

## Research Article

## Autoimmune Hepatitis is more severe in Asian Australians

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## Abstract

Increasingly there is more information in the literature on patients with Autoimmune Hepatitis (AIH) from Eastern countries, with evidence suggesting these patients present with a different clinical phenotype than patients from Western countries. A retrospective analysis of AIH patients at 2 Australian Health services with a mix of Asian and Caucasian patients, was performed. Data on 53 patients (11 Asian and 42 Caucasian) was assessed. Asian patients had a trend to higher AIH score at diagnosis (14.9 vs 13.4;  $p = 0.33$ ), and a higher percentage of Asian patients were cirrhotic at diagnosis (45% vs 21%;  $p = 0.22$ ). Only 36% of Asian patients had a complete response to standard therapy (normal ALT), compared to 57% of Caucasian patients ( $p = 0.22$ ). Relapse was more common in Asian patients (36% vs 28%,  $p = 0.62$ ). Asian Australian patients may have a more severe and more refractory clinical phenotype of AIH compared with Caucasian Australian patients.

## Introduction

Autoimmune hepatitis (AIH) is a chronic progressive inflammatory liver disease that affects children and adults of all ethnicities and races. It has similarities with other autoimmune disorders with the pathogenesis hypothesised to involve a combination of environmental triggers, a loss of immunological self-tolerance and genetic predisposition. This induces a T cell-mediated immune attack upon liver antigens, leading to a progressive necro-inflammation of the liver [1,2]. AIH is considered relatively rare, with early prevalence studies from Europe showing 16 to 18 cases per 100,000 inhabitants [3-6]. However, further studies have shown that the prevalence and clinical expression seems to vary according to ethnicity [7]. Previous studies have suggested patients of Asian or other non-European background may have poorer outcomes [8-10]. The aim of this study was to compare the clinical phenotype and response to therapy of Caucasian and Asian Australian patients in a diverse, multicultural Australian city.

## Methods

A retrospective analysis of liver databases was conducted of patients with known AIH from the last 10 years at two Australian tertiary Health services. The diagnosis of AIH was determined by the diagnostic criteria of definite or probable disease set by the International Autoimmune Hepatitis Group [11]. Phenotypic features including clinical features at presentation, response to standard therapy, and relapse rates were compared.

## Statistical analysis

Differences in prevalence between ethnicities were compared by using the Student  $t$  tests to compare continuous variables and chi-squared test for categorical variables. A  $p$  value of  $<0.05$  was considered significant. Ethics was approved by the respective Human Research Ethics Committees at both health services.

## Results

Between the two health services, 98 patients with AIH were identified. Twenty-eight patients were excluded because they were not

Caucasian or Asian. A further seventeen patients (all Caucasian) were excluded due to incomplete data on baseline characteristics, or response to treatment. Data was complete for 42 Caucasian and 11 Asian patients (four Chinese, four South East Asian and three South Asian). Baseline demographics are shown in table 1.

The majority of patients were female ( $n = 44$ , 83%) with a higher female to male ratio in Asian compared to Caucasian patients (10:1 vs 17:4;  $p = 0.43$ ). The median age at diagnosis was similar for the two groups; 53.6 years for Asians and 54.6 years for Caucasians ( $p = 0.37$ ). Caucasian patients demonstrated the typical bimodal age of presentation with 7/42 (16.7%) patients presenting at age  $<35$  years. In contrast, no Asian patients presented at age  $<35$  years. Furthermore, Asian patients appeared to suffer less comorbid autoimmune disease compared with Caucasian patients (36.4% vs 45.2%;  $p = 0.60$ ).

The AIH score at diagnosis was only marginally higher in the Asian patients (14.9 vs 13.4;  $p = 0.33$ ), and a higher percentage of Asian patients were cirrhotic (45% vs 21%  $p = 0.22$ ), but neither were statistically significant. At diagnosis, both the median ALT and the average total gamma globulin titres were higher in Asians compared to Caucasians (349IU/L vs 331IU/L;  $p = 0.70$  and 20.9g/L vs 19.1g/L;  $p = 0.08$  respectively), however these differences did not reach statistical significance.

