Abstract

**Purpose:** To evaluate a possible relationship between the size of the spleen and values of circulating blood elements in patients with schistosomatic splenomegaly.

**Methods:** Sixty one patients with hepatosplenic schistosomiasis mansoni underwent a clinical exam and peripheral venous blood was collected for a hemogram. The erythrocyte, hemoglobin, hematocrit, leukocyte, and platelet values were determined. All patients underwent abdominal ultrasound to measure the spleen. The hematological test results were compared to the size of the spleen.

**Results:** The size of the spleen varied from 14.0 to 28.4 (19.9 ± 3.7) cm according to the ultrasound image. Thrombocytopenia was observed 58 (95%) patients, leukopenia in 55 (90%) patients, and anemia in 32 (52.4%) patients. Leukopenia was proportional to splenomegaly.

**Conclusion:** Schistosomal splenomegaly leads to leukopenia in direct proportion to the size of the spleen.

**Key words:** Schistosomiasis mansoni. Splenomegaly. Leukopenia. Thrombocytopenia. Anemia.
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Introduction

Symmers-Bogliolo is a typical hepatosplenic lesion of Schistosomiasis mansoni (SM), which culminates in presinusoidal portal hypertension. After five to 15 years of schistosomatic hepatopathy, scheral congestive splenomegaly, hyperdynamic porto-systemic collateral circulation, and the reduction in the number of peripheral blood elements begin to appear.

The association between scheral congestive splenomegaly and hematological alterations of leukopenia, plateletopenia, and anemia is still not fully understood, considering that the blood elements remain within the spleen without being destroyed, as occurs in leukosis and hypersplenism. By contrast, in emergency, such as severe infections and intense bleeding, leukocytes and platelets are released in the quantity that the organism needs. In this sense, patients with intense leukopenia begin to present leukocytosis during septic complications at the same level as people with a normal spleen. As regards thrombocytopenia, no schistosomal patient, even those with platelet levels of below 10.000/mm³, presents hemorrhagic disorders, purple spots, or bruises, and their bleeding time is normal. Thus, surgical procedures are performed on these patients with no difficulty in vascular coagulation and without the need for a transfusion of platelet concentrates. Therefore, leukopenia and thrombocytopenia are only laboratorial, with no clinical manifestation and without hypersplenism. The spleen plays the role of storing the blood elements, without destroying them, and releases them into systemic circulation when necessary.

In a line of research, the purpose of this study was to verify a possible relationship between the size of the spleen and values of circulating blood elements in patients with schistosomatic splenomegaly.

Methods

This study was approved by the Research Ethics Committee from Universidade Federal de Minas Gerais (UFMG), logged under protocol number ETIC 006/08, as well as by the Teaching, Research, and Extension Board from the UFMG Clinical Hospital, logged under protocol number 065/09.

This study was performed on 61 patients with hepatosplenic schistosomiasis, 36 men and 25 women. The age of the patients varied from 18 to 65 (42 ± 11) years. Regarding the skin color, 17 were caucasian, 30 light-skinned black, and 14 dark-skinned black. All of the patients, upon undergoing a physical exam, presented hepatosplenomegaly. Patients with any other clinically manifested disease or who were undergoing complementary exams were excluded. All patients were advised as regards the purpose of this research and only those who agreed to the terms of the study and who signed the Free and Informed Consent Form were included.

For the hemogram dose, 4 ml of peripheral venous blood was collected, aimed at quantifying the erythrocyte, leukocyte, and thrombocyte series. The collection was conducted by a vacuum blood collection system in EDTA tubes. The samples were processed in a specific automation device, by electric impedance and flow cytometry (Cell Dyn 3000® System, Abbott Diagnostics Division, Mountain View, California, USA), and the results were manually confirmed by a hematoscopy exam, performed by a Clinical Pathologist.

Anemia was considered when hemoglobin was less than 13.0 g/dl in men and 12.0 g/dl in women. Thrombocytopenia was classified as serum platelets of less than 150.000/mm³. Leukopenia was considered when total serum leukocyte values were below 4.000/mm³.

