

CORRELATION BETWEEN SPLENOMEGALY AND THROMBOCYTOPENIA IN HEPATOSPLENIC SCHISTOSOMIASIS

Correlação entre esplenomegalia e plaquetopenia na forma hepatoesplênica da esquistossomose mansônica

Rubens Nascimento **MARTINS**, Roberto de **CLEVA**, Éder Maxwel **GOUVEIA**, Nagilton Bou **GHOSN**, Paulo **HERMAN**

Work done at Department of Gastroenterology, Faculty of Medicine, University of São Paulo, São Paulo, Brazil

ABSTRACT – Background – It is known that both leukopenia and thrombocytopenia were significantly correlated with splenomegaly, but there is no studies correlating directly or precisely the size of the spleen with the number of platelets. It is controversial whether the thrombocytopenia observed in patients with chronic liver disease is more related to splenomegaly or portal hypertension itself. **Aim** – To correlate the serum level of platelets in pre and postoperative weight and volume of the spleen in patients with hepatosplenic schistosomiasis with indication for surgical treatment of portal hypertension. **Methods** – The medical records of patients with hepatosplenic schistosomiasis mansoni who underwent surgical treatment of portal hypertension were revised. Were included patients with the disease confirmed by pathologic diagnosis of liver biopsy performed during surgery, and excluded all patients who had a history of chronic alcoholism, viral hepatitis, clinical and laboratory evidence of hepatic or histopathological changes compatible with liver cirrhosis. Evaluation of the size and volume of the spleen, the serum level of platelets, the platelet count was done. **Results** – Were identified 141 patients who met the inclusion criteria of the 160 charts analyzed. The mean age was 39.03 ± 12.74 years (15 to 74 years) and 84 men (59.5%) and 57 women (40.5%). The average weight of the spleen was 966.27 ± 464.61 g (120-2700 g). The elliptical volume averaged 966.68 ± 499.12 cm³ (from 236.13 to 2782.36 cm³). There was a statistically significant correlation between weight and volume of elliptical spleen ($p < 0.0001$). The average number of platelets in preoperative period was $76.84 \pm 43.64 \times 10^3/\text{mm}^3$ below normal values ($150-400 \times 10^3/\text{mm}^3$). There was a statistically significant correlation between the numbers and logarithmic value of platelets in both preoperative with weight ($p < 0.01$) with the elliptical volume ($p < 0.05$) spleen. The number of platelets in the immediate postoperative period was correlated inversely with the weight of the spleen removed ($p = 0.0297$), the logarithm value of platelets is also correlated with weight. The model used did not predict the serum concentrations of platelets based on weight and spleen volume. **Conclusion** – The variations in serum levels of platelets in both pre and postoperative period in patients with hepatosplenic schistosomiasis were directly correlated to changes in weight and volume of the spleen. Splenomegaly was directly responsible for the variation in the number of platelets.

HEADINGS – Hypertension, portal. Schistosomiasis mansoni. Blood platelets.

Correspondence:

Paulo Herman.
Rua Eneas de Carvalho Aguiar, 255 -
Cerejeira Cesar - Sao Paulo, SP - Brasil.

Fonte de financiamento: não há

Conflito de interesses: não há

Recebido para publicação: 02/08/2010

Aceito para publicação: 27/10/2010

DESCRITORES – Hipertensão portal. Esquistossomose mansoni. Plaquetas.