Only 36% of Asians patients had a complete response to standard treatment (corticosteroids and azathioprine or 6-Mercaptopurine) with ALT returning to normal range, compared to 57% of Caucasian patients,  $p = 0.22$ . Furthermore, a lower percentage of Asian patients had their total gamma globulins returned to normal with treatment compared to Caucasian patients (57.1% vs 63.6%;  $p = 0.08$ ).

Biochemical relapse was more common in Asian patients (36% vs 28%;  $p = 0.62$ ). Second and third line therapies such as mycophenolate,

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**Table 1.** Baseline characteristics

	Caucasians n (%)	Asians n (%)	
Number (% of total)	42 (79.2%)	11 (20.8%)	
Nationality			
Chinese		4	
SE Asian		4	
South Asian		3	
Female: Male	34: 8	10: 1	$p = 0.43$
Median Age (years) $\pm$ IQR	54.6 $\pm$ 18.8	53.6 $\pm$ 12.2	$p = 0.37$
Age <35 years	7 (16.7%)	0 (0%)	
Age >35 years	35 (83.3%)	11 (100%)	
Comorbid Autoimmune Disease	19 (45.2%)	4 (36.4%)	$p = 0.60$
Mean AIH score (at diagnosis)	13.4	14.9	$p = 0.33$
Cirrhosis at diagnosis	9 (21.4%)	5 (45.5%)	$p = 0.22$
ALT at diagnosis (IU/L) Median $\pm$ IQR	331 $\pm$ 1032	349 $\pm$ 538	$p = 0.70$
Mean Total Gamma Globulin (g/L) Median $\pm$ IQR	19.1 $\pm$ 12.5	20.9 $\pm$ 19.1	$p = 0.08$

budesonide, methotrexate and cyclosporine were used similarly in Asian patients and Caucasian patients (54.5% compared to 52.4%,  $p = 0.90$ ).

## Discussion

This study adds to the current literature that Asian patients with AIH often have a different clinical phenotype to Caucasians, and this should be taken into consideration when planning management. With a multicultural population that includes large numbers of both Asian and Caucasian individuals, the city of Melbourne provides an opportune cohort to investigate these differences in greater detail. Our pilot data suggests Asian patients appear to have a different clinical phenotype for autoimmune hepatitis compared with Caucasian patients in our cohort, with a possible trend towards more severe and treatment refractory disease. This is the first Australian study to describe and characterize the differences between these two groups. Although there were no significant results, our study provides interesting preliminary results which we hope to expand to other Australian health services given Australia's multicultural population.

Ethnic differences in AIH have previously been considered. A study from King's College Hospital in the United Kingdom compared their 12 non-European AIH patients with 180 European AIH patients [8]. However, the non-European cohort included only 5 Asian patients and were significantly younger compared to the Europeans. They found no significant differences between the two groups in the proportions presenting acutely or with cirrhosis, and similar to our study, a significantly lower proportion of non-European patients showed a complete initial response to standard therapy. A study from the United

States comparing Caucasians, Asians and Hispanics demonstrated similar findings [9]. In their cohort, Asians had a higher AIH score at diagnosis compared to Caucasians, and Asians were more likely to be cirrhotic. The Kaplan-Meier survival analysis showed a trend toward poorer outcomes among Asians.

Our study was limited by factors typical of retrospective research, including lack of complete data for all patients, especially detailed information pertaining to the severity of illness, HLA status and details of immunosuppressive therapies. Furthermore, the sample size of our cohort was small, in particular our small number of Asian patients, hence there was insufficient power to demonstrate a statistical significant difference between our two cohorts.

In summary, our study presents a comparison between the clinical phenotypes of Caucasian and Asian Australian patients with AIH. It demonstrates that Asian patients may potentially have a different clinical phenotype compared to Caucasian patients, with a possible trend towards more severe and more treatment refractory disease further highlighting the race/ethnicity-specific variations in the clinical features of autoimmune hepatitis.

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