



Systematic Review & Meta Analysis

Predictor of Spontaneous Rupture of Malarial Spleen: A Systematic Review and Meta-analysis

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Abstract

Background: Spontaneous pathological rupture of the malarial spleen (SPRMS) is a rare but serious complication that has no known predictor in the medical literature. This study aims to report a systematic review of the search for a predictor for SPRMS and the recent changes in the management trends and outcomes of this problem.

Methods: A systematic review of 122 cases from January of 2000 through March of 2024 was conducted and linear regression was computed to search for predicting factors for SPRMS.

Results: Plasmodium vivax (*P. vivax*) was the most common cause of SPRMS among local citizens, while Plasmodium falciparum (*P. Falciparum*) was predominant among infected travelers. Fifty patients underwent splenectomy. Despite the possibility of the presence of a confounding factor, blood pressure could be the sole predictor of SPRMS.

Conclusion: Recent management trends have shown a tendency toward conservative treatment to preserve splenic immunological functions. To our knowledge, this is the first report on a predicting factor for SPRMS. This is important for early diagnosis and health management, as securing patient safety is a cornerstone of clinical governance in emergency settings.

Keywords: spleen, rupture, malaria

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1. Introduction

In 2017, the World Health Organization (WHO) recorded 445,000 malaria-related fatalities and 216 million cases of malaria globally [1]. The rarity of spontaneous pathological rupture of the malarial spleen (SPRMS) is due to underdiagnosis and underreporting. However, compared to 10% mortality in residents diagnosed with SPRMS, the death rate among travelers suffering from the same problem was found to be around 38% [2]. This difference relates to people's immunity in regions where malaria is endemic. In contrast, the mortality rate of overwhelming post-splenectomy infection (OPSI) was reported at around 50% [3]. To address SPRMS, we systematically reviewed the relevant literature published between January 1st, 2000 and March 31st, 2024 to search for a predictive factor for SPRMS and look for changes in its management trends. Linear regression revealed that blood pressure is a predictor for SPRMS. This is important for early diagnosis and management to secure patient safety as a cornerstone of professional commitment and clinical governance.

The current study aims to find the outcomes of changes in management trends and predicting factors for SPRMS.

2. Materials and Methods

PubMed was searched and the digital objective identifiers were followed to find manuscripts published from January 1st, 2000 through March 31st, 2024 using the keywords "spleen," "rupture," and "malaria." Three investigators independently reviewed the retrieved literature, discussed the differences, and solved them with consensus (Figure 1).

(i) *Inclusion criteria*: Relevant case reports, case series, and relevant abstracts.

(ii) *Exclusion criteria*: Duplicates, titles with unavailable literature, and insufficient abstracts.

We added to the residents, expatriates, and emigrants who visited their home country where they contracted malaria. Then the data on age, sex, residence, symptoms (fever and left upper abdominal pain), vital signs (hypotension, tachycardia, and respiratory distress), laboratory findings (hemoglobin, platelets, and blood film, and/or serology test for plasmodia), ultrasound and/or CT scan report, and treatment outcomes were collected.

2.1. Statistical analysis

Data were fed to the Statistical Package for Social Sciences (SPSS) version 26. Means and standard deviations were computed where appropriate. Data were examined for independence using the Dubin-Watson test and histogram. Partial regression plots were drawn to test the linear relationship graphically and collinearity statistics were tested using Casewise Diagnostics for outliers. Logistic regression was set to find the impact of fever, pain, blood pressure, splenomegaly, and platelet count as independent variables on the dependent variable of splenic rupture or infarction.

3. Results

A total of 122 cases of SPRMS were retrieved. They were 103 males and 19 females with a mean (\pm SD) age of 33.3 (\pm 14.7) years. This sample included 78 local citizens, 32 travelers, and 12 military personnel. One-hundred and fifteen patients presented with fever (temperature $>37.3^{\circ}\text{C}$), 111 had abdominal pain, and 77 had a systolic blood

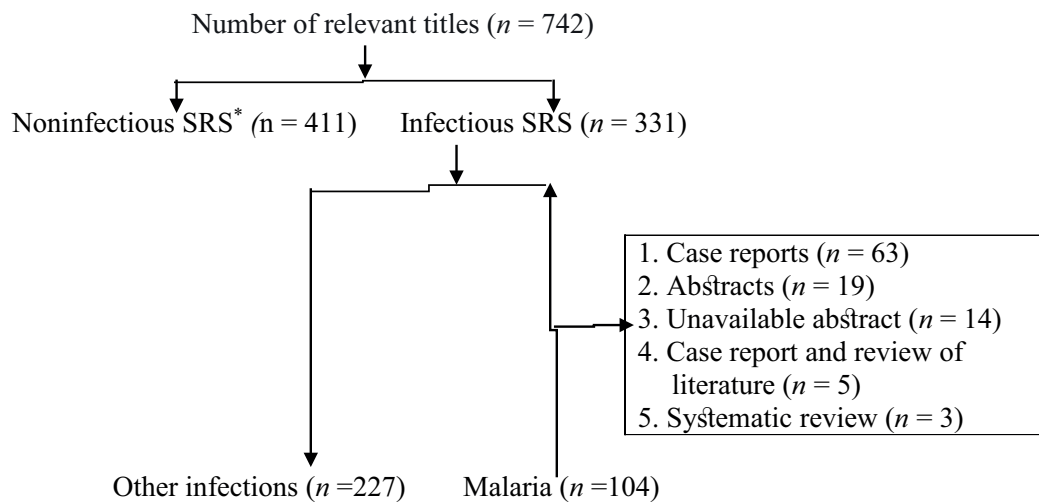


Figure 1: The PRISMA flow chart for the selection of retrieved literature.

pressure (BP) <100 mmHg. Left-sided abdominal tenderness was reported in 97 cases, palpable spleen in 49, and hepatosplenomegaly in 21. Investigations showed that 66 patients had Hb <7 g/dl and 54 had platelet count <150,000 × 10⁹ mL. The ultrasound and/or CT scan report is depicted in Table 1.

Plasmodium falciparum was more predominant than *P. vivax* among travelers, while *P. vivax* was more prevalent among citizens and military personnel, as shown in Table 2.

The tendency to preserve splenic function in 57 patients, along with three patients treated with pulmonary artery embolization, is shown in Table 3.

Our review findings were compared with the previously published reviews in Table 4.

The dependent variable (spleen rupture) was regressed on the independent variables (fever, pain, BP, splenomegaly, and platelet counts). The independent variables significantly predicted splenic rupture: $F = 5.142$ (in the model summary table, $df = 6$, and in the ANOVA table residual = 0.110, Sig $F = 0.002$). This indicated that the independent variables had a significant role in

splenic rupture. Moreover, $R^2 = 0.584$ indicated that the model explained 58.4% of the variance in splenic rupture. The coefficients were further assessed to ascertain the influence of each independent variable on splenic rupture. The results revealed that only BP (Figure 2) impacts splenic rupture (B -value = 0.595, $t = 4.345$, $P = 0.000$). The regression plots showed that the rest of the variables had either a negative impact (pain and splenomegaly) or a minimal positive impact (fever and thrombocytopenia) on the splenic rupture. However, we could not exclude a confounding factor at this stage.

4. Discussion

Edward Atkinson reported the first case of spontaneous rupture of the spleen (SRS) in 1874 [4]. In 1958, Orloff and Peskin described the criteria for diagnosing SPRMS, one of which was that the SRS should not have an identifiable cause such as infection, malignancy, drugs, or other medical interventions [5]. Hence, the term “pathological spontaneous rupture” was suggested [6].

Table 1: Correlation of the type of plasmodia and ultrasound and CT reports of the spleen.

	Splenic infarction	Splenic hematoma	Splenic infarction hematoma and hemoperitoneum	Total
<i>P. falciparum</i>	10	9	24	43
<i>P. vivax</i>	9	3	36	48
<i>P. ovale</i>	3	1	04	08
<i>P. falciparum</i> and <i>vivax</i>	5	2	04	11
<i>P. knowlesi</i>	0	0	02	02
Total	27	15	70	112

Table 2: The frequency of plasmodial infection among citizens, travelers, and soldiers.

	Local citizens	Travelers	Military	Total
<i>P. falciparum</i>	23	18	02	43
<i>P. vivax</i>	37	06	09	52
<i>P. ovale</i>	03	06	01	10
<i>P. falciparum</i> and <i>vivax</i>	10	01	00	11
<i>P. knowlesi</i>	02	00	00	02
Total	75	31	12	118

Table 3: Distribution of the final treatment with the different types of plasmodia.

