World Journal of Pharmaceutical and Life Sciences

www.wjpls.org

Impact Factor: 8.21 Coden USA: WJPLA7

HEPATIC SARCOIDOSIS: CLINICAL FEATURES, PORTAL HYPERTENSION, AND TREATMENT OUTCOMES IN A MONOCENTRIC COHORT OF 16 PATIENTS

I. Qarch*, N. Lagdali, F. Z. Chabib, S. Sabbah, M. Borahma, F. Z. Ajana, M. Kadiri

Department of Gastroenterology C, Ibn Sina Hospital, Mohammed V University in Rabat.

***Corresponding Author: I. Qarch**

Department of Gastroenterology C, Ibn Sina Hospital, Mohammed V University in Rabat.

DOI: https://doi.org/10.5281/zenodo.21020575

How to cite this Article: I. Qarch*, N. Lagdali, F. Z. Chabib, S. Sabbah, M. Borahma, F. Z. Ajana, M. Kadiri. (2026). Hepatic Sarcoidosis: Clinical Features, Portal Hypertension, and Treatment Outcomes In A Monocentric Cohort of 16 Patients. World Journal of Pharmaceutical and Life Sciences, 12(7), 94–99.

Article Received on 25/05/2026 **Article Revised on 15/06/2026** **Article Published on 01/07/2026**

ABSTRACT

Background: Hepatic involvement in sarcoidosis is common but often asymptomatic. However, it can progress to severe complications such as cirrhosis and portal hypertension (PHT). This study aims to characterize the clinical, biological, histological features, and therapeutic outcomes in a monocentric cohort. **Methods:** We conducted a retrospective descriptive study of 16 patients followed for hepatic sarcoidosis in the gastroenterology department of a Moroccan hospital between 2017 and 2026. Diagnosis was based on liver biopsy (non-caseating granulomas), systemic evidence, and exclusion of other causes. Statistical analysis was performed using Jamovi. **Results:** All 16 patients were female, with a mean age of 49.1 ±13.5 years. Hepatic involvement was symptomatic in 68.7% (n=11), primarily presenting as pruritus (45.5%) and abdominal pain. Biological cholestasis was found in 81.2% (n=13), while angiotensin-converting enzyme (ACE) was elevated in 73%. Extra-hepatic involvement was present in 75% (n=12), dominated by pulmonary Stage II sarcoidosis. PHT was identified in 43.7% (n=7), with 3 patients experiencing hemorrhagic decompensation. Treatment included ursodeoxycholic acid (n=12) and/or systemic corticosteroids (n=8). A favorable biological response was significantly more frequent in treated patients (p=0.04). Despite PHT and advanced fibrosis, overall outcome remained stable over a median follow-up of 56 months. **Conclusion:** Hepatic sarcoidosis is a heterogeneous condition characterized by a cholestatic profile and portal granulomatous inflammation. The high prevalence of PHT (43.7%) suggests that disease severity may be underestimated. While treatment effectively improves biochemical abnormalities, the potential for severe complications necessitates rigorous long-term follow-up.

KEYWORDS: Hepatic sarcoidosis, portal hypertension, cholestasis, non-caseating granuloma, corticosteroids, ursodeoxycholic acid, liver biopsy, hepatic fibrosis.

1. INTRODUCTION

Sarcoidosis is a systemic granulomatous disease of unknown etiology, characterized by the presence of non-caseating granulomas in various organs.[1] This multisystemic condition preferentially affects the lungs and the intrathoracic lymphatic system, but can also affect other organs such as the liver, spleen, lymph nodes, salivary glands, heart, nervous system, muscles, and bones.[2]

Although hepatic involvement is frequent — with hepatic granulomas identified in 50 to 70% of patients at autopsy — the disease is often asymptomatic.[1,3] Clinical manifestations such as hepatomegaly, abdominal pain, or biological alterations of intrahepatic cholestasis type can occur, although granulomatous hepatitis is mostly asymptomatic.[4] In rare cases, hepatic sarcoidosis can progress to cirrhosis and severe complications, including portal hypertension, which may sometimes require liver transplantation.[5]

The diagnosis of hepatic sarcoidosis typically relies on liver biopsy, which reveals characteristic non-caseating granulomas, often in patients whose initial presentation is abdominal pain or pruritus.[6] Distinguishing isolated hepatic sarcoidosis from other forms of granulomatous liver disease can be challenging, as the disease can remain latent with only biochemical abnormalities or

progress to cirrhosis, which affects approximately 33% of hepatic sarcoidosis patients.[7,8,9]

The aim of this study is to further characterize the clinical, biological, histological, and evolutionary aspects of hepatic sarcoidosis, given its varied presentation and potential for severe outcomes.

