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# Clinical Profile and Treatment Outcomes of Patients with Autoimmune Hepatitis in a Tertiary Care Hospital: A Retrospective Observational Study.

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## Abstract

***Background:*** ***Aim:*** Autoimmune hepatitis (AIH) is an immune-mediated chronic liver disease with significant geographic variability in clinical presentation. Data from South India remain sparse. This study aimed to evaluate the clinical profile, disease severity at presentation, and predictors of biochemical response to immunosuppressive therapy in South Indian patients with AIH. ***Methods:*** This was a retrospective observational study of 100 patients (≥18 years) diagnosed with AIH at a tertiary care centre in Mysuru, Karnataka, between January 2022 and December 2025. Diagnosis was based on IAIHG criteria and/or compatible histopathological findings. All patients received standard immunosuppressive therapy (prednisolone and azathioprine). Biochemical response was assessed at three months, defined as normalization of ALT and AST to <40 U/L. Bivariate and multivariate logistic regression analyses were performed to identify independent predictors of treatment response. ***Results:*** The cohort comprised 72% females, with a mean age of 38.6 ± 14.2 years. Cirrhosis was present in 61% of patients at diagnosis, with 42.6% having decompensated disease. Seronegative AIH accounted for 32% of cases and was significantly associated with severe portal tract inflammation (OR 5.42; P = 0.012), oesophageal varices (OR 3.56; P = 0.018), and advanced fibrosis (OR 3.14; P = 0.024). Good biochemical response was achieved in 63% of patients at three months. On multivariate analysis, independent predictors of good response were: pre-treatment serum IgG >16 g/L (OR 3.42; 95% CI 1.38–8.47; P = 0.008), presence of pseudorosettes on liver biopsy (OR 2.91; 95% CI 1.12–7.56; P = 0.028), and three-month post-treatment total bilirubin <2 mg/dL (OR 5.74; 95% CI 2.18–15.12; P <0.001). ***Conclusions:*** AIH in South India predominantly affects young to middle-aged women and carries a high burden of cirrhosis at diagnosis, reflecting delayed recognition. Seronegative AIH is frequent and associated with more severe disease, underscoring the indispensable role of liver biopsy. Standard immunosuppressive therapy achieves good biochemical response in approximately two-thirds of patients. Pre-treatment serum IgG, presence of pseudorosettes, and early post-treatment bilirubin normalization are reliable independent predictors of favourable treatment response.

**Keywords:** Autoimmune hepatitis; South India; cirrhosis; seronegative; immunoglobulin G; pseudorosettes; treatment response; biochemical remission.

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## INTRODUCTION

Autoimmune hepatitis (AIH) is a chronic, progressive, immune-mediated inflammatory liver disease characterized by hyper gammaglobulinemia, circulating autoantibodies, elevated hepatic transaminases, and interface hepatitis on histo pathological examination [1]. The disease affects individuals of all ages, ethnicities, and both sexes, although a distinct female preponderance has been consistently demonstrated across populations worldwide [2]. Left untreated, AIH carries a significant risk of progressive hepatic fibrosis, cirrhosis, liver failure, and death, with reported five-year mortality rates exceeding 50% in the absence of immunosuppressive therapy [3]. The pathogenesis of AIH involves a complex interplay of genetic susceptibility, environmental triggers, and dysregulated immune responses directed against hepatocyte antigens. Molecular mimicry between infectious agents and self-antigens, defective regulatory T-cell function, and human leukocyte antigen (HLA)-associated predisposition are considered central mechanisms in disease initiation and perpetuation [4].

Histologically, AIH is characterized by portal and periportal lymphoplasmacytic infiltration, interface hepatitis, hepatocyte rosette formation, and emperipolesis, features that are pivotal for accurate diagnosis especially in seronegative cases [5]. The clinical spectrum of AIH is remarkably heterogeneous, ranging from asymptomatic transaminase elevation detected incidentally during routine screening to fulminant hepatic failure requiring emergent liver transplantation [1]. This wide variability in presentation poses considerable diagnostic challenges, particularly in settings where clinical awareness of the disease remains suboptimal. Classification into Type I and Type II AIH is based on autoantibody profiles, with anti-nuclear antibody (ANA) and anti-smooth muscle antibody (ASMA) positivity defining Type I, and anti-liver kidney microsomal type 1 (anti-LKM-1) antibody characterizing Type II disease [2]. However, a significant proportion of patients may present with negative autoimmune serology despite having compatible histopathological features, a condition termed seronegative AIH, which further complicates timely diagnosis and initiation of treatment [6].

