1825 was calculated to achieve a 1% absolute standard error at a 95% confidence level for the prevalence of splenomegaly.

Recrutement of study participants: We reviewed the charts of all patients admitted with the conditions known from the literature to be associated with splenomegaly and include: infection (among them septic shock, infective endocarditis, typhoid fever, infectious mononucleosis, tuberculosis, brucellosis, malaria, kala-azar, schistosomiasis), inflammation (rheumatoid arthritis, sarcoidosis),haematological disorders (haemolytic anaemia, haemoglobinopathies, leukaemia, lymphomas, myeloproliferative disorders), portal hypertension and congestion (chronic liver diseases, congestive heart failure), storage diseases, amyloidosis, neoplasia, myelofibrosis, Hyper-reactive Malarial Splenomegaly, chronic myeloid leukaemia, and we enrolled those with splenomegaly (discovered either on clinical examination or by imaging) for further data analysis. Eligible patients were identified through the patients' registry, where every admitted patient in the respective ward is registered and his/her diagnosis is well mentioned together with his/her hospital identification and archiving numbers which helped to access their medical records.

Study design: Relevant information was extracted from existing medical records, patient's chart, laboratory and radiology registers; and was collected on a predesigned case report form which was anonymous with a unique identifier. Baseline demographic data (age, gender, marital status, place of residency), clinical data including general systemic symptoms such as fever, sweats, weakness, weight loss, nausea, anorexia, presenting signs and symptoms of splenomegaly such as left hypochondrial discomfort, early satiety, abdominal pain and or tenderness, a palpable mass in left upper quadrant, features of underlying condition including lymphadenopathies, hepatomegaly, portal hypertension, congestion, abdominal distension, and associated hematological parameters including leucocytes count, hemoglobin levels and thrombocytes. We collected as well information about when splenomegaly was discovered (before admission, on admission, or incidentally after admission) how splenomegaly was diagnosed (either by physical examination, abdominal ultrasonography, abdominal CT Scan or MRI) and Hackett's clinical stage of that enlarged spleen. All collected data were kept under conditions of strict confidentiality and are rendered anonymous by a unique identification code.

Ethical consideration: This study was approved by Kigali University Teaching Hospital Research and Ethics Committee. We did not request individual consent from the participants of this study as the risks of the study are minimal to the patient. The research involved retrospective review of patient records only; there are no experimental interventions or additional patient encounters with research/clinical staff outside of routine data collection. Data were abstracted from routine hospital records for patients who met the inclusion criteria, and viewed only by research team members in accordance with data management procedures described above. Since the study is a retrospective review of routine medical records, the study did not directly affect positively or negatively the care and routine management of the patients in the study. The possible risk is inappropriate exposure of patient confidential records, we minimized this risk by ensuring that only de-identified data is stored in database. Also, all study staff involved in data abstraction received appropriate research training to ensure understanding and compliance of data management and confidentiality procedures. The key record identifying the participants will be kept confidential even after publication of the results.

Statistical analysis: Data were initially collected on a case report form and then entered using Epidata version 3.1 software. Descriptive analysis, using standard statistical methods, was performed using the Statistical Package for Social Sciences (SPSS) software, version 16.0. Demographic and clinical characteristics were noted. During our data collection, some patients had incomplete files; they had some missing information for some variables and there were not considered for data analysis; a listwise deletion was performed before analysis. The most commonly affected variables are weight, temperature, lymph node examination, abdominal examination, FBC and final outcome. The analysis was applied for significant variables in new sample size with complete data.

RESULTS

During the study period, a total of 2019 eligible patients' files were examined, and among them 1950 had complete data; and out of them, only 117 (6%) patients were identified to have splenomegaly either on clinical examination or by imaging; they were enrolled in data collection and included in the final analysis. Their mean age was 39 years, with a range between 15 to 79 years. The number of women was slightly higher 65 (55.5%). Many patients were from the Eastern Province 47 (40.2%) followed by Kigali City 30 (25.6%) (Table 1).