2. PATIENTS AND METHODS

2.1 Study Design and Population

We conducted a retrospective descriptive monocentric study including patients followed for hepatic sarcoidosis in the gastroenterology department of a Moroccan hospital between 2017 and 2026. All patients with a confirmed diagnosis of hepatic sarcoidosis, based on a combination of clinical, biological, radiological, and histological arguments, were included.

2.2 Diagnostic Criteria

The diagnosis of hepatic sarcoidosis was established in the presence of

- Non-caseating epithelioid and giant cell granulomas on liver biopsy,
- Associated with evidence supporting systemic sarcoidosis,
- After exclusion of other causes of hepatic granulomatosis: infections, autoimmune diseases, and drug-related causes.

2.3 Data Collection

Data were collected from medical records and included:

- Demographic data: age at diagnosis, sex.
- Clinical data: symptomatic or asymptomatic nature, hepatic manifestations, clinical signs of portal hypertension.
- Biological data: liver function tests (AST, ALT, ALP, γ-GT, bilirubin), ACE levels, immunological workup.
- Cholestasis was defined by an elevation of ALP and/or γ-GT above the upper limit of normal.
- Radiological and endoscopic data: abdominal ultrasound and/or CT scan, signs of portal hypertension, upper gastrointestinal endoscopy.
- Portal hypertension was diagnosed in the presence of at least one clinical, radiological, or endoscopic criterion.
- Extra-hepatic involvement: pulmonary involvement classified according to the Scadding classification, other sites.
- Histological data: presence of non-caseating granulomas, location, degree of fibrosis (METAVIR score).

2.4 Therapeutic Management

Therapeutic modalities analyzed included ursodeoxycholic acid (UDCA), systemic corticosteroid therapy with description of the initial dosage and tapering regimen, and therapeutic abstention.

2.5 Response Evaluation

Biological response was assessed based on the evolution of cholestatic parameters and defined as:

- Complete response: normalization of ALP and γ-GT.
- Partial response: decrease ≥50% without normalization.
- No response: decrease <50% or worsening.

A biological relapse was defined by the re-elevation of cholestatic parameters after an initial response.

2.6 Statistical Analysis

Statistical analysis was performed using Jamovi software. Quantitative variables were expressed as mean ± standard deviation or median according to their distribution. Qualitative variables were expressed as numbers and percentages. Comparisons between groups were performed using Fisher's exact test for qualitative variables, and Student's t-test or Mann-Whitney test for quantitative variables, according to applicability conditions. A significance threshold of $p < 0.05$ was adopted.

2.7 Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. Data collection was performed anonymously and confidentially.

3. RESULTS

3.1 Demographic Characteristics and Clinical Profile

This study included 16 female patients. The mean age at diagnosis was 49.1 ± 13.5 years, ranging from 23 to 72 years.

Hepatic involvement was symptomatic in 11 patients. The hepatic clinical manifestations were distributed as follows: pruritus (n=5, 45.5%), right hypochondrium pain (n=3, 27.3%), left hypochondrium pain (n=1, 9.1%), and gastrointestinal bleeding (n=2, 18.2%). The remaining five patients were asymptomatic.

On physical examination, splenomegaly was present in 50% of patients and hepatomegaly in 31%. Signs of portal hypertension were observed in 31% of cases.

3.2 Biological and Immunological Abnormalities

Biological testing revealed cholestasis in 13 patients: elevation of gamma-glutamyltransferases (n=13) and elevation of alkaline phosphatases (n=12). Hepatic cytolysis was significant in only 3 patients.

ACE levels were elevated in 73% of evaluated patients. The immunological workup was negative in all patients, thus excluding associated autoimmune hepatitis or primary biliary cholangitis.