Standard treatment of AIH consists of corticosteroids, either alone or in combination with azathioprine, which achieves biochemical remission in approximately 80–90% of patients within two years of therapy initiation [3]. The American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) guidelines recommend prompt treatment of all patients with active AIH to prevent disease progression [7]. However, treatment response is variable, with approximately 10–15% of patients demonstrating incomplete response and up to 9% experiencing treatment failure with standard regimens [8]. Alternative immunosuppressive agents including mycophenolate mofetil and tacrolimus are employed in cases of azathioprine intolerance or inadequate response, though evidence supporting their use remains comparatively limited [3]. Epidemiological data on AIH demonstrate significant geographic and ethnic variability. Studies from Western populations report an incidence of approximately 1.0–1.9 per 100,000 persons per year and prevalence ranging from 10 to 25 per 100,000 [2]. However, data from the Asian subcontinent remain sparse and fragmented. Reports from India have demonstrated that AIH is frequently underdiagnosed and that patients often present with advanced disease, including cirrhosis, at the time of initial diagnosis [9]. The proportion of cirrhotic presentation at diagnosis has been reported to be substantially higher in South Asian populations compared to Western cohorts, suggesting potential differences in disease behaviour attributable to genetic predisposition, environmental factors, and healthcare access disparities [6].

Studies from the Indian subcontinent have further highlighted the unique characteristics of AIH in this population, including a higher proportion of seronegative cases, younger age at presentation, and more aggressive disease progression [9,10]. However, the majority of Indian studies have originated from North and Western India, and robust data from the South Indian population remain conspicuously absent. Given the documented ethnic and geographic heterogeneity in AIH phenotype and the limited applicability of Western data to Indian patients, there is a compelling need for region-specific studies that characterize the clinical profile and treatment outcomes of AIH in the South Indian context. Identifying predictors of treatment response is of paramount clinical importance, as early recognition of patients likely to have an unfavourable outcome enables timely modification of therapeutic strategies and closer monitoring. Several clinical, biochemical, and histological parameters including age, baseline liver fibrosis stage, serum immunoglobulin G (IgG) levels, and post-treatment bilirubin values have been variably associated with treatment response in different populations [6,8]. However, there remains no consensus on universally applicable prognostic markers, and the relevance of these predictors in the Indian setting has not been adequately studied.

The present study was therefore undertaken to systematically evaluate the clinical profile, disease severity at presentation, and treatment outcomes of patients with AIH at a tertiary care hospital in South India, and to identify clinical, biochemical, immunological, and histopathological factors that predict biochemical response to standard immunosuppressive therapy.

**AIMS AND OBJECTIVES**

The present study was undertaken with the primary aim of evaluating the clinical profile of patients diagnosed with autoimmune hepatitis (AIH) at a tertiary care hospital in South India, encompassing demographic characteristics, clinical presentation, biochemical parameters, immunological markers, radiological findings, and histopathological features. The study additionally aimed to provide comprehensive descriptive data on the spectrum of disease presentation in this population, with particular attention to the prevalence of cirrhosis and decompensated liver disease at the time of initial diagnosis.

The secondary objectives of the study were directed toward assessing the treatment outcomes of patients with AIH following standard immunosuppressive therapy, as defined by biochemical response at three months of follow-up. The study sought to determine the proportion of patients achieving good versus poor biochemical response to treatment. Furthermore, it aimed to identify clinical, biochemical, immunological, and histopathological factors that predicted response to treatment, including baseline serum IgG levels, total bilirubin levels, autoimmune serology status, and presence of cirrhosis. An additional objective was to evaluate the frequency and characteristics of seronegative autoimmune hepatitis and to determine its association with disease severity and treatment response in the South Indian population.

## MATERIALS AND METHODS

### Study Design and Setting

This was a retrospective observational study conducted at the Department of Medical Gastroenterology, JSS Medical College and Hospital, JSS Academy of Higher Education and Research, Mysuru, Karnataka, India. The hospital is a tertiary care academic medical centre providing specialized hepatology and gastroenterology services to patients from Karnataka and neighbouring states in South India.

### Study Duration and Period

The study was conducted over a period of three years, with patient data retrieved from medical records spanning from January 2022 to December 2025. The study protocol was approved by the Institutional Ethical Committee (IEC) of JSS Medical College, Mysuru, prior to commencement of data collection.

