LIVER DISEASE

Characteristics of autoimmune hepatitis in patients who are not of European Caucasoid ethnic origin

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Background: Significant diversity in disease severity has been identified for autoimmune disorders among different ethnic groups but there is a lack of data on autoimmune hepatitis (AIH) in populations other than those of European Caucasoid (EC) or Japanese extraction.
Aims: To assess the clinical features, response to therapy, and eventual outcome in AIH patients of non-EC ethnicity.
Methods: A retrospective review of a regularly updated database of patients with AIH referred to liver outpatient clinics at King's College Hospital, London, since 1983.
Results: Twelve patients were identified (10 female; six African, five Asian, one Arabic; median age at presentation 30 years (range 12–58)) who satisfied international criteria for type 1 (11 cases) or type 2 (one case) AIH. Nine (75%) had cholestatic serum biochemistry and three (25%) had mild biliary changes on liver biopsy without definitive features of primary biliary cirrhosis or cholangiographic evidence of primary sclerosing cholangitis. Four showed a complete biochemical response to standard prednisolone with or without azathioprine therapy, three partial, and five no response. Four have required liver transplantation for intractable disease. By comparison with 180 EC patients with definite AIH attending during the same period, the non-EC patients were younger ($p<0.05$), presented with cholestatic biochemistry ($p=0.014$), and morphological biliary features more frequently ($p<0.0005$) and showed a poorer initial response to standard therapy ($p<0.0005$).
Conclusions: Clinical expression of AIH in non-EC patients seems to differ in important respects from that in EC or Japanese patients. Management of such patients is challenging and may require alternative or more aggressive treatment strategies.

Autoimmune hepatitis (AIH) is a rare disease occurring predominantly in women which is characterised by the morphological changes of interface hepatitis on liver biopsy, hypergammaglobulinaemia, elevated serum aminotransferases, and circulating autoantibodies.[1] Affected individuals often have concurrent extrahepatic autoimmune disorders. Although the pathogenesis is unclear, AIH is thought to have a basis in aberrant autoreactivity to hepatocytes in genetically susceptible individuals. The condition is frequently associated with inheritance of the HLA A1-B8-DR3 haplotype and with the DR3 and DR4 allotypes in northern European Caucasoid patients.[1–7] AIH is notably heterogeneous with respect to its clinical expression and laboratory features. Onset is typically associated with non-specific symptoms such as fatigue, right upper quadrant pain, and/or malaise but a significant proportion of patients either present with an acute hepatitis or have no obvious clinical evidence of liver disease.[1] The majority of patients are peri- or postmenopausal females but AIH can present at any age and also affects males.[1] Most patients show a characteristically rapid response to immunosuppressive therapy and the disease can usually be maintained in remission on low doses of prednisolone or on azathioprine alone.[1 8]

Almost all of the current knowledge of both the natural history and management of AIH has derived from studies on patients of European Caucasoid (EC) or Japanese extraction. The condition is not exclusive to these ethnic groups but there is very little information available about the disease in patients of other ethnic backgrounds. However, it has been our impression that the manifestations of AIH in non-EC patients attending our clinics tend to be more severe and the disease activity more difficult to control than in EC patients. In other autoimmune diseases, such as systemic lupus erythematosus and type 1 diabetes mellitus, significant differences have been identified both in the clinical features and severity of disease between African Americans and whites.[9–16] Analogous data exist for rheumatoid arthritis in which differences in the manifestations of the disease in patients of African American, North Indian, or Pakistani origin compared with whites have been reported.[17 18] To investigate whether such racial differences may also apply in AIH, we have undertaken a systematic review of EC and non-EC patients referred to our outpatient clinics between 1983 and 1999 with respect to their presenting features, response to therapy, and outcome.

MATERIALS AND METHODS

Interrogation of a regularly updated database on AIH patients identified a total of 27 non-EC patients with suspected AIH who had been referred to the liver outpatient clinics at King's College Hospital during the period 1983–1999. Fifteen patients were excluded due to: concomitant hepatitis B virus infection, overlap syndrome (with primary sclerosing cholangitis (PSC) or with primary biliary cirrhosis (PBC)), history of potentially hepatotoxic drug use, inadequate documentation received on referral, and/or loss to follow up. The remaining 12 patients (10 females, two males) comprised the study cohort (table 1).

Abbreviations: AIH, autoimmune hepatitis; ALP, serum alkaline phosphatase; AMA, antimitochondrial antibodies; ANA, antinuclear antibodies; anti-LKM1, type 1 antiliver-kidney microsomal antibodies; AST, serum aspartate aminotransferase; EC, European Caucasoid; HCV, hepatitis C virus; IAIHG, International Autoimmune Hepatitis Group; MMF, mycophenolate mofetil; OLT, orthotopic liver transplantation; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis; SMA, antismooth muscle antibodies; UDCA, ursodeoxycholic acid.

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Table 1 Demographic, clinical, biochemical, and immunological data for the 12 patients at presentation

Patient No	M/F	Ethnic origin	Age (y)	Acute onset	AST (<50 IU/l)	Bilirubin (<20 μmol/l)	ALP (<130 IU/l)	IgG (<18 g/l)	ANA	SMA	LKM
1	F	African	39	Yes	1803	22	232	25.3	1:10	1:160	Neg
2	M	African	16	Yes	2181	320	360	60.0	1:640	Neg	Neg
3	F	African	13	No	601	59	618	42.3	1:40	1:640	Neg
4	F	Arabic	13	Yes	1576	400	657	37.7	Neg*	Neg*	Neg*
5	F	African	28	No	579	43	262	29.2	1:1280	1:1280	Neg
6	F	Asian	33	No	191	227	466	22.7	1:20	1:80	Neg
7	F	African	32	No	980	90	647	70.7	Neg	1:160	Neg
8	F	African	12	Yes	850	280	850	36.0	Neg	Neg	1:640
9	F	Asian	19	Yes	847	469	186	46.8	1:40	1:320	Neg
10	F	Asian	51	Yes	1259	246	318	41.3	1:40	1:40	Neg
11	M	Asian	47	No	108	26	315	23.2	Neg	1:80	Neg
12	F	Asian	58	No	140	45	203	33.3	Neg	1:40	Neg

AST, aspartate aminotransferase; ALP, alkaline phosphatase—upper reference limits in parentheses; ANA, antinuclear antibodies; SMA, smooth muscle autoantibodies; LKM, type 1 antiliver-kidney microsomal antibodies.
*Presented with thyroid microsomal and thyroglobulin autoantibodies, became seropositive for ANA at 1:40 three months after starting immunosuppressive therapy.

Six patients were of African or Afro-Caribbean ethnic background, five were of Asian origin (India or Pakistan), and one was Arabic (Kuwait). Seven were born in the UK and five were immigrants who had lived in the UK for 7–19 years prior to accession. All were seronegative for markers of concurrent hepatotropic viral infections (hepatitis B surface antigen, hepatitis C virus antibody (anti-HCV), and RNA (HCV-RNA), as well as for IgM antibodies to hepatitis A virus, Epstein-Barr virus, and cytomegalovirus), and for antimitochondrial antibodies (AMA). All patients had normal serum levels of ferritin, ceruloplasmin, copper, and α_1 antitrypsin. Careful anamnesis revealed no recent history of hepatotoxic drug usage (including herbal remedies) or excessive alcohol consumption. Eleven fulfilled the criteria for a diagnosis of definite AIH and one for probable AIH according to the International Autoimmune Hepatitis Group (IAIHG) scoring system.[1] Age at presentation ranged from 12 to 58 years (median 30). Ten presented with antinuclear (ANA) and/or smooth muscle (SMA) antibodies and one had type 1 liver-kidney microsomal antibodies (anti-LKM1). The 12th patient was seronegative for these antibodies at presentation but had thyroid microsomal and thyroglobulin autoantibodies (with normal thyroid function tests) and became ANA positive (at 1:40) three months after starting therapy. Four patients had a history of other concomitant disorders: Sjogren's syndrome, psoriasis with lichen ruber planus, non-insulin dependent diabetes, and alopecia areata with non-insulin dependent diabetes. Of six non-EC patients who were HLA typed, one was DR3 positive and four had DR4 (one with the A1-B8-DR4 haplotype).

All patients underwent ultrasound and/or computerised tomography scanning of the abdomen, and liver biopsy. Liver biopsies were reviewed by one of the authors (BCP) with particular attention to features of interface hepatitis (portal and periportal lymphoplasmacytic infiltration, and periportal piecemeal necrosis), lobular necroinflammation, and any other features (particularly biliary changes) that might be suggestive of other aetiologies of chronic hepatitis. Semiquantitative histological assessment of the severity of chronic hepatitis was performed according to Batts and Ludwig,[19] whereby necroinflammatory activity is graded as: 0, none; 1, minimal or patchy; 2, mild; 3, moderate; and 4, severe, and extent of fibrosis is staged as: 0, none; 1, portal only; 2, periportal; 3, septal; and 4, cirrhosis. Five patients had established cirrhosis at presentation.