All of the patients were submitted
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To a bidimensional ultrasound study. The exams were conducted by a single ultrasound technician, following the same evaluation standard for the spleen and other abdominal organs, including the portal system. The size of the spleen was defined by measuring its craniocaudal length. The size of the spleen was correlated with the values of the hematological exams.

The statistical tests were carried out using the Statistical Package for Social Sciences (SPSS) version 12.0 for Windows® (SPSS Incorporation, Chicago, Illinois, USA, 2005). Spearman’s correlation coefficient was used to compare the size of the longitudinal axis of the spleen with the hematological parameters. The significance level was set at p < 0.05 corresponding 95% CI.

### Results

Data referent to age, weight, height, and body mass index (BMI) of the 61 patients are presented in Table 1.

**Table 1 – Characteristics of 61 patients with splenomegaly caused by Schistosomiasis mansoni.**

| Characteristics  | Results |
|------------------|---------|
|                  | M ± SDM | Minimum | Maximum |
| Age (years)      | 42 ± 11  | 18      | 65      |
| Weight (kg)      | 62.4 ± 12.2 | 42      | 94      |
| Height (cm)      | 162.9 ± 9.3 | 144     | 183     |
| BMI (kg/m²)      | 24.2 ± 3.5 | 18.6    | 32.3    |

Mean ± standard deviation of mean (M ± SDM); BMI = Body Mass Index.

Table 2 presents the sizes of the spleens measured by ultrasound and the evaluated hematological results.

**Table 2 – Hematological exams and craniocaudal length of the spleen of 61 patients with splenomegaly caused by Schistosomiasis mansoni.**

| Parameters                  | Results M ± SDM | Minimum | Maximum | Reference Intervals |
|-----------------------------|-----------------|---------|---------|---------------------|
| Red blood cells (10⁶/mm³)   | 4.24 ± 0.60     | 2.76    | 5.40    | 4.5 – 5.5 (M) 3.8 – 5.4 (F) |
| Hemoglobin (g/dL)           | 11.2 ± 2.10     | 7.2     | 16.0    | 13.0 – 17.5 (M) 12.0 – 16.0 (F) |
| Hematocrit (%)              | 34.4 ± 5.10     | 25.0    | 47.3    | 40 – 50 (M) 36 – 46 (F) |
| Total leukocytes (cels/mm³) | 2.710 ± 1.348   | 900     | 7.600   | 4.000 – 11.000    |
| Platelets (cels/mm³)        | 55.918 ± 33.253 | 15.000  | 167.000 | 150.000 – 450.000 |
| Craniocaudal length of spleen (cm) | 19.9 ± 3.7  | 14.0    | 28.4    | 8 – 12             |

Mean ± standard deviation of mean (M ± SDM); M = Male, F = Female.

At the ultrasound exam, no patient presented parenchymal alterations of cirrhosis, tumor, or thrombosis of the main veins of the portal system, which would serve as a reason to exclude the patient from this study. Splenomegaly was confirmed in all patients,
whose measurements of the craniocaudal length varied between 14 and 28.4 (19.9 ± 3.7) cm.

Regarding the hematological results, the thrombocytopenia was the most common alteration, which was observed in 58 (95%) patients. Leukopenia and anemia were observed in 55 (90%) and in 32 (52.4%) of the cases, respectively.

The correlations between the size of the spleen and the hematological parameters are presented in Table 3.

Table 3 – Correlation between splenomegaly and results from hematological exams from 61 patients with splenomegaly caused by Schistosomiasis mansoni.

| Parameters       | Splenomegaly (n = 61) | Spearman Coefficient (r) | Significance level (p) |
|------------------|-----------------------|--------------------------|------------------------|
| Red blood cells  |                       | 0.164                    | 0.208                  |
| Hemoglobin       |                       | 0.088                    | 0.498                  |
| Hematocrit       |                       | 0.091                    | 0.485                  |
| Total leukocytes |                       | -0.295                   | **0.021**              |
| Platelets        |                       | -0.150                   | 0.247                  |

Proportionality was observed between leukopenia and the splenic dimensions, larger spleens were accompanied by proportionally more intense leukopenia (p = 0.021). In the other evaluated hematological parameters, no difference or proportionality was found. No difference between the sexes nor between the patients with different skin colors. No alterations stemming from patient age and BMI were found.