### Study Population

The study population comprised all patients aged 18 years and above who were diagnosed with autoimmune hepatitis and attended the Medical Gastroenterology outpatient or inpatient services at JSS Medical College Hospital during the defined study period. A purposive sampling technique was employed to identify eligible patients from hospital records.

### Sample Size

The sample size was calculated using the formula for comparison of two means: $N = (Z\alpha + Z\beta)^2 \times \sigma^2 / d^2$, where $Z\alpha = 1.96$ (for 95% confidence level), $Z\beta = 0.84$ (for 80% power), $\sigma = 4.7$ (standard deviation derived from a previous study by Tasneem and Luck, 2020), and $d = 2.5$ (expected clinically meaningful difference). The calculation yielded approximately 48–50 patients per group, and with two groups (good responders and poor responders), the total required sample size was determined to be 100 patients.

### Inclusion Criteria

Patients aged 18 years and above who were diagnosed with AIH based on the International Autoimmune Hepatitis Group (IAIHG) criteria and/or compatible clinical, biochemical, immunological, and histological findings were included. Only patients with availability of baseline clinical data, laboratory investigations, and follow-up records for at least three months after initiation of treatment were considered eligible for inclusion.

### Exclusion Criteria

Patients with coexisting causes of chronic liver disease including viral hepatitis (hepatitis B and C), alcohol-related liver disease, non-alcoholic fatty liver disease, drug-induced liver injury, Wilson's disease, and hemochromatosis were excluded from the study. Patients with overlap syndromes (AIH–PBC or AIH–PSC) analysed separately, those with incomplete medical records, patients who had undergone liver transplantation prior to assessment of treatment response, and paediatric patients below 18 years of age were also excluded.

### Data Collection

Medical records of eligible patients were systematically reviewed and relevant data were extracted using a pre-designed proforma. The following parameters were recorded: demographic details including age and sex; clinical features including mode of presentation (acute, chronic, or incidental), presence of cirrhosis and its complications (ascites, hepatic encephalopathy, variceal bleeding); baseline laboratory investigations including complete blood picture (haemoglobin, total leukocyte count, platelet count), liver function tests (total and direct bilirubin, AST, ALT, alkaline phosphatase, serum albumin), renal function tests, and prothrombin time/INR; immunological markers including serum IgG levels, ANA, ASMA, anti-LKM, and anti-SLA antibodies; abdominal ultrasound findings including features of chronic liver disease and splenomegaly; upper gastrointestinal endoscopy findings including presence and grade of oesophageal varices and portal hypertensive gastropathy; and liver biopsy findings including grade and stage of disease according to the Ishak Modified HAI scoring system and presence or absence of pseudo rosettes.

### Treatment Protocol

All patients were treated with standard immunosuppressive therapy as per AASLD guidelines. Initial treatment consisted of weight-based corticosteroids (prednisolone) in combination with azathioprine. Patients who demonstrated inadequate response or intolerance to azathioprine were switched to alternative immunosuppressive agents including mycophenolate mofetil or tacrolimus. Treatment modifications and dose adjustments were performed at the discretion of the treating gastroenterologist based on individual patient response and tolerability.

**Outcome Assessment**

Biochemical response to treatment was assessed at three months after initiation of immunosuppressive therapy. Response was categorized as good if hepatic transaminases (ALT and AST) normalized to below 40 U/L, or as poor if transaminases remained persistently elevated or showed only partial improvement at the three-month follow-up assessment.

**Statistical Analysis**

All data were entered into a Microsoft Excel spreadsheet and analyzed using SPSS version 28 (IBM Corp., Armonk, NY, USA) under institutional license. Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. The chi-square test and Fisher's exact test were used to identify associations between categorical variables. Independent samples t-test was used for comparison of means between two groups. Multivariate logistic regression analysis was performed to identify independent predictors of treatment response. A P value of less than 0.05 was considered statistically significant. Odds ratios with 95% confidence intervals were calculated for predictors of treatment response.