Autoantibody tests were performed by the hospital's clinical immunology laboratory. Sera were initially screened at 1:10 dilution and positive samples were titrated to negativity in doubling dilutions. ANA, SMA, anti-LKM1, and AMA were tested for by indirect immunofluorescence on sections of rodent liver, kidney, and stomach. Thyroid autoantibodies were detected by commercial particle agglutination assays (Serodia AMC and ATG; Fujirebio, Tokyo, Japan).

All patients were initially treated according to the standard therapeutic protocol of King's College Hospital with prednisolone (0.5 mg/kg/day) with or without azathioprine (1–2 mg/kg/day) as first choice therapy. Other immunosuppressive drugs (tacrolimus, cyclosporin, and/or mycophenolate mofetil), or ursodeoxycholic acid (UDCA) were introduced when necessary as indicated below. The IAIHG scoring system was applied to features at presentation as directed,[1] and was reapplied subsequently for confirmation when it was possible to include assessment of response to therapy. According to this system, scores of 10–15 before institution of therapy define "probable" and >15 indicate "definite" AIH and, when outcome of treatment is included, the corresponding values are 12–17 and >17, respectively. Complete response to therapy and relapse were defined according to the revised IAIHG criteria.[1] As these do not include definitions of other possible outcomes, the original IAIHG criteria were used to define "partial response" and "no response".[20]

Findings in non-EC patients were compared with those in 180 consecutive EC patients (136 female) with definite AIH referred to our clinics during the same period. The study was undertaken under the supervision of the local ethics committee in accordance with the 1996 Helsinki Declaration guidelines.

Statistical analysis

The Mann-Whitney U test was applied for comparison of continuous variables, and the χ^2 test with Yates' correction for small numbers or Fisher's exact test (as appropriate) were used for comparing dichotomous variables. A two tailed probability (p) value of less than 0.05 was considered significant.

RESULTS

Eleven patients presented with typical symptoms and/or signs associated with AIH (table 2). In six of the 11 patients, including one (No 9, table 3) with cirrhosis, onset was acute and severe, with a short history (6–28 days; median 14) of increasing jaundice (in five) and rapid deterioration of biochemical liver tests. Three of these developed encephalopathy, two had ascites, and one (No 10) had haematemesis. In five patients (including four with cirrhosis) onset was insidious, with ascites in one and haematemesis in another. The remaining patient (No 6) was completely asymptomatic. Her liver disease was revealed by the finding of splenomegaly and abnormal biochemical liver tests during investigation of repeated miscarriages.

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Table 2 Symptoms and signs at presentation in the 12 patients

	Patient No											
	1	2	3	4	5	6	7	8	9	10	11	12
Lethargy		+			+		+	+	+	+		+
Malaise	+	+					+					
Abdominal pain	+						+		+			
Nausea		+	+					+		+		
Vomiting			+					+		+		
Diarrhoea		+										
Pruritus							+					
Anorexia			+				+	+				+
Weight loss							+					
Rigors							+					
Epistaxes							+	+				
Miscarriages						+	+					
Arthralgia			+									
Jaundice		+	+	+			+	+	+	+		
Ascites									+	+	+	
Peripheral oedema												+
Encephalopathy		+		+						+		+
Haematemesis										+		+
Fever												+
Hepatomegaly	+	+		+			+					
Splenomegaly	+		+	+		+		+	+		+	
Anaemia			+	+					+			+

Nine patients (75%) presented with serum alkaline phosphatase (ALP) activities greater than twice the upper normal limit (130 IU/l). One of these (No 3, table 3) also had biliary changes (pericholangitis, apparent ductopenia, ductular proliferation) and a second (No 8) had evidence of mild cholestasis in their liver biopsies either at presentation or subsequently but no definitive features of PSC or PBC. In both, cholangiography revealed only very minor abnormalities attributable to their underlying extensive fibrosis or cirrhosis and there was no evidence of PSC. In three others cholangiography showed no abnormalities. Examination of the explanted livers in those who underwent orthotopic liver transplantation (OLT; see below) also revealed no evidence of PBC or PSC. One patient (No 9) whose ALP at presentation was only slightly abnormal (186 IU/l) but whose liver biopsy showed mild pericholangitis and copper associated protein deposition has not yet had cholangiography but her ALP is still only 225 IU/l three years later.