RESUMO – Racional – Sabe-se que tanto a leucopenia quanto a plaquetopenia têm relação direta com a esplenomegalia, mas não existem estudos correlacionando de forma direta ou precisa o tamanho do baço com o número de plaquetas. Ainda há controvérsia se a plaquetopenia observada em pacientes com doenças hepáticas crônicas está mais relacionada à esplenomegalia ou à própria hipertensão portal. **Objetivo** – Correlacionar o nível sérico das plaquetas nos períodos pré e pós-operatório imediato com peso e volume do baço em pacientes portadores da forma hepatoesplênica da esquistossomose com indicação para tratamento cirúrgico da hipertensão portal. **Método** – Foram analisados os prontuários de pacientes portadores da forma hepatoesplênica da esquistossomose mansônica submetidos a tratamento cirúrgico da hipertensão portal. Foram incluídos portadores com a doença confirmada pelo diagnóstico anatomopatológico da biópsia hepática realizada no período intra-operatório. Foram excluídos todos os doentes que apresentavam antecedentes de etilismo crônico, hepatite viral, evidências clínico-laboratoriais de insuficiência hepática ou alterações histopatológicas compatíveis com cirrose hepática. Foram avaliados: o tamanho e volume do baço; o nível sérico de plaquetas; o número de plaquetas. **Resultados** – Foram identificados 141 pacientes que preenchem os critérios de inclusão do total de 160 prontuários analisados. A idade média foi de $39,03 \pm 12,74$ anos (15 a 74 anos), sendo 84 homens (59,5%) e 57 mulheres (40,5%). O peso médio do baço foi de $966,27 \pm 464,61$ g (120 a 2700 g). O volume elíptico médio foi de $966,68 \pm 499,12$ cm³ (236,13 a 2782,36 cm³). Houve correlação estatisticamente significativa entre o peso

e o volume elíptico do baço ($p < 0,0001$). O número médio de plaquetas no período pré-operatório foi $76,84 \pm 43,64 \times 10^3/\text{mm}^3$, abaixo dos valores considerados normais ($150 - 400 \times 10^3/\text{mm}^3$). Observou-se correlação estatisticamente significativa entre o número e valor logarítmico das plaquetas no período pré-operatório tanto com peso ($p < 0,01$) quanto com o volume elíptico ($p < 0,05$) do baço. O número de plaquetas no pós-operatório imediato esteve correlacionado de modo inverso com o peso do baço retirado ($p = 0,0297$); o valor logaritmo das plaquetas também se correlacionou com o peso. Não se conseguiu, através do modelo empregado, prever o valor sérico das plaquetas baseando-se no peso e volume esplênicos. **Conclusão** - As variações do nível sérico de plaquetas tanto no pré como no pós-operatório, em pacientes portadores da forma hepatoesplênica da esquistossomose mansônica, apresentam-se diretamente correlacionadas às variações de peso e volume do baço. A esplenomegalia foi diretamente responsável pela variação do número de plaquetas.

INTRODUCTION

Schistosomiasis is a parasitic disease endemic in over 70 countries worldwide, affecting approximately 200 million individuals¹². In Brazil, the only parasitic disease is caused by *Schistosoma mansoni* and represents an important public health impact, estimating that 3 million to 4 million people are infected and 20 million exposed to infection. The most severe form of the disease, hepatosplenic, is an important cause of morbidity and mortality in 30-10% of infected⁶, characterized by splenomegaly and widespread fibrosis of the liver with portal hypertension, collateral circulation and risk of variceal bleeding esophagus.

From the standpoint of laboratory these patients have leukopenia and thrombocytopenia important and sometimes pancytopenia and the loss or iron deficiency anemia and leukopenia and thrombocytopenia secondary to large splenomegaly hepatosplenic^{3,4,10}. We know that as much as leukopenia thrombocytopenia were significantly correlated with splenomegaly¹³, but no studies correlating directly or precise size of the spleen with the number of platelets. There is still controversy over whether the thrombocytopenia observed in patients with chronic liver disease is more related to splenomegaly or very high blood pressure portal.

The main complication of portal hypertension in schistosomiasis is bleeding from esophagogastric varices not known and the role of thrombocytopenia in these bleeding episodes. Despite major advances in therapeutic endoscopic surgical treatment is still indicated as prophylaxis in patients with previous episode of upper gastrointestinal bleeding, with the esophagogastric devascularization and splenectomy the most used in our environment by eliminating the quota of the splenic vein portal flow, and restrict the flow to the portal venous flow into the territory esophagogastric esophagogastric^{11,16}.