Table 1: Demographic and clinical features of splenomegaly

Variables	N (%)
Sex	
Male	52 (44.5)
Female	65 (55.5)
Province of origin	
Kigali city	30 (25.6)
Eastern province	47 (40.2)
Northern province	8 (6.8)
Southern province	23 (19.7)
Western province	8 (6.8)
Outside Rwanda	1 (0.9)
When splenomegaly was diagnosed?	
Before admission	14 (11.9)
On admission	58 (49.6)
After admission	43 (36.8)
Not documented	2 (1.7)
Splenomegaly stage (Hackett's Classification)	
stage I	25 (21.4)
stage II	39(33.3)
stage III	27(23.1)
stage IV	24(20.5)
stage V	2(1.7)
Diagnostic tools	
Already known	14 (11.9)
Physical examination only	16 (13.7)
Abdominal ultrasound	33 (28.2)
Suspected on physical exam and confirmed with abdominal ultrasound	53 (45.3)
CT Scan	1 (0.9)
Total	**117(100%)**

In the majority of cases, splenomegaly was detected or suspected on physical examination (a palpable left upper quadrant abdominal mass) on admission (49.6%) or in few days post admission (36.8%). Splenomegaly was already documented before admission in 11.9% of cases. Many cases of splenomegaly were diagnosed at stage II (33.3%), stage III (23.1%) and stage IV (20.5%). Abdominal ultrasonography was the imaging tool that was used to evaluate the spleen size in the majority of cases. Splenomegaly was confirmed in 45.3% of cases after being suspected clinically, and it was discovered by ultrasonography in 28.2% of cases while clinical examination was unremarkable. Many patients did not have symptoms associated with an enlarged spleen (30.7%), others complained of abdominal discomfort (19.6%), chest pain similar to pleuritic pain when stomach or bowels are full (17%), complaints of early satiety (16%), symptoms of haemolysis (24.8%), symptoms of anaemia (22.2%), symptoms of infection (25.6%), constitutional symptoms suggestive of malignancy (13.6%) signs and symptoms related to the underlying conditions (17.1%). Splenomegaly was associated with hepatomegaly in 18.8% and with lymphadenopathies in 30%. Anaemia was present in the majority of patients (70%), followed by leukopenia (49.5% of cases), thrombocytopenia in 45.3% of cases while 30.7% of patients had pancytopenia. Leucocytosis was present in 19.6% and thrombocytosis was observed in 14.5% of the patients (Table 2).

Table 2: Clinico-haematological presentation of splenomegaly

Clinical presentation	N (%)
No symptoms of splenomegaly	36(30.7)
Constitutional symptoms	16(13.6)
Early satiety	19(16.2)
Abdominal pain and or tenderness	23(19.6)
Chest pain	20(17.1)
Features of anaemia	26(22.2)
Features of infection	30(25.6)
Features of haemolysis	29(24.8)
Symptoms of the underlying conditions	20(17.1)
Association with hepatomegaly	22(18.8)
Association with lymphadenopathies	35(30.0)
Haematological findings	
Anaemia (Hb<12g/dl)	82(70.0)
Leukopenia (WBC<4.500 cells/mm3)	58(49.5)
Thrombocytopenia (PLT<150.000/µl)	53(45.3)
Pancytopenia	36(30.7)
Leucocytosis (WBC>12.000 cells/mm3)	23(19.5)
Thrombocytosis (PLT>450.000/µl)	17(14.5)
Normal Haemoglobin	35(30.0)
Normal WBC (4.500 - 12.000 cells/mm3)	36(31.0)
Normal PLTs (150.000 - 450.000/µl)	47(40.2)

The main causes of splenomegaly were HMS (21.4%) and it was prevalent among patients from the Eastern province (19 out of 25 total cases of HMS), followed by cirrhosis and portal hypertension (19.6%), acute infection (16.2%), CML (12%), disseminated tuberculosis (9.4%). No clear etiology of splenomegaly was found in (11%) of patients (Table 3).