## RESULTS

**Demographic and Clinical Characteristics**

A total of 100 patients diagnosed with autoimmune hepatitis were included in the study. The demographic and clinical characteristics of the study population are summarized in Table 1. Among the 100 patients, 72 (72%) were female and 28 (28%) were male, yielding a female-to-male ratio of approximately 2.6:1. The mean age of the study population was 38.6 ± 14.2 years, with ages ranging from 18 to 74 years. Forty-two patients (42%) were below 35 years of age, while 26 (26%) were above 50 years. Regarding the mode of presentation, 54 (54%) patients presented with chronic symptoms, 31 (31%) had acute presentation, and 15 (15%) were diagnosed incidentally during evaluation for other conditions.

Cirrhosis was present in 61 (61%) patients at the time of diagnosis. Among the cirrhotic patients, 35 (57.4%) had compensated cirrhosis and 26 (42.6%) had decompensated cirrhosis. Esophageal varices were documented in 48 (48%) patients on upper gastrointestinal endoscopy. Ascites was present in 34 (34%) patients, while hepatic encephalopathy was noted in 11 (11%) patients. Both esophageal varices and ascites coexisted in 28 (28%) patients. Child-Turcotte-Pugh (CTP) classification among cirrhotic patients revealed CTP class A in 24 (39.3%), class B in 22 (36.1%), and class C in 15 (24.6%) patients.

**Table 1: Demographic and Clinical Characteristics of Patients with AIH (n = 100)**

| Characteristic | Category | Number (n) | Percentage (%) |
|---|---|---|---|
| Gender | Female | 72 | 72.0 |
| | Male | 28 | 28.0 |
| Age group (years) | <35 | 42 | 42.0 |
| | 35–50 | 32 | 32.0 |
| | >50 | 26 | 26.0 |
| Mode of presentation | Chronic | 54 | 54.0 |
| | Acute | 31 | 31.0 |
| | Incidental | 15 | 15.0 |
| Cirrhosis at diagnosis | Yes | 61 | 61.0 |
| | No | 39 | 39.0 |
| Cirrhosis status (n=61) | Compensated | 35 | 57.4 |
| | Decompensated | 26 | 42.6 |
| Esophageal varices | Present | 48 | 48.0 |
| | Absent | 52 | 52.0 |
| Ascites | Present | 34 | 34.0 |
| | Absent | 66 | 66.0 |
| Hepatic encephalopathy | Present | 11 | 11.0 |
| | Absent | 89 | 89.0 |
| CTP class (n=61) | A | 24 | 39.3 |
| | B | 22 | 36.1 |
| | C | 15 | 24.6 |
| Response to treatment | Good | 63 | 63.0 |
| | Poor | 37 | 37.0 |

**Baseline Biochemical Parameters**

The baseline biochemical parameters of the study population are presented in Table 2. The mean pre-treatment total bilirubin was 3.14 ± 2.86 mg/dL, while the mean direct bilirubin was 1.72 ± 1.94 mg/dL. The mean serum ALT was 148.3 ± 112.6 U/L and the mean serum AST was 162.7 ± 98.4 U/L. The mean alkaline phosphatase was 142.6 ± 68.3 U/L. Serum

albumin levels were low with a mean of 3.1 ± 0.74 g/dL. The mean platelet count was 148,200 ± 72,400 per mm³ and the mean hemoglobin was 10.8 ± 2.1 g/dL. The mean INR was 1.34 ± 0.42. After three months of immunosuppressive therapy, substantial improvement in biochemical parameters was observed, with mean post-treatment total bilirubin, ALT, and AST values decreasing to 1.82 ± 1.46 mg/dL, 58.4 ± 42.8 U/L, and 64.2 ± 38.6 U/L, respectively.

**Table 2: Baseline and Post-Treatment Biochemical Parameters (n = 100)**

| Parameter | Pre-Treatment (Mean ± SD) | Post-Treatment (Mean ± SD) | P value |
|---|---|---|---|
| Total bilirubin (mg/dL) | 3.14 ± 2.86 | 1.82 ± 1.46 | <0.001 |
| Direct bilirubin (mg/dL) | 1.72 ± 1.94 | 0.86 ± 0.92 | <0.001 |
| ALT (U/L) | 148.3 ± 112.6 | 58.4 ± 42.8 | <0.001 |
| AST (U/L) | 162.7 ± 98.4 | 64.2 ± 38.6 | <0.001 |
| Alkaline phosphatase (U/L) | 142.6 ± 68.3 | 118.4 ± 52.1 | 0.004 |
| Serum albumin (g/dL) | 3.1 ± 0.74 | 3.4 ± 0.62 | 0.001 |
| Platelet count (×10³/mm³) | 148.2 ± 72.4 | 156.8 ± 68.2 | 0.389 |
| Hemoglobin (g/dL) | 10.8 ± 2.1 | 11.4 ± 1.8 | 0.032 |
| INR | 1.34 ± 0.42 | 1.22 ± 0.34 | 0.026 |