The aim of this study was to correlate serum levels of platelets in pre-and postoperative weight and volume of the spleen in patients with

hepatosplenic schistosomiasis with indication for surgical treatment of portal hypertension.

METHOD

The medical records of patients with hepatosplenic schistosomiasis mansoni who underwent surgical treatment of portal hypertension in the period between 1991 and 2006.

This study was approved by the Commission for the Analysis of Research Projects of the Hospital of the Faculty of Medicine, University of São Paulo.

We included patients with hepatosplenic disease confirmed by pathologic diagnosis of liver biopsy performed during surgery.

We excluded all patients who had a history of chronic alcoholism, viral hepatitis, clinical and laboratory evidence of hepatic or histopathological changes consistent with liver cirrhosis.

Evaluation of spleen size and

Ultrasonography was used preoperative measurement of the anteroposterior diameter, spleen longitudinal and transverse in the coronal and axial after deep inspiration, adopting as reference the splenic hilum⁹.

The spleen volume in cubic centimeters, was calculated using the formula of ellipse: long axis (cm) x anteroposterior (cm) x cross (cm) x 0.523, which is used to estimate the volume of irregular bodies^{2,5,14}. The organ weight in grams was obtained immediately after completion of the splenectomy in the surgical center.

Evaluation of serum platelet

It was expressed in units per cubic millimeter, using the method automated equipment in Counter-Cell-Dyn®, and its value also logarithmic. Results were collected in the preoperative period (one to seven days before surgery) and postoperative (up to one month of surgery).

We determined the relationship between serum levels of platelets in the preoperative and postoperative weight and volume of the spleen.

We used the logarithmic increase of platelets to the correlation existing between the times of collection of serum platelet and the variables of volume and weight of the spleen.

Model for determining the number of platelets

From the data obtained we attempted to evaluate the possibility of determining serum levels of platelets in pre-or post-operative only by weight or volume.

To this was employed linear models with gamma distribution and identity link. The gamma distribution is used to evaluate the difference between platelets in pre-and postoperatively. We chose this model of distribution due to the fact the results show only positive values.

Evaluation of parameters obtained

We calculated the relationships between the parameters of interest: platelets in the preoperative and postoperative volume and weight of the spleen.

The evaluation of the parameters was performed using the Spearman correlation test to perform non-parametric correlation, ie, it was assumed the normality assumption of the values studied. Were considered as statistically significant p values <0.05.

RESULTS

We identified 141 patients who met the inclusion criteria of the 160 charts analyzed. The mean age was 39.03 ± 12.74 years (15 to 74 years) and 84 men (59.5%) and 57 women (40.5%).

The average weight of the spleen was 966.27 ± 464.61 g (120-2700 g). The elliptical volume averaged 966.68 ± 499.12 cm³ (from 236.13 to 2782.36 cm³), a significant splenomegaly compared with the values considered normal (164.3 ± 62.9 cm³)^{13,16}. There was a statistically significant correlation between weight and volume of elliptical spleen (p <0.0001).

The average number of platelets in the preoperative period was $76.84 \pm 43.64 \times 10^3 / \text{mm}^3$, below normal values (150 to $400 \times 10^3 / \text{mm}^3$). We observed a statistically significant correlation between the numbers and logarithmic value of platelets in both pre-operative weight (p <0.01) with the elliptical volume (p <0.05) of the spleen (Table 1 and Figures 1 and 2).

The number of platelets in the immediate postoperative period was correlated inversely with the weight of the spleen removed (p = 0.0297), the logarithm value of platelets also correlated with weight. The parameters for the spleen, obtained in the pre surgery and immediate postoperative period, can be seen in Table 2 and Figure 3.