Three of the six patients (Nos 1, 4, and 8) with an acute onset had a complete response to standard immunosuppressive therapy with prednisolone (plus azathioprine in one). Of the remaining three, one (No 10) deteriorated rapidly and required emergency OLT but died 10 days postoperatively from multiorgan failure. The second (No 2), who admitted to defaulting therapy, also deteriorated and his disease could not be controlled on restarting prednisolone. He subsequently did not respond to addition of either first tacrolimus (2 mg/day) or later mycophenolate mofetil (MMF, 2 g/day). Following plasmapheresis his condition slowly improved and during the next 12 months there was gradual normalisation of his serum aspartate aminotransferase (AST) and bilirubin on 20 mg/day of prednisolone with MMF (2 g/day), although his ALP and gammaglutamyl transferase have remained elevated (336 IU/l and 418 IU/l, respectively). The third patient (No 9) showed some improvement initially on 40 mg/day of prednisolone but required addition of tacrolimus and UDCA to achieve complete normalisation of her liver biochemistry over the following five months but, shortly thereafter, she relapsed when prednisolone was reduced to 15 mg/day. Tacrolimus was changed to MMF without any effect and after three months she underwent plasmapheresis which resulted in some improvement. However, despite high doses of prednisolone (20–30 mg/day) with MMF (2 g/day) her disease activity remains suboptimally controlled three years after diagnosis, although she is clinically asymptomatic.

Of the six patients with an insidious onset (Nos 3, 5, 6, 7, 11, and 12), including four with cirrhosis (Nos 3, 6, 11, and 12), one (No 6) showed a complete response to prednisolone and azathioprine. Two others (Nos 3 and 7) initially had a partial response, with marked improvement in AST activity but without normalisation of biochemical parameters after one year. One of these (No 3) has since shown a complete response after two years. The other (No 7) continues to require 20–30 mg/day of prednisolone with tacrolimus (2–4 mg/day) to maintain symptomatic remission. Of the remaining three patients who had no initial response to standard therapy, one (No 5) had an eight month trial of cyclosporin (serum level 100–200 µg/l) which was unsuccessful. Prednisolone was restarted at 30 mg/day but there has been little improvement in her liver biochemistry after five years and she is still periodically symptomatic despite receiving 20 mg/day of prednisolone with azathioprine (50 mg/day), tacrolimus (2 mg/day), and UDCA (600 mg/day), and is now cirrhotic (Child's B). The second patient (No 11) also showed little improvement in liver biochemistry after three years while continuing on 30 mg/day of prednisolone, at which point he was listed for OLT and started on tacrolimus (2 mg/day). Despite this, while awaiting OLT he died in the setting of spontaneous bacterial peritonitis, encephalopathy, and gastrointestinal bleeding. The third (No 12) had significant deterioration and required OLT three months after diagnosis. She remains alive seven years post-transplant.

Of the four patients (three with acute and one with insidious onset) who initially had a complete response to standard therapy, one (patient No 1, table 3) has relapsed clinically and biochemically on each of three occasions over six years when attempts were made to reduce her steroid dose below 10 mg/day. She continues in clinical and biochemical remission on this dose but has refused a further liver biopsy. The second (No 4) continued in remission for four years on 7.5 mg/day of prednisolone alone but then her biochemical liver tests gradually became abnormal. Despite increasing the steroid dosage and starting tacrolimus (2 mg/day), she continued to deteriorate and eventually required OLT. She survived this procedure but died three years later of sepsis on a background of chronic graft rejection. The third patient (No 6) was asymptomatic for 14 years after withdrawal of prednisolone despite two minor biochemical relapses (which resolved spontaneously) but became cirrhotic. Very recently she suddenly decompensated, necessitating OLT. The fourth (No 8) had three clinical and biochemical relapses over 27 years when attempts were made to reduce her prednisolone dose below 7.5 mg/day. She has continued in remission on this dose for the past nine years but has developed cirrhosis (Child's A) and portal hypertension.