**Immunological Profile**

The immunological characteristics of the study population are detailed in Table 3. Positive autoimmune serology was present in 68 (68%) patients, while 32 (32%) patients had negative autoimmune serology and were diagnosed on the basis of compatible liver histopathology and subsequent response to immunosuppressive therapy. Among the 68 seropositive patients, 62 (91.2%) had Type I AIH (positive ANA or ASMA), while 6 (8.8%) had Type II AIH (positive anti-LKM antibody). None of the patients tested positive for anti-soluble liver antigen (anti-SLA) antibody. Among seropositive patients, the serum ANA titer was low (≤1:80 dilution) in 38 (55.9%) and high (>1:80 dilution) in 30 (44.1%) patients. Serum IgG levels were elevated above 16 g/L in 74 (74%) patients and above 25 g/L in 41 (41%) patients. The mean serum IgG level was 24.8 ± 8.6 g/L.

**Table 3: Immunological Profile of Patients with AIH (n = 100)**

| Parameter | Category | Number (n) | Percentage (%) |
|---|---|---|---|
| Autoimmune serology | Positive | 68 | 68.0 |
| | Negative | 32 | 32.0 |
| AIH type (n=68) | Type I (ANA/ASMA+) | 62 | 91.2 |
| | Type II (anti-LKM+) | 6 | 8.8 |
| ANA titer (n=68) | ≤1:80 | 38 | 55.9 |
| | >1:80 | 30 | 44.1 |
| Serum IgG (g/L) | >16 | 74 | 74.0 |
| | ≤16 | 26 | 26.0 |
| Anti-SLA | Positive | 0 | 0.0 |
| | Negative | 100 | 100.0 |

**Histopathological Findings**

Liver biopsy was performed in 82 (82%) patients. Portal tract inflammation was mild to moderate in 46 (56.1%) and severe in 36 (43.9%) patients. The histology activity index (HAI) score for necroinflammation (grade) was >6/18 in 34 (41.5%) patients. A fibrosis stage of >4/6 on the Ishak scale was observed in 58 (70.7%) patients, with stage 4/6 in 8 (9.8%), stage 5/6 in 18 (22.0%), and stage 6/6 (established cirrhosis) in 32 (39.0%) patients. Pseudo rosettes were identified in 28 (34.1%) patients. Interface hepatitis was present in 74 (90.2%) and lymphoplasmacytic infiltration in 78 (95.1%) of the biopsied cases.

**Treatment and Response**

All 100 patients were initiated on standard immunosuppressive therapy with weight-based prednisolone and azathioprine. Due to inadequate response or intolerability to azathioprine, 22 (22%) patients were subsequently switched to mycophenolate mofetil (n = 14) or tacrolimus (n = 8). At the three-month follow-up assessment, good biochemical response (normalization of transaminases to <40 U/L) was achieved in 63 (63%) patients, while poor response (persistent or partial elevation of transaminases) was observed in 37 (37%) patients.

**Factors Associated with Seronegative AIH**

Bivariate analysis of clinical factors associated with seronegative AIH revealed significant associations with severe portal tract inflammation (P = 0.012), presence of oesophageal varices (P = 0.018), and higher fibrosis stage on liver biopsy (P = 0.024). No statistically significant association was found with age, gender, BMI, serum IgG levels, or CTP class.

**Predictors of Treatment Response**

The bivariate and multivariate analyses of factors predicting treatment response are presented in Table 4. On bivariate analysis, good response to treatment was significantly associated with pre-treatment serum IgG level >16 g/L (P = 0.006), presence of pseudo-rosettes on histopathology (P = 0.018), absence of ascites at presentation (P = 0.032), and three-month post-treatment serum total bilirubin <2 mg/dL (P <0.001). Age, gender, BMI, autoimmune serology status, portal inflammation severity, overlap syndrome, presence of cirrhosis, CTP score, and presence of esophageal varices did not demonstrate statistically significant associations with treatment response. Multivariate logistic regression analysis confirmed that pre-treatment serum IgG >16 g/L (OR 3.42; 95% CI 1.38–8.47; P = 0.008), presence of pseudo-rosettes on liver biopsy (OR 2.91; 95% CI 1.12–7.56; P = 0.028), and three-month post-treatment serum total bilirubin <2 mg/dL (OR 5.74; 95% CI 2.18–15.12; P <0.001) were independent predictors of good response to treatment.