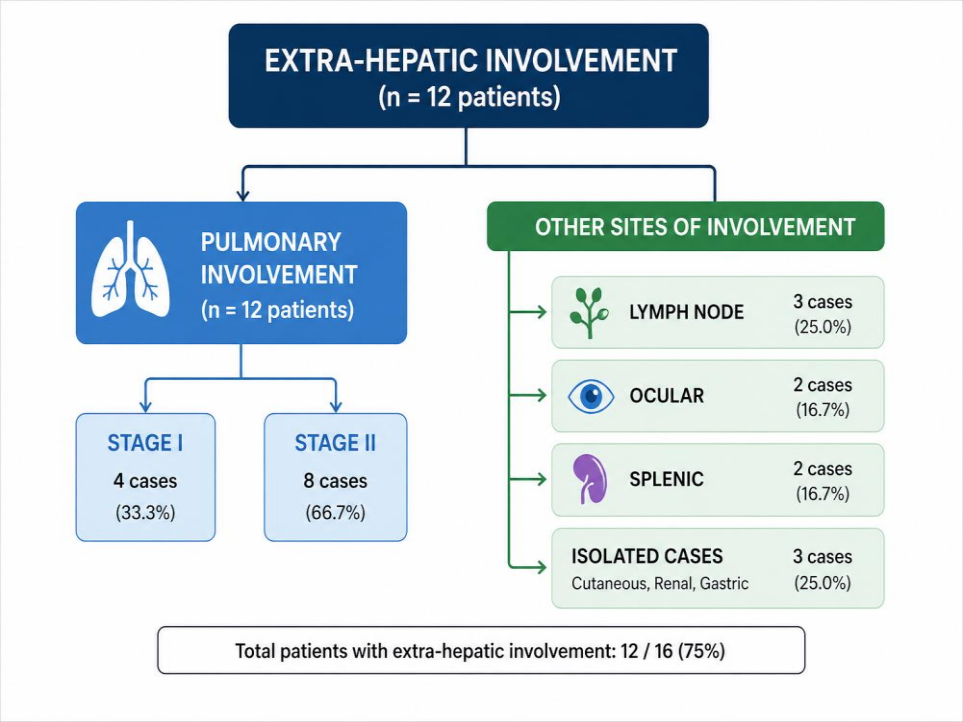
3.3 Signs of Portal Hypertension

Clinical signs of PHT were observed in 5 patients. Ultrasound signs of PHT were found in 7 patients. Endoscopic signs of PHT were noted in 5 patients. In

total, 7 patients had PHT defined by at least one clinical, radiological, or endoscopic criterion. PHT decompensation occurred in 3 patients: hemorrhagic in all 3 cases, and with ascites in 2 cases.

3.4 Extra-Hepatic Involvement

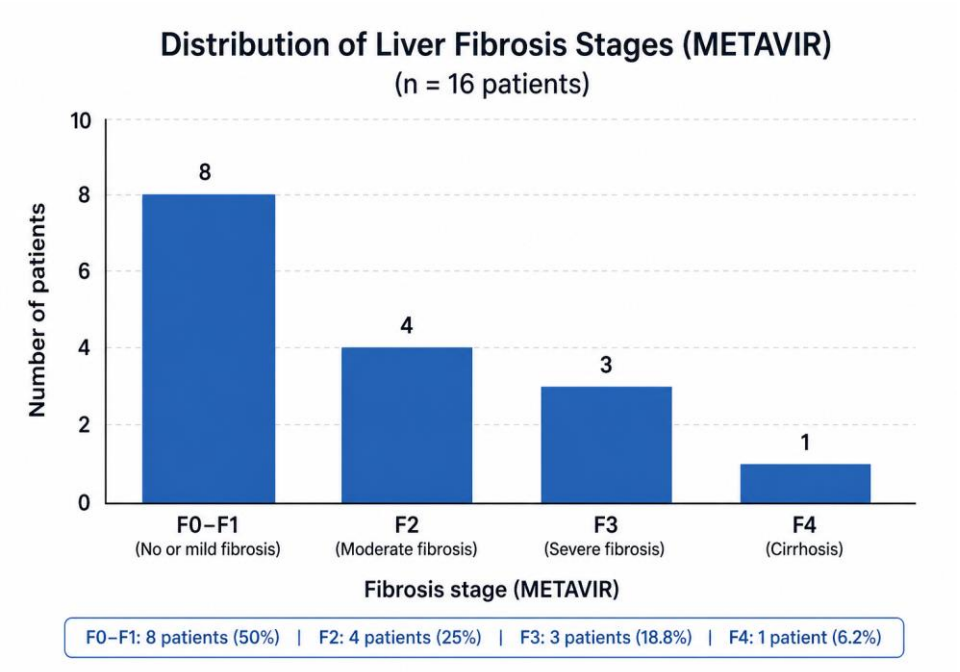
Extra-hepatic involvement was present in 12 patients, dominated by pulmonary involvement (n=12): stage I (n=4), stage II (n=8). Other sites included: lymph node (n=3), ocular (n=2), splenic (n=2), and isolated cases of cutaneous, renal, and gastric involvement.



3.5 Histopathological Study

Liver biopsy, performed in all patients, revealed non-caseating epithelioid and giant cell granulomas in 15 cases. The location of granulomas was: portal (n=14), lobular (n=1), and mixed (n=1).

Liver fibrosis was distributed as follows: F0–F1 (n=8), F2 (n=4), F3 (n=3), F4 (n=1).



3.6 Therapeutic Management and Outcome

UDCA was administered to 12 patients at doses of 10 to 14 mg/kg/day. A biological response to UDCA was observed at month 3 in 9 patients and at month 6 in 10 patients. Overall: complete response (n=10), partial response (n=1), no response (n=1).

Corticosteroid therapy was prescribed to 8 patients, according to extra-hepatic or biological indications, with adapted regimens and progressive tapering over 6 to 12 months. Therapeutic abstention was decided for 3 patients.

The overall outcome was favorable, with a biological response in 11 patients, defined by normalization or a >50% decrease in cholestatic parameters. The median follow-up duration was 56 months, marked by overall clinical stability despite advanced fibrosis stages in some patients.

Regarding survival, 15 out of 16 patients were alive at the end of follow-up. One death was recorded, related to neuroblastoma and considered unrelated to hepatic sarcoidosis.

3.7 Statistical Analysis

A bivariate analysis was performed to explore factors associated with severity and treatment response. Elevation of ACE was more frequent in patients with pulmonary involvement, without reaching statistical significance ($p > 0.05$). Similarly, the presence of biological cholestasis was more often observed in patients with portal hypertension, without statistically significant association.

The biological response to treatment was significantly more frequent in treated patients compared to untreated patients ($p = 0.04$). The presence of advanced fibrosis was associated with a higher frequency of portal hypertension, without statistically significant difference ($p > 0.05$).

Table 1: Univariate Analysis of Factors Associated with Biochemical Response.

Variable	Favorable response (n=11)	No response (n=5)	p-value
Treatment (UDCA ± corticosteroids)	10 (90.9%)	3 (60%)	**0.04***
Pulmonary involvement	9 (81.8%)	3 (60%)	>0.05
Baseline cholestasis	10 (90.9%)	3 (60%)	>0.05
Advanced fibrosis (≥F3)	2 (18.2%)	2 (40%)	>0.05
Portal hypertension	4 (36.4%)	3 (60%)	>0.05
Symptomatic presentation	8 (72.7%)	3 (60%)	>0.05

** Statistically significant (Fisher's exact test, $p < 0.05$)*

4. DISCUSSION

4.1 Principal Findings

In this monocentric cohort of 16 middle-aged women with hepatic sarcoidosis, liver involvement was frequently associated with systemic disease, particularly pulmonary manifestations. The hepatic presentation was primarily cholestatic, with non-caseating granulomas predominantly located in portal tracts on histology. Despite portal hypertension in nearly half of patients, the outcome remained generally favorable under treatment.

4.2 Clinical and Biological Profile

Hepatic involvement is among the most frequently observed extrapulmonary manifestations of sarcoidosis, with a reported prevalence of 10–20% in clinical series.[10] However, this prevalence is likely underestimated, as post-mortem studies suggest hepatic involvement in up to 45–70% of cases.[11] Although most cases occur in association with systemic disease, isolated hepatic sarcoidosis has been reported in approximately 13% of patients.[12]

Clinically, hepatic sarcoidosis is highly heterogeneous, ranging from asymptomatic biochemical abnormalities to severe complications such as cirrhosis and portal hypertension. Although most patients are asymptomatic, up to 60% may present with systemic symptoms such as fever, weight loss, or fatigue, and approximately 20–25% report hepatomegaly or abdominal pain.[13,14]

Biologically, the predominance of a cholestatic pattern, observed in up to 66–90% of cases, is well established in the literature.[10] In contrast, cytolysis is less frequent and usually mild, supporting the concept that hepatic sarcoidosis primarily affects the biliary microenvironment rather than hepatocellular integrity. Serum ACE levels were elevated in a majority of tested patients but showed no clear correlation with hepatic severity, in line with previous studies demonstrating that ACE lacks both sensitivity and specificity as a reliable diagnostic or prognostic marker.[12,15]

4.3 Histological Features and Disease Severity

Histological confirmation remains a cornerstone of diagnosis, as sarcoidosis is fundamentally a diagnosis of exclusion, requiring the identification of non-caseating granulomas in the appropriate clinical context and after exclusion of other granulomatous diseases.[14] In our cohort, granulomas were predominantly located within portal tracts, consistent with previous studies reporting portal or periportal distribution in approximately 60–70% of cases.[3] This distribution likely explains the predominance of cholestatic abnormalities and may contribute to the development of portal hypertension.