Discussion

Among the exams available to determine the size of the spleen, the ultrasound is the most common. Splenic dimensions can vary according to age, nutritional state, anthropometric dimensions, and the presence of diseases. In healthy adults, the normal spleen measures approximately 8 cm to 12 cm along its craniocaudal length, of 4 cm to 7 cm in width (anteroposterior), and 3 cm to 4 cm in thickness (laterolateral).

Since the measures were taken by a single professional in all patients, according to health protocols of the World Health Organization (WHO), potential errors were maintained constant, and the dimensions followed a similar pattern.

According to the literature, the cytopenias associated with splenomegaly and portal hypertension of any etiology occur in a percentage that varies between 30% and 70% of the cases and, specifically in schistosomiasis, between 50% and 95% of the cases. According to the literature, the majority of the patients presented pancytopenia. Among the cytopenias observed, plateletopenia was the most common, followed by leukopenia and anemia. These findings were also reported in other studies.

Although pancytopenia is common among patients with splenomegaly, the reduction of erythrocyte, leukocyte, and thrombocyte series is not always associated with the size of the spleen. Cytopenia does not necessarily occur in all peripheral blood elements, as the patient may present only anemia or leukopenia or thrombocytopenia, as well as the reduction of only two of the three series. This situation also remains unexplained in current knowledge, which ignores the etiopathogenesis of the reduction of each one of the series.

In this study, the splenomegaly was correlated only to leukopenia. Such findings were similar to those from Khishen et al., although these authors had also observed...
a correlation with thrombocytopenia. By contrast, Wadenvik et al.\textsuperscript{5} verified that the dimensions of the spleen, measured by ultrasound, had a correlation with the low levels of hemoglobin and platelets but not with the count of circulating leukocytes. Neither thrombocytopenia, present in 95\% of the patients evaluated, nor the intensity of anemia proved to be correlated to the size of the spleen. Such results contradict studies conducted by Martins et al.\textsuperscript{25}, who found a correlation between splenomegaly and plateletopenia. However, these authors evaluated neither the leukocyte nor the erythrocyte series. Leite et al.\textsuperscript{26} also observed a correlation between splenomegaly and thrombocytopenia in 55 patients in the hepatosplenic stage of Schistosomiasis mansoni.

According to Eichner\textsuperscript{7}, augmented spleens are not necessarily abnormal, much like hyperfunctioning spleens are not always augmented. Grover et al.\textsuperscript{23} observed no hematological alterations in the presence of splenomegalies stemming from different causes, while Gielchinsky et al.\textsuperscript{6} found pancytopenia in the presence of small spleens, with no perceivable disorders.

The divergence in findings in the literature reinforces how difficult it is to understand the physiopathology of pancytopenia in patients with splenomegaly\textsuperscript{4}. Most authors erroneously describe cytopenia as necessarily pertaining to a medical condition of hypersplenism\textsuperscript{4,5}. This idea began with studies that considered hypersplenism as an increase in hemocatheretic activity resulting from structural hyperplasia of the spleen, always accompanied by a destructive autoimmune mechanism of the blood elements\textsuperscript{29,30}. However, this situation rarely occurs\textsuperscript{10}. The more common is splenomegaly, associated only with an increase in the storage of blood elements without provoking any clinical disorder\textsuperscript{8,9,12}. This concept is reinforced by the fact that partial and subtotal splenectomies have normalized the number of peripheral blood elements, thereby maintaining the splenic tissue. In this sense, the immune response hypothesis no longer contains a substrate\textsuperscript{10}.

A weakness aspect of this study was the use of ultrasound to determine the longitudinal measurement of the spleen, rather than the volumetric dimensions of the organ, since the process of leukocyte accumulation and other blood components in the spleen occurs in the three dimensions. In fact, ideally, splenic index calculated for the splenic volume, using the craniocaudal dimension, width, and thickness, would be the most reliable measurement for diagnosing splenomegaly. However, according to literature\textsuperscript{18-20,31}, a single measurement, for example the craniocaudal length, is not different to emphasise the splenic index from the one calculated for the splenic volume.

\section*{Conclusion}

The size of the spleen was proportionally correlated with leukopenia when in the presence of schistosomal splenomegaly.

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