**Table 4: Predictors of Treatment Response in Patients with AIH (n = 100)**

| Variable | Category | Good (n=63) | Poor (n=37) | OR (95% CI) | P value | Multivariate P |
|---|---|---|---|---|---|---|
| Age (years) | <40 | 37 | 20 | 1.12 (0.49–2.56) | 0.784 | — |
| | ≥40 | 26 | 17 | | | |
| Gender | Female | 46 | 26 | 1.08 (0.44–2.64) | 0.868 | — |
| | Male | 17 | 11 | | | |
| BMI (kg/m²) | <25 | 52 | 30 | 1.04 (0.36–2.98) | 0.942 | — |
| | ≥25 | 11 | 7 | | | |
| Autoimmune serology | Positive | 44 | 24 | 1.22 (0.52–2.87) | 0.648 | — |
| | Negative | 19 | 13 | | | |
| Serum IgG (g/L) | >16 | 52 | 22 | 3.38 (1.42–8.04) | 0.006 | 0.008 |
| | ≤16 | 11 | 15 | | | |
| Portal inflammation | Severe | 24 | 12 | 1.25 (0.53–2.95) | 0.612 | — |
| | Mild-Mod | 39 | 25 | | | |
| Pseudorosettes | Present | 22 | 6 | 2.96 (1.09–8.06) | 0.018 | 0.028 |
| | Absent | 41 | 31 | | | |
| Cirrhosis | Yes | 37 | 24 | 0.77 (0.33–1.79) | 0.542 | — |
| | No | 26 | 13 | | | |
| CTP class (n=61) | A | 16 | 8 | 1.24 (0.44–3.48) | 0.682 | — |
| | B or C | 21 | 16 | | | |
| Esophageal varices | Yes | 28 | 20 | 0.72 (0.32–1.64) | 0.434 | — |
| | No | 35 | 17 | | | |
| Ascites | Yes | 17 | 17 | 0.43 (0.19–1.01) | 0.032 | 0.076 |
| | No | 46 | 20 | | | |
| Pre-Tx bilirubin | <2 mg/dL | 36 | 16 | 1.75 (0.77–3.97) | 0.182 | — |
| (mg/dL) | ≥2 mg/dL | 27 | 21 | | | |
| Post-Tx bilirubin | <2 mg/dL | 58 | 22 | 7.92 (2.70–23.26) | <0.001 | <0.001 |
| (mg/dL) | ≥2 mg/dL | 5 | 15 | | | |

**Clinical Factors Associated with Seronegative AIH**

The clinical factors associated with seronegative AIH are presented in Table 5. Among the 32 seronegative patients, severe portal tract inflammation was present in 20 (62.5%) compared to 16 (23.5%) of seropositive patients (OR 5.42; 95% CI 2.12–13.84; P = 0.012). Esophageal varices were present in 22 (68.8%) seronegative patients versus 26 (38.2%) seropositive patients (OR 3.56; 95% CI 1.44–8.80; P = 0.018). Advanced fibrosis (Ishak stage >4/6) was more frequent in seronegative AIH (OR 3.14; 95% CI 1.16–8.52; P = 0.024).

**Table 5: Clinical Factors Associated with Seronegative AIH (n = 100)**

| Variable | Category | Seroneg (n=32) | Seropos (n=68) | OR (95% CI) | P value |
|---|---|---|---|---|---|
| Age (years) | <40 | 22 | 42 | 1.36 (0.54–3.42) | 0.516 |
| | ≥40 | 10 | 26 | | |
| Gender | Female | 22 | 50 | 0.79 (0.31–2.04) | 0.634 |
| | Male | 10 | 18 | | |
| Serum IgG (g/L) | >16 | 25 | 49 | 1.48 (0.56–3.92) | 0.426 |
| | ≤16 | 7 | 19 | | |
| Portal inflammation | Severe | 20 | 16 | 5.42 (2.12–13.84) | 0.012 |
| | Mild-Mod | 12 | 52 | | |
| Esophageal varices | Present | 22 | 26 | 3.56 (1.44–8.80) | 0.018 |
| | Absent | 10 | 42 | | |
| Ascites | Present | 14 | 20 | 1.87 (0.78–4.46) | 0.162 |
| | Absent | 18 | 48 | | |
| Fibrosis >4/6 | Yes | 26 | 32 | 3.14 (1.16–8.52) | 0.024 |
| (n=82 biopsied) | No | 4 | 20 | | |
| CTP class | B or C | 16 | 21 | 2.28 (0.88–5.92) | 0.084 |
| (cirrhotic, n=61) | A | 6 | 18 | | |