Beyond granulomas, hepatic sarcoidosis is characterized by a wide spectrum of histological alterations. Biliary lesions are reported in up to 60% of cases, including ductopenia, cholangiolar proliferation, and nonspecific biliary changes, which may mimic primary biliary cholangitis or primary sclerosing cholangitis. Vascular involvement, including sinusoidal dilatation and nodular regenerative hyperplasia, has been described in approximately 20% of patients[16], suggesting a multifactorial pathophysiology of portal hypertension.

Notably, portal hypertension was identified in 43% of our patients, a proportion higher than that reported in several historical series.[1,13] This finding suggests that hepatic sarcoidosis may be more severe than traditionally considered, particularly in referral centers. The mechanisms underlying portal hypertension are likely multifactorial, including granulomatous compression of portal venules and secondary biliary cirrhosis related to chronic intrahepatic cholestasis.[17]

4.4 Treatment and Response

The management of hepatic sarcoidosis remains poorly standardized, with no randomized controlled trials available to date. Current practices are largely based on observational studies and expert opinion.[6,9] Given the high rate of spontaneous remission reported in the literature (up to 60–70%), treatment is generally reserved for patients with symptomatic disease or significant biochemical abnormalities.

In our cohort, treatment with UDCA and/or corticosteroids was associated with a significant improvement in cholestatic parameters, consistent with previous reports.[13,14] UDCA has been shown to induce complete biochemical response in approximately 57% of patients, and in some studies may even outperform corticosteroids in terms of response.[18] Corticosteroids remain the first-line therapy, with clinical remission observed in approximately 60% of patients and partial response in 40%, although biochemical response rates are more variable.[19] Relapse is common, particularly after treatment tapering.

Second-line therapies, including azathioprine and methotrexate, have been used in refractory cases or for steroid-sparing purposes, with reported response rates of 40–60%.[18] Biologic agents such as infliximab have also shown promising results in small case series.

4.5 Prognosis

Despite the presence of portal hypertension and advanced fibrosis in some patients, the overall prognosis of hepatic sarcoidosis remains favorable. In our cohort, no patient progressed to liver failure or required liver transplantation, and survival was excellent, with only one death unrelated to hepatic disease.

These findings are consistent with previous studies indicating that clinically significant liver disease remains relatively uncommon despite frequent histological involvement.[3,10] However, severe forms exist: portal hypertension-related complications including ascites and variceal bleeding, and cirrhosis may develop after several years of disease evolution.[1] Hepatic involvement accounts for approximately 5% of sarcoidosis-related deaths.[20] Emerging data also suggest an increased risk of hepatocellular carcinoma, even in non-cirrhotic livers, highlighting the need for long-term surveillance in selected patients.[21]

4.6 Limitations

This study has several limitations, including its retrospective design, small sample size, and the absence of complete longitudinal quantitative biological data, limiting the ability to perform robust statistical analyses. In addition, the monocentric nature of the study may introduce selection bias toward more severe cases.

5. CONCLUSION

Hepatic sarcoidosis is a frequent yet often underrecognized manifestation of sarcoidosis. Although it is commonly associated with systemic disease, isolated hepatic involvement remains uncommon, accounting for approximately 10% of cases.

Clinical presentation is highly heterogeneous, ranging from isolated biochemical abnormalities to severe complications including portal hypertension and cirrhosis. Diagnosis relies on a combination of clinical, biological, and radiological findings, but ultimately requires histological confirmation demonstrating non-caseating granulomas. Importantly, hepatic sarcoidosis remains a diagnosis of exclusion, necessitating careful evaluation to rule out other causes of hepatic granulomatosis, such as primary biliary cholangitis, viral hepatitis, or drug-induced liver injury.