TABLE 1 – Parameters obtained in the pre - operative

Parameters	Mean \pm SD	Median	Normal Value
Spleen weight	966,27 \pm 464,61	890,00	150
Spleen	966,68 \pm 499,12	871,31	164,3 \pm 62,9
Platelets pre-op	76,84 \pm 43,64	65,00	150 – 400

Legend: Weight (g) Volume (cm³); platelets (10³/mm³)

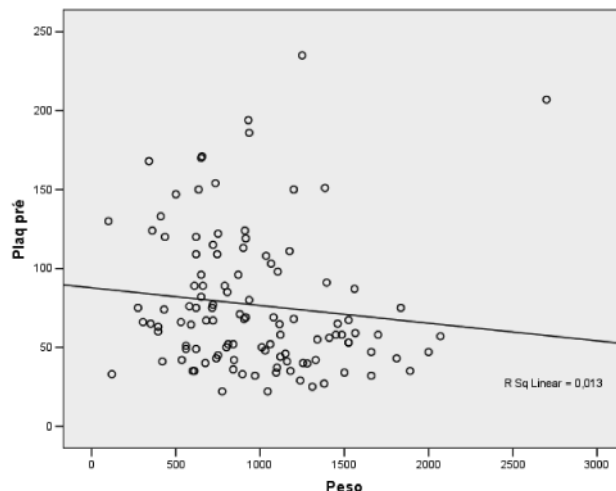


FIGURE 1 - Relationship between platelet counts preoperatively and spleen weight

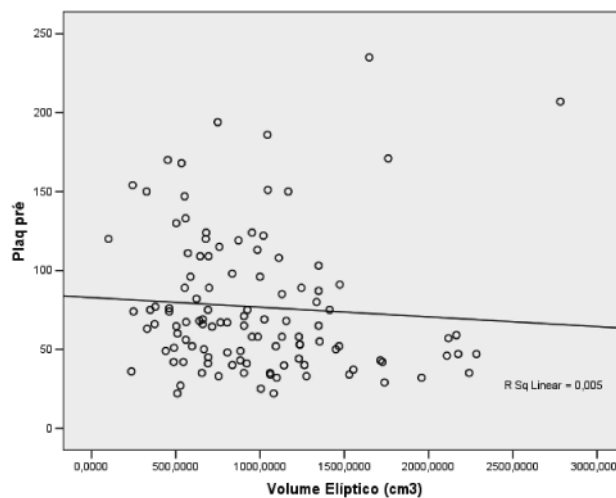


FIGURA 2 - Relationship between platelet counts and preoperative splenic volume elliptical

TABLE 2 – Parameters obtained in the pre-operative and postoperative

Parameters	Mean \pm SD	Median	Normal Value
platelets pré-op	76,84 \pm 43,64	65,00	150 – 400
platelets PO imediat	415,84 \pm 241,33	374	150 – 400
platelets PO	349,17 \pm 148,77	314	150 – 400

Legend: platelets (10³/mm³)

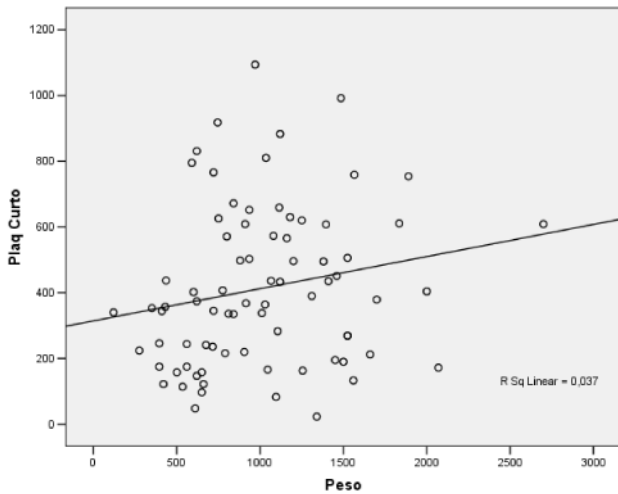


FIGURE 3 - Relationship between platelets in the immediate postoperative period and spleen weight

Could not get through the model used to predict the serum concentrations of platelets based on the weight and volume of the spleen.