**Treatment Modalities**

Table 6 presents the treatment details. All 100 patients were commenced on prednisolone and azathioprine as first-line therapy. The mean initial prednisolone dose was 38.2 ± 8.4 mg/day and the mean azathioprine dose was 62.4 ± 14.6 mg/day. Ten patients (10%) required a switch to second-line agents due to inadequate response (n = 8) or drug intolerance (n = 2). Of these, All ten patients were switched to mycophenolate mofetil. Among the 10 patients who required treatment modification, 8(80%) eventually achieved good biochemical response by the three-month assessment, while 2 (20%) continued to demonstrate poor response.

**Table 6: Treatment Details and Outcomes (n = 100)**

| Treatment Parameter | Category / Value | Number (n) / Mean ± SD | Percentage (%) |
|---|---|---|---|
| Initial therapy | Prednisolone + Azathioprine | 100 | 100.0 |
| Mean prednisolone dose | mg/day | 38.2 ± 8.4 | — |
| Mean azathioprine dose | mg/day | 62.4 ± 14.6 | — |
| Switch to second-line | Yes | 10 | 10.0 |
| | No | 90 | 90.0 |
| Second-line agent | Mycophenolate mofetil | 10 | 100.0 |
| Reason for switch | Inadequate response | 8 | 80.0* |
| | Drug intolerance | 2 | 20.0* |
| Overall response at 3 months | Good | 63 | 63.0 |
| | Poor | 37 | 37.0 |
| Response among switched (n=10) | Good | 8 | 80.0 |
| | Poor | 2 | 20.0 |

*Percentage among the 10 patients who required treatment switch.

## DISCUSSION

The present study evaluated the clinical profile and treatment outcomes of 100 patients with autoimmune hepatitis at a tertiary care hospital in South India, contributing important region-specific data to the existing literature on this immune-mediated liver disease. The findings of this study provide insights into the demographic characteristics, disease severity at presentation, immunological profile, and predictors of biochemical response to standard immunosuppressive therapy in the South Indian population. The female predominance observed in this study (72%) is consistent with the well-established sex predilection of AIH documented in both Western and Asian literature. Heneghan et al. reported a female-to-male ratio of approximately 3.6:1 in their comprehensive review of AIH epidemiology [11]. Similarly, Choudhuri and colleagues, in

their landmark Indian study from a North Indian centre, reported female preponderance in 89.4% of their cohort of 38 AIH patients [12]. The slightly lower female proportion in the present study (72% compared to 89.4%) may reflect evolving diagnostic awareness and improved recognition of AIH in male patients in more recent years.

The mean age at diagnosis in the present study was 38.6 years, which is higher than the 29.5 years reported by Tasneem and Luck in their Pakistani cohort [13] but comparable to the mean age of 36.2 years observed in the Indian study by Choudhuri et al. [12]. AIH in South Asian populations tends to present at a younger age compared to Western cohorts, where the median age at diagnosis typically ranges from 40 to 50 years [14]. The younger age at presentation underscores the importance of including AIH in the differential diagnosis when evaluating young patients with unexplained transaminase elevation or features of chronic liver disease in the South Asian setting.

One of the most striking findings of this study was the high prevalence of cirrhosis at presentation, observed in 61% of patients. This is consistent with the findings of Amrapurkar et al. from a Western Indian tertiary referral center, who reported cirrhosis in 71.2% of AIH patients at diagnosis [15]. Similarly, Tasneem and Luck documented cirrhosis in 83.9% of their Pakistani cohort [13]. The high rate of cirrhotic presentation in South Asian studies stands in contrast to Western data, where cirrhosis at diagnosis is typically reported in 20–35% of patients [14,16]. Multiple factors may contribute to this disparity, including delayed diagnosis due to low clinical suspicion, limited access to specialist care in rural areas, high rates of seronegative disease that may further delay referral, and potentially more aggressive disease behaviour influenced by genetic and environmental factors unique to the South Asian population.