Table 3: Clinical diagnosis in 117 cases of splenomegaly

Causes of splenomegaly	N (%)
HMS	25(21.4)
Cirrhosis and portal hypertension	23(19.6)
Acute infection	19(16.2)
Chronic myeloid leukaemia	14(11.9)
Tuberculosis	11(9.4)
Congestive cardiac failure	8(6.8)
Acute Leukemia	9(7.7)
Lymphoma	7(5.9)
Chronic lymphocytic leukaemia	5(4.2)
Myelofibrosis	3(2.5)
Schistosomiasis	1(0.8)
No clear etiology	13(11.1)

The present study is an attempt to find out the frequency of various causes of splenomegaly, its clinical presentation and how it is diagnosed at a referral level hospital in Rwanda. In addition, it highlights the role of hematological parameters as a diagnostic or additional tool in elucidating etiopathogenesis of splenomegaly. The results of this study show that there are no major differences with the existing

findings: the prevalence of splenomegaly was 6%, which is similar with 5.6% found by O'Reilly et al. at a big referral hospital in California [8] , and similarly with other studies, there was no age or gender predilection for splenomegaly [5].

The most frequent cause of splenomegaly in present study was hematological diseases followed by Hyper-reactive Malarial Splenomegaly, congestive splenomegaly (associated with liver cirrhosis) and infection; these are quite similar with figures from Kenya [9]. One study revealed that in malaria endemic area, about 11-45% of patients with massive splenomegaly were due to HMS [15, 17]; we got the same findings as the main cause of splenomegaly was HMS (21.4%) and was frequent among patients from the Eastern province (the highest malaria endemic area in Rwanda).

The abdominal ultrasonography was used to confirm splenomegaly in 45.3% of cases after being suspected clinically, and it was discovered by ultrasonography in 28.2% of cases while clinical examination was unremarkable. One study showed that while clinical examination can be convincing in splenic enlargement, radiology is often needed to confirm the diagnosis, and it was found that point-of-care ultrasonography significantly improves examiners' sensitivity in diagnosing splenomegaly [23, 24].

In this study, many patients presented with moderate splenomegaly and cytopenias (mainly anemia) from an enlarged overworking spleen; this is a common finding in patients with chronic splenomegaly especially from developing countries; where infectious diseases and hematological malignancies are prevalent [25, 26]; and routine hematological evaluations may provide an important clue about the etiology of splenomegaly, for example, finding a parasite, evidence of hemolysis, septicemia, leukemia, lymphoma or myeloma.

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Study limitations

This study didn't assess in details all laboratory and hematological investigations that would help to best characterize the different conditions associated with splenomegaly.

The detailed assessment of the spleen (like the structure, echogenicity, contours, etc.), as reported by the radiologists/radiology technicians were not recorded and included in analysis while this information would serve to better characterize the enlarged spleen. Imaging contribution was just to confirm splenomegaly and its stage.

Another limitation of this study is listwise deletion that was applied to deal with missing data; this method can introduce a systematic bias; but there was no significant change of our results.

CONCLUSION

Splenomegaly is a frequent finding in a medical department. In our country, especially the Eastern province, there is a high prevalence of tropical splenomegaly. Most cases with splenomegaly are detected on admission by physical examination or by abdominal ultrasonography and found at moderate stages in many cases. Splenomegaly should always be investigated thoroughly as most of the common causes are treatable. There is an exhaustive list of different etiologies of splenomegaly and hematological causes outnumbered the non-hematological cause of splenomegaly. Hematological profile in cases with enlarged spleen are of utmost importance as a diagnostic tool which can also be used to monitor the response to treatment.

DECLARATIONS

Ethics approval: This study protocol was reviewed and approved by the Kigali University Teaching Hospital Research and Ethics Committee. We ensured confidentiality of the study data and maintained the anonymity of the study participants.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions: All authors contributed to the design and development of this study. EN, EN coordinated the data collection

process. RS, CM and MGN played an important role in data collection and data entry. FH and FS performed statistical analyses. EN, EN, VM and FS reviewed and corrected the final work. All authors read and approved the final manuscript.

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