Analysis of the data for the 180 European (EC) patients revealed that median age at presentation was 45 years (range 3–79), 42.6% presented with an acute hepatitic illness, 35.0% had ALP activities greater than twice the upper normal limit but only one (0.6%) had biliary features on liver biopsy, 28.6% had cirrhosis, 95.0% showed a complete initial response to standard therapy, 4.4% had a partial response, and one (0.6%) showed no response. During the period of study, six (3.3%) required OLT for end stage disease, 15 (8.3%) died of liver failure after a median of 12 years (range 1–28), and 22 (12.2%) died of causes unrelated to their liver disease (median duration 10.5 years (range 3–32)). Patients with liver related deaths or requiring OLT for end stage disease were significantly younger (median age 45 years (range 17–89)) than those dying of liver unrelated causes (median 70.5 years (range 24–89); $p=0.007$).

Although the proportion of EC patients who required OLT or died of liver failure (21/180; 11.7%) was much lower than in the non-EC group (4/12; 33.3%), this difference was not

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Table 3 Histological findings at presentation, HLA data, and outcome following standard steroid therapy in the 12 patients

Patient No	Liver histology			HLA			Outcome	IAIHG score
	Grade	Stage	Biliary changes	A	B	DR		
1	3	0	No	na	na	na	Complete response + relapse	20
2	4	3	No	na	na	na	No response. Still requires multiple therapy after 3 y.	19
3	3	4	Yes	1, 10	7, 17	4, 13	Partial response. Complete response after 2 y.	18
4	4	0	No	3, 28	18, 35	4, 11	Complete response + relapse. OLT after 4 y. Died 3 y post-OLT.	21
5	4	0	No	na	na	na	No response. Still requires multiple therapy after 5 y.	19
6	3	4	No	1, 24	8, 39	4, 4	Complete response. No relapse. Recent OLT (after 14 y).	21
7	4	0	No	na	na	na	Partial response. Still requires multiple therapy after 10 y.	19
8	3	3	Yes	1, 2	35, 35	7, 13	Complete response + relapse	25
9	2	4	Yes	na	na	na	Partial response. Still requires multiple therapy after 4 y.	21
10	4	0	No	1, 32	51, 51	3, 7	No response. Emergency OLT. Died 10 days post-OLT .	16
11	0	4	No	na	na	na	No response. Listed for OLT 3 y later but died pre-OLT.	14
12	1	4	No	1, 2	5, 7	4, 11	No response. OLT after 3 mo. Still alive 7 y post-OLT.	16

Histological grading and staging according to Batts and Ludwig,[19] as described in patients and methods.
Biliary changes include one or more of the following: pericholangitis, apparent ductopenia, ductular proliferation, copper associated protein deposition, cholestasis.
na, data not available; OLT, orthotopic liver transplant; IAIHG score, International Autoimmune Hepatitis Group score (including scoring for initial response to therapy).[1 20]

statistically significant (p=0.080). There were also no significant differences between EC and non-EC patients in the proportions presenting acutely or with cirrhosis. However, by comparison with EC patients, the non-EC group were significantly younger (p<0.05), a significantly higher proportion presented with more than twofold elevations in ALP (p<0.02) and biliary changes on liver biopsy (p<0.0005), and a significantly lower proportion showed a complete initial response to standard therapy (p<0.0005).

DISCUSSION

Non-European Caucasoid (non-EC) patients represent a minority of cases of AIH seen in clinical practice in the UK but with the increasingly multiracial nature of our society it is likely that the numbers will increase. To date there have been no substantive data to guide management of such patients and the present study points to some noteworthy caveats. Firstly, the 12 non-EC patients described here presented with a severe form of liver disease that was compatible in all respects with international criteria for a diagnosis of AIH[1] but, by comparison with EC AIH patients attending our clinics, a high proportion had biochemical or histological changes suggestive of an underlying cholangiopathy. Despite this, cholestatic features were not of sufficient magnitude to affect the scoring for AIH using a system which has been previously validated[1] and, more recently, has been shown to have a high degree of specificity for excluding PSC.[21] Additionally, the mild biliary changes observed in liver biopsies from three patients are not uncommonly associated with severe fibrosis or cirrhosis[1] (which all three had at presentation) and none of the patients had AMA or histological or cholangiographic evidence of either PBC or PSC. Therefore, this cohort did not appear to constitute cases of "overlapping" syndromes variously described as autoimmune cholangitis, autoimmune cholangiopathy, or (in children) autoimmune sclerosing cholangitis[1 22 23]; but we cannot exclude the possible involvement of some other aetiological factor (for example, an unidentified virus or toxin). Secondly, the non-EC patients were significantly younger at presentation and had a significantly poorer initial response to standard immunosuppressive therapy than our EC patients. Importantly, the doses of corticosteroids and the requirement for second line agents such as cyclosporin, tacrolimus, or MMF to achieve or maintain remission was greater in the non-EC group.