DISCUSSION

The splenomegaly observed in schistosomiasis is due both to the presence of portal hypertension as the inflammatory reaction triggered by the presence of parasites or their eggs, causing venous congestion of the splenic vein and impoundment of erythrocyte lineages, granulocytic and megakaryocytic, leading to increased functional organ¹⁵.

Morphological and structural changes of the spleen associated with hematologic and subsequently called hypersplenism^{2,15} leukopenia, thrombocytopenia, and anemia caused by this change. Increased functional spleen as the initial process in the formation of hypersplenism was described^{2,15}, while Andrade¹ showed that this process results from hyperplasia and increased cell function of the reticuloendothelial system secondary to venous congestion of splanchnic system.

Hyperplasia of the spleen described by various authors in this study was checked by increasing the average weight, dimensions and volume of the organ when compared to the average normal population. Weights and elliptical volume were directly related.

Splenic involvement with the development of splenomegaly, due to the emergence of hepatic fibrosis secondary to the granulomatous reaction caused by *Schistosoma* eggs were loaded into the liver. The flow becomes hepatofugal liver, resulting in increased flow and stasis in the collateral venous system, especially in the splenic vein. This event results in an increase in the fairing of the bloodlines

in the spleen, with subsequent development of this organ hyperplasia, seen in this study as an increase in mean and median when compared to normal values.

Thrombocytopenia observed in patients with schistosomiasis occurs concomitantly with the progressive increase in the spleen as in autoimmune diseases such as idiopathic thrombocytopenic purpura and severe thrombocytopenia observed with small splenomegaly. Little is studied whether the thrombocytopenia observed in patients with chronic liver diseases, is more related to splenomegaly or portal hypertension itself.

To analyze the linearity of this relationship in the hepatosplenic form of schistosomiasis, this study was to correlate the serum level of platelets with the size and volume of the spleen, it was observed that both weight and volume are directly correlated with splenic platelets in pre-and post- operatively.

The treatment of choice for most services involved in the treatment of portal hypertension in schistosomiasis is to esophagogastric devascularization and splenectomy⁷. In this study, the patients underwent surgical treatment showed increased serum levels of platelets in the immediate postoperative period compared to preoperative. This result refers to the splenic sequestration that occurs in schistosomiasis¹⁵.

One of postoperative complications common to patients submitted to esophagogastric devascularization and splenectomy is thrombosis of the portal system caused by stasis of blood flow within the portal vein and its branches and increasing the blood cells especially platelets⁶.

Increased serum levels of platelets in the immediate postoperative period correlated inversely with the weight of the spleen is significantly removed showing that the effect of splenic sequestration that occurs in schistosomiasis.

The changes in spleen volume and mass obtained in this study were directly related to the serum level of platelets in the preoperative period, ie the larger the spleen the lowest platelet counts preoperatively, just as the larger the spleen increased the elevation of platelets in the immediate postoperative period, demonstrating that the spleen acts as an organ which sequesters platelets. Based on these findings, it should be noted that in patients with hepatosplenic schistosomiasis splenomegaly, and no portal hypertension, is responsible for varying the number of platelets.

Similarly, when splenectomy is carried out ligation of the splenic vessels, observing the change of the action of sequestration by the spleen of bloodlines, with an increase during surgery of the hemoglobin level - a phenomenon termed "auto-transfusion" - and subsequently increased serum level of platelets in the immediate postoperative period.

CONCLUSION

The variations in serum levels of platelets in both pre and postoperatively in patients with hepatosplenic schistosomiasis, have directly correlated to changes in weight and spleen. Splenomegaly is directly responsible for the variation in the number of platelets.