	Conservative	Splenectomy	Splenic artery embolization	Laparoscopic converted to open splenectomy	Total
<i>P. falciparum</i>	21	20	1	0	42
<i>P. vivax</i>	23	23	2	0	48
<i>P. ovale</i>	4	3	0	1	8
<i>P. falciparum</i> and <i>P. vivax</i>	8	3	0	0	11
<i>P. knowlesi</i>	1	1	0	0	2
Total	57	50	3	1	111

SPRMS is a rare but fatal complication of malaria. Figure 1 shows malaria is the most common infection leading to SPRMS (104; 31.3%). Ozsoy et al. found 18 reported cases since 1960 [7] and Aubrey-Bassler and Sowers published a systematic review covering 613 cases, in which 62 cases of SPRMS were present [6]. Renzulli et al., in their systematic review, found 23 cases infected with *P. vivax* and 20 infected with *P. falciparum* [8], and another review reported 22 cases of SPRMS, predominately related to *P. vivax* [9].

Additionally, a systematic review from 1960 to 2012 found 40 cases of splenic infarction,

of which 23 were due to *P. vivax* [10]. In contrast, we analyzed 122 cases (Tables 1–4). In our country, Sudan, the prevalence of *P. falciparum* and *P. vivax* was reported as 87.6% and 8.1% respectively [11]. Malaria leads to severe architectural disorganization of the spleen [12]. The reported median time from the onset of symptoms to the diagnosis of spleen rupture was 8.5 days (range 3–90 days) [10]. In comparison, we encountered 112 cases of SRPMS, with predominant *P. vivax* in 55 cases (Table 4), and the mean (\pm SD) duration from diagnosis to the time of splenic rupture in 45 cases was 7.16 (\pm 18.02) days.

Table 4: Comparison of our review with previously published review articles on SRPMS.

	Our review 2000–2023	Patrick Imbert et al. [2] 1958–2008
Literature titles:		
Case reports	(n = 63)	Case reports
Abstracts	(n = 19)	
Case report and literature review	(n = 05)	
Systematic review	(n = 03)	
Sex:		
Males	103	42
Females	19	13
Age mean (\pm SD)	33.3 (\pm 14.6)	Median 31.5
Local citizens of endemic areas	78	21
Travelers	32	24
Soldiers	12	0
Expatriates	0	6
Migrants	0	4
Causative plasmodia:		
<i>Falciparum</i>	44	23
<i>Vivax</i>	55	26
<i>Ovalle</i>	10	2
<i>Malariae</i>	0	2
<i>Vivax and falciparum</i>	11	2
<i>Knowlesi</i>	2	0
Management:		
Splenectomy	51	33
Conservative	57	14
Splenic artery embolization	3	0
Laparoscopic surgery	2	0
Laparoscopic converted to open splenectomy	1	0
Mortality	04*	12 (22%)
Post splenectomy vaccination	22 patients	09 patients
Reported the follow-up period	77 patients**	22 patients

*Three patients died before surgery, one was in coma due to cerebral malaria, another was hemodynamically unstable and was kept under mechanical ventilation and hemodialysis, and the third was gasping on arrival and had dyslipidemia and hypertension. The fourth patient died after a splenectomy.

**During the follow-up of 77 cases, 66 were reported alive and well. In three patients, the splenic infarct disappeared, in two the splenic hematoma resolved, and three post-splenectomy patients developed further attacks of malaria.

While reports showed that *P. vivax* is more common among citizens, *P. falciparum* is common among travelers [13]. These frequencies seem to be related to the number and geographical sites of publications because, in our study, the maximum

number of cases were reported from India (24 cases), Turkey (12 cases), and Korea (10 cases), where *P. vivax* is predominant.