Consistent with these findings are preliminary results from a single North American centre reported at a recent Single Topic Conference of the American Association for the Study of Liver Disease[24] showing that, at diagnosis, African American patients with AIH were younger and had a significantly higher frequency of cirrhosis (86% *v* 33%) compared with Caucasoids, although the study did not take account of the possible impact of socioeconomic factors. The latter are unlikely to have influenced the findings in the present study because all UK residents have unrestricted access to free health care. Cultural factors may however be important. For example, patients may have been slow to seek medical attention when they first felt unwell or may not have described their symptoms sufficiently to their family practitioners to immediately raise suspicions of liver disease. Thus delay in diagnosis and treatment might have resulted in progression of their disease to an advanced stage which can be difficult to control with standard therapy.[1] Additionally, non-responsiveness due to non-compliance (or only partial compliance) with therapy cannot be excluded because patients were not continuously supervised taking their medication, and it is worth noting that one patient was known to default.

On the other hand, racial differences in the severity of other autoimmune diseases and responses to immunosuppressive therapy are now well recognised. Several studies have shown significant differences in age at presentation, frequency and nature of complications, and responses to treatment between patients of different ethnic backgrounds with systemic lupus erythematosus.[9–13] Similarly, a higher mortality and higher rate of complications have been reported in African Americans with type 1 diabetes than in whites, even when account is taken of differences in socioeconomic background.[14–16] In rheumatoid arthritis patients of African American, North Indian, or Pakistani origin, different manifestations of the disease are apparent compared with whites.[17 18] These include objective differences in the degree of joint destruction and subjective diversity in pain scores, and the observation that patients of North Indian or Pakistani origin have more severe symptoms and require more analgesics.[17 18] It seems likely that at least some of these differences may relate to genetic variations in the metabolism of the immunosuppressive agents used to control the diseases, evidence for which comes predominantly from studies in the transplant setting. For example, racial differences in the pharmacokinetics of methylprednisolone have been demonstrated, with blacks reportedly being more resistant to standard doses (and therefore requiring higher doses to prevent allograft rejection) than whites[25] and Koreans showing a larger volume of distribution

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of the drug than blacks, lower clearance rates than whites, and a longer drug half life than both blacks and whites.[26]

Data on azathioprine metabolism in different races are somewhat conflicting, with some studies reporting lower[27] and others higher[28] conversion of the drug to inactive metabolites in those of African origin than in Caucasoids. However, racial differences in the pharmacokinetics of the other immunosuppressive agents (tacrolimus, MMF, and cyclosporin) that were used in our patients have been described. African-American renal allograft recipients reportedly require a 37% higher mean dose of tacrolimus to achieve and maintain equivalent blood concentrations of the drug than Caucasoid patients[29] and a significant reduction in bioavailability of tacrolimus in blacks compared with non-blacks has been demonstrated, both in healthy individuals and in renal allograft recipients.[30] This has also been noted for cyclosporin,[31] while MMF has been shown to be less effective for reducing the risk of acute renal allograft rejection in African-Americans than in Caucasoids.[32 33]

For patients with AIH, failure to respond to conventional therapy usually results in fairly rapid development of cirrhosis and an increased likelihood of a requirement for liver transplantation. In the transplant arena, the consequences of racial differences in drug metabolism translate into chronic rejection and graft loss. Non-European liver allograft recipients have been shown to have inferior graft survival compared with European recipients at one, two, and three years after transplantation, with chronic allograft rejection developing in 12.6% of non-European recipients versus 5.9% of Europeans.[34] Similarly, in kidney transplant recipients, chronic rejection and graft loss are significantly more likely in African American recipients than in Caucasoids.[35 36]

Whether the cases described here are broadly representative of AIH in non-EC patients is unclear. Selection bias is a possibility but, as a tertiary referral centre, we tend to see patients with disease at the more severe end of the spectrum and, since this also applies to our EC patients, the two populations are probably reasonably comparable in terms of patients presenting with severe disease. Indeed, apart from the features mentioned above, there were no other significant differences between the two groups. Although this is a relatively small series, the present findings point to the importance of considering race as a factor in the diagnosis and management of the condition. In particular, non-EC patients may require greater levels of immunosuppression from an early time point after diagnosis. The present data also emphasise a need for more information about AIH in different racial groups and for further investigation to determine whether differences are related to cultural, environmental, or genetic factors.

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