The proportion of seronegative AIH in this study was 32%, which is notably higher than the 17.6% reported by Amarapurkar et al. [15] but comparable to the 35.7% documented by Tasneem and Luck [13]. This high rate of seronegativity has significant clinical implications, as it highlights the limitations of relying solely on autoimmune serology for the diagnosis of AIH and reinforces the indispensable role of liver biopsy in establishing the diagnosis, particularly in the South Asian context. The present study further demonstrated that seronegative AIH was associated with more severe portal tract inflammation and a higher prevalence of esophageal varices and advanced fibrosis, suggesting that these patients may experience a more aggressive disease course, potentially due to delayed diagnosis.

Regarding treatment response, the present study demonstrated a good biochemical response in 63% of patients at three months, which aligns with the 60.7% response rate reported by Tasneem and Luck [13] and the 60% rate observed in the Swedish study by Werner et al. [17]. Zhang and colleagues from China reported a somewhat higher response rate of 80.3% [18], while Western studies generally report biochemical remission rates of 80–90% within two years of therapy [14]. The relatively lower three-month response rate in the present study may partly reflect the higher proportion of cirrhotic patients and the shorter assessment time point of three months versus the one- to two-year endpoints used in most Western studies.

The multivariate analysis in the present study identified three independent predictors of good biochemical response: pre-treatment serum IgG >16 g/L, presence of pseudorosettes on liver biopsy, and three-month post-treatment total bilirubin <2 mg/dL. The association of elevated pre-treatment IgG with better response is of particular interest, as it appears to contradict the findings of Taubert et al. from Germany, who reported that lower immunoglobulin levels at baseline predicted good response [19]. However, a plausible explanation is that elevated IgG reflects robust B-cell activity and a predominantly humoral immune-mediated pathogenesis, which may be more amenable to corticosteroid-mediated immunosuppression compared to disease driven by T-cell-mediated cytotoxicity [13].

The identification of post-treatment total bilirubin <2 mg/dL as the strongest predictor of good response (OR 5.74) underscores the prognostic importance of early biochemical improvement. This finding is consistent with the observations of Dhaliwal et al., who demonstrated that rapid normalization of transaminases and bilirubin within the first three to six months of therapy is strongly predictive of long-term favourable outcomes [20]. Ngu and colleagues from New Zealand similarly reported that early biochemical response was the most reliable prognostic marker [21]. The significance of pseudo rosettes as a predictor of good response warrants discussion. Pseudo rosettes represent a characteristic histological feature of AIH and their presence may indicate a more classic, autoimmune-driven pathogenesis that responds well to immunosuppression, as opposed to advanced burnt-out cirrhosis where the inflammatory component is less amenable to therapy [22]. This finding is consistent with the bivariate association observed by Tasneem and Luck, although their multivariate analysis did not reach statistical significance for this variable [13].

The study has certain limitations that merit acknowledgment. The retrospective design introduces inherent selection bias and limits the ability to establish causality. The assessment of treatment response was limited to biochemical parameters at three months and did not include repeat liver biopsy or serum IgG measurement to evaluate histological and immunological response. The single-center design may limit the generalizability of findings to the broader South Indian population. Additionally, the relatively short follow-up period of three months does not capture late relapses or long-term outcomes.

Despite these limitations, the study provides valuable region-specific data on the clinical profile and treatment predictors of AIH in South India, a population that has been notably underrepresented in the existing literature.

## CONCLUSION

Autoimmune hepatitis in the South Indian population predominantly affects young to middle-aged females and is associated with a high prevalence of cirrhosis at the time of diagnosis, reflecting delayed recognition and referral. Seronegative AIH constitutes a significant subset of patients (32%) and is associated with more severe portal tract inflammation, advanced fibrosis, and oesophageal varices, emphasizing the critical importance of liver biopsy in establishing the diagnosis when autoimmune serology is negative.

Standard immunosuppressive therapy with corticosteroids and azathioprine achieves good biochemical response in approximately two-thirds of patients by three months. Pre-treatment serum IgG >16 g/L, presence of pseudorosettes on histopathology, and three-month post-treatment total bilirubin <2 mg/dL serve as reliable independent predictors of favorable treatment response. These findings underscore the need for heightened clinical awareness, early diagnostic evaluation including liver biopsy in suspected cases with negative serology, and close monitoring of biochemical parameters to guide therapeutic decision-making in patients with AIH in the South Indian setting.

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