The risk of overwhelming post-splenectomy infection was reported to be 0.23–0.42% per year,

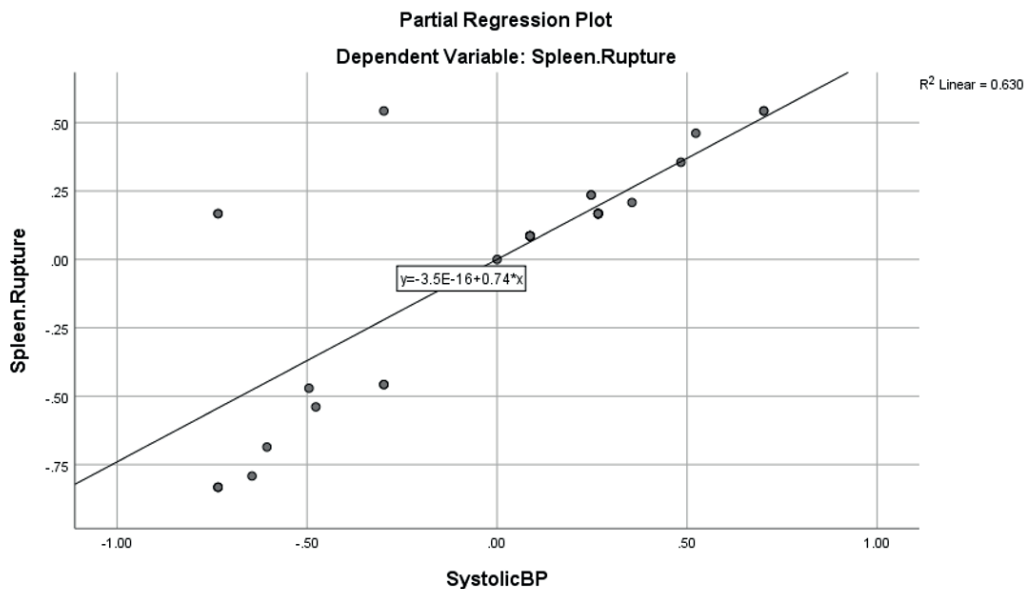


Figure 2: The scatter plot of blood pressure.

with a lifetime risk of 5% [14]. This dictates that conservative management of the spleen is the gold standard approach [15–18]. The percentage of patients who received vaccination against *Pneumococci* in our study and the paper by Imbert et al. [2] was 43.1% and 27.3% respectively (Table 4). When we relate this finding to the time frame of our study (2000–2023) and that of Imbert et al.'s (1958–2008) [2], there is a definite increase in the trend of vaccination that reduces and prevents the overwhelming post-splenectomy infection. Furthermore, if facilities are available, splenic artery embolization is a favorable change in management trends to preserve the immunological function of the spleen.

A splenic infarction may lead to a rupture of the spleen. Although the mechanism of splenic rupture is not fully elucidated, macrophage hyperplasia and increasing venous congestion [9, 10, 19] may lead to an elevation of the intrasplenic pressure that stretches the thin capsule of the spleen that may contain minor areas of infarctions or ischemia due to local thrombosis. These changes predispose the capsule to tear and the

spleen to rupture. Our finding explains that the spontaneous rupture of the malarial spleen is due to the discrepancy between the high intrasplenic pressure, resulting from systemic systolic BP, and the local inflammatory process in the congested spleen stretched thin infarcted splenic capsule. Although we could not exclude the presence of a confounding factor, to our knowledge, this is the first study that proves BP is possibly the main predictor of splenic rupture. This is important for the awareness of doctors in emergency settings.

5. Conclusion

The higher number of *P. vivax* cases is most likely related to the higher reporting rate from countries with prevalent *P. vivax*. In this review, the change in management trend is toward conservative treatment and immunization to reduce and prevent the overwhelming post-splenectomy infection. Our finding that BP as a possible predictor for SPRMS paves the way for the compelling, best-available evidence for early diagnosis and management to secure patient safety as a cornerstone of

clinical governance. It opens the door for further research to explain the changes in BP inside the congested and inflamed malarial spleen and the intraperitoneal pressure at the moment of splenic rupture.

6. Study Limitations

Medical journals in tropical countries could not be retrieved because of their unavailability on the World Wide Web.

Declarations

Acknowledgments

None.

Ethical Considerations

Ethical clearance was obtained from our medical school's Ethical Committee.

Competing Interests

None declared.

Availability of Data and Material

Data are available upon reasonable request to the corresponding author.

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None.

Abbreviations and Symbols

SPRMS: Spontaneous pathological rupture of the malarial spleen

WHO: World Health Organization

OPSI: Overwhelming post-splenectomy infection

SPSS: Statistical Package for Social Sciences

BP: Blood pressure

SRS: Spontaneous rupture of the spleen

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