The natural course is generally favorable, with spontaneous resolution reported in a substantial proportion of patients. However, a subset may progress to chronic disease requiring treatment. First-line therapy typically includes corticosteroids and/or ursodeoxycholic acid, which lead to biochemical remission in most cases. In refractory or steroid-dependent disease, second-line agents such as azathioprine, methotrexate, or biologics may be considered. Liver transplantation remains a valid option in advanced cases, although data on long-term outcomes are limited.

Despite the overall favorable prognosis, the relatively high prevalence of portal hypertension observed in our cohort suggests that disease severity may be underestimated. These findings highlight the importance of early recognition, individualized management, and long-term follow-up in patients with hepatic sarcoidosis.

REFERENCES

1. Fauter M et al. Hepatic sarcoidosis with symptomatic portal hypertension: A report of 12

cases with review of the literature. Front Med., 2022; 9. doi:10.3389/fmed.2022.995042.
2. Faini C et al. Sarcoidosis presenting with splenomegaly and abdominal pain: a case report. Clin Manag Issues, 2012; 6(3): 91. doi:10.7175/cmi.v6i3.443.
3. Sedki M et al. Hepatic Sarcoidosis: Natural History and Management Implications. Front Med., 2019; 6. doi:10.3389/fmed.2019.00232.
4. Redon F. Sarcoidosis and anti-TNF: a paradoxical class effect? HAL, Feb. 2011.
5. Majumder TK et al. Hepatic Sarcoidosis — An Unusual Cause of Jaundice: A Case Report. SN Compr Clin Med., 2024; 6(1). doi:10.1007/s42399-024-01681-7.
6. Sollors J et al. Management of Hepatic Sarcoidosis. J Gastrointest Liver Dis., 2022; 31(3): 323. doi:10.15403/jgld-4122.
7. Mu X et al. Isolated hepatic sarcoidosis: A case series. Can Liver J., 2024; 7(2): 316. doi:10.3138/canlivj-2023-0030.
8. Deliwala S et al. Sarcoidosis Masquerading as Long-Standing Cholestasis. Gastroenterol Res., 2021; 14(2): 112. doi:10.14740/gr1360.
9. Valeyre D et al. How to Tackle the Diagnosis and Treatment in the Diverse Scenarios of Extrapulmonary Sarcoidosis. Adv Ther., 2021; 38(9): 4605. doi:10.1007/s12325-021-01832-5.
10. Graf C et al. Hepatic sarcoidosis: Clinical characteristics and outcome. JHEP Rep., 2021; 3(6): 100360. doi:10.1016/j.jhepr.2021.100360.
11. Moser A, Cheung A. Hepatic Sarcoidosis: A Review of the Diagnosis and Management. Curr Hepatol Rep., 2024; 23(1): 137. doi:10.1007/s11901-024-00634-x.
12. Chebbi D et al. Pure extra-thoracic sarcoidosis: about 24 cases. Rom J Intern Med., 2021; 59(3): 312. doi:10.2478/rjim-2021-0012.
13. Ungprasert P et al. Clinical Characteristics and Outcome of Hepatic Sarcoidosis: A Population-Based Study, 1976–2013. Am J Gastroenterol. 2017; 112(10): 1556. doi:10.1038/ajg.2017.231.
14. Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med., 2007; 357(21): 2153. doi:10.1056/nejmra071714.
15. Uehara K et al. Liver biopsy as a useful diagnostic tool for hepatic sarcoidosis: A case report. Med Int., 2024; 4(4). doi:10.3892/mi.2024.162.
16. Devaney KO et al. Hepatic Sarcoidosis. Am J Surg Pathol, 1993; 17(12): 1272. doi:10.1097/00000478-199312000-00009.
17. Hillaire S et al. Idiopathic non-cirrhotic intrahepatic portal hypertension in the West: a re-evaluation in 28 patients. Gut., 2002; 51(2): 275. doi:10.1136/gut.51.2.275.
18. Sinnanaidu RP et al. The clinical management of hepatic sarcoidosis: A systematic review. JGH Open, 2024; 8(6). doi:10.1002/jgh3.13076.
19. Judson MA. Corticosteroids in Sarcoidosis. Rheum Dis Clin North Am., 2015; 42(1): 119. doi:10.1016/j.rdc.2015.08.012.
20. Ibrahim A et al. Hepatic Involvement in Systemic Sarcoidosis. Am J Case Rep., 2018; 19: 1212. doi:10.12659/ajcr.910600.
21. Bonifazi M et al. Sarcoidosis and Cancer Risk. CHEST J., 2014; 147(3): 778. doi:10.1378/chest.14-1475.