REFERENCES

1. Andrade Z. A. Aspectos experimentais da esplenomegalia da esquistossomose. *Rev Inst Med Trop.* 1962;4:249-55.
2. Cerri CG, Alves VA, Magalhães A. Hepatosplenic schistosomiasis mansoni: ultrasound manifestations. *Radiology* 1984;153:777-80
3. de Cleve R, Genzini T, Laudanna AA. Hipertensão portal na Esquistossomose. *Revista de Medicina de São Paulo* 1996; 75:126-9
4. de Cleve R, Herman P, Saad WA, Pugliese V, Zilberstein B, Rodrigues JJ, Laudanna AA. Postoperative portal vein thrombosis in patients with hepatosplenic mansonic schistosomiasis: relationship with intraoperative portal pressure and flow. A prospective study. *Hepatogastroenterology.* 2005 Sep-Oct;52(65):1529-33..
5. De Odorico I, Spaulding KA, Pretorius DH, Lev-Toaff AS, Bailey TB, Nelson TR. Normal splenic volumes estimated using three-dimensional ultrasonography. *J Ultrasound Med* 1999;18:231-6.
6. Ferreira FG, Chin EWK, Santos MF, de Carvalho DLM, De Capua Junior A. Índice de congestão portal e a ocorrência de congestão portal pós-DAPE. *Rev Assoc Med Bras* 2005; 51(4): 233-6
7. Ferreira FG, Chin EWK, Santos MF, Carvalho DLM, de Capua Jr A. Índice de Congestão Portal e a Ocorrência de Trombose Portal Pós-Dape. *Rev. Assoc Méd Bras* 2005; 51(4): 233-6
8. Guerra CCC, Haddad CM, Matsumoto M, Luzzi JR, Silva MP, Chacon JP. Comportamento do hiperesplenismo após anastomose esplenorrenal seletiva. *Rev Ass Med Bras* 1985;31:65-70.
9. Guerra CCC, Haddad CM, Matsumoto M, Luzzi JR, Silva MP, Chacon JP. Novos conceitos do hiperesplenismo na esquistossomose mansônica. *Rev Ass Med Bras* 1982;28:42-4
10. Janini DS, Oliveira IRS, Widman A, Ianhez LE, Cerri GG. Aspectos morfológicos e hemodinâmicos do baço em indivíduos normais: estudo por ultrassom Doppler. *Radiol Brás* 2003; 36(4): 213-218.
11. Makdissi F. Trombose do sistema portal no pós-operatório da desconexão ázigo-portal e esplenectomia em portadores e esquistossomose hepato-esplênica: avaliação de incidência, fatores preditivos, evolução clínica, laboratorial, endoscópica e de ultrassonografia com Doppler. *Dissertação de Mestrado, FMUSP,* 2004.
12. Makdissi FF, Herman P, Machado MAC, Pugliese V, D'Albuquerque LAC, Saad WA. Trombose de veia porta após desconexão ázigo-portal e esplenectomia em pacientes esquistossomóticos. Qual a real importância? *Arq. Gastroenterol* 2009; 1:50-56.
13. Organização mundial da Saúde - Departamento de Controle de Doenças Tropicais Negligenciadas.
14. Petroianu A, Oliveira AE, Alberti LR. "Hiperesplenismo" em hipertensão porta por esquistossomose mansônica. *Rev Bras Hematol Hemoter.* 2004;26(3):195-20
15. Santos GT, Sales DM, Leão AR, Santos JEM, de Aguiar LAK, Brant PE, Shigueoka DC, Neto RC, D'Ippolito G. Reproducibility of ultrasonography in the assessment of periportal fibrosis according to Niamey criteria in patients with schistosomiasis mansoni. *Radiol Bras, nov./dez.* 2007, vol.40, no.6, p.377-381.
16. Souza MRA, Bordin JO, Borges DR. Hiperesplenismo. In: Petroianu A, editor. *O Baço.* CLR Balieiro, São Paulo, p.161-164. 2003
17. Widman A, Oliveira IRS de, Speranzini MB, Cerri GG, Saad WA, Gama-Rodrigues J. Hipertensão portal por esquistossomose mansônica hepatoesplênica: efeito da desconexão ázigo-portal com esplenectomia no diâmetro e na velocidade média de fluxo do sistema portal (estudo ultra-sonográfico com Doppler). *Arq. Gastroenterol.* 2001; 38(1):19-23.