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Intrahepatic Cholestasis of Pregnancy: Prevalence and Ethnic Distribution

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ABSTRACT

We undertook a retrospective analysis of the prevalence of obstetric cholestasis in the population of the South Birmingham area in the various ethnic subgroups. A diagnosis of intrahepatic cholestasis of pregnancy was made on the basis of symptoms of generalised pruritis along with biochemical evidence of the condition, after ruling out other liver diseases. We found an overall prevalence of 0.7%, with an occurrence in the white population of 0.62%, compared to that in the Asians of Pakistani origin of 1.46%. In the Asians of Indian origin it was found to be 1.24%. The prevalence of obstetric cholestasis was significantly higher in the Pakistani and Indian subgroups compared to the whites.

INTRODUCTION

Intrahepatic cholestasis of pregnancy, commonly known as 'obstetric cholestasis' is a liver disease characterised by generalised pruritis that appears in the later half of pregnancy, and resolves in the puerperium. It was previously thought to be a benign and relatively harmless condition, but more recent research has shown that it is associated with significant perinatal mortality and maternal morbidity. In one study,[1] a perinatal mortality rate of 110/1000 livebirths was attributed to it. In a later study,[2] it was reported that intensive fetal surveillance, including induction of labour before term, and amniocentesis for meconium staining of liquor, was associated with a perinatal mortality of 35/1000 liverbirths. The incidence of stillbirths (in women with the condition) was found to be 30/1000 livebirths. There is also an increased risk of preterm birth ranging from 30% to 44%,[3] along with meconium staining of amniotic fluid in up to 58% and intrapartum fetal distress in 15% of labours.

The prevalence of obstetric cholestasis has not been reported in the UK, but studies from other countries indicate a varying geographical distribution. The prevalence in France has been reported to be around 0.2%,[7] compared with Finland and Sweden where it varies between 1 and 2%.[4] It is less frequent in North America, with a review by Johnson and Baskett[5] suggesting an incidence of 1 in 1293 pregnancies. However, there has been a general trend in over-diagnosis based on symptomatology alone without recourse to biochemical testing. A prime example is the study on intrahepatic cholestasis of pregnancy in Chile done by Reyes *et al.*,[6] which has quoted a prevalence rate as high as 12.6–22.1% depending on the ethnic population. Their diagnostic criteria for intrahepatic cholestasis was generalised pruritis without jaundice, that appeared in the pregnancy with an absence of skin lesions or biliary colicky pain, and no signs or symptoms of liver

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TABLE 1. *Comparison of prevalence rates of obstetric cholestasis (oc) in the various ethnic subgroups*

Ethnic subgroup	Total no. of women with OC	Total no. of women delivering	% Women with OC	Odds ratio (95% CI)		*p* value
White	42	6790	0.62			
Pakistani	23	1574	1.46	2.38	(1.43–3.97)	0.0009
Indian	7	564	1.40	2.02	(0.9–4.5)	0.087
Bangladeshi (ns)	1	232	0.43	0.696	(0.095–5.07)	0.72
Total Asian (from Indian subcontinent)	31	2370	1.26	2.13	(1.34–3.40)	0.0015

CI, confidence interval.

diseases. They obtained blood samples for testing serum bilirubin, alkaline phosphatase and glutamic-pyruvic transaminase, all of which are unreliable for diagnosing the condition, 15–40 hours after delivery. Incidentally, this study found a higher incidence of the condition in Araucanians, descendants of the original inhabiters of the central zone of Chile, as compared to Caucasoids, who are an ethnic admixture between European colonizers and native South American Indian groups.

METHODS

Our study comprised of patients diagnosed with obstetric cholestasis between 1 April 1995 and 31 March 1997. As ours is a tertiary referral centre, with referrals from beyond our immediate area, to ensure that our study was representative of the population we included patients only with addresses and postcodes within the South Birmingham area. We did the same with our figures for the number of deliveries in the hospital.

Due to large-scale migrations of Asians from the Indian subcontinent in the 1960s and 1970s, the population our hospital serves is an interesting mixture of whites, Asians of Indian, Pakistani and Bangladeshi origin, and some of Afro-Caribbean descent.

Women presenting with generalised pruritis to the hospital undergo biochemical testing which includes serum bile acids, aspartate and alanine transaminase, and serum bilirubin. Alkaline phosphatase is not measured because the placental contribution makes it unreliable for diagnosis. We usually diagnose obstetric cholestasis when serum bile acids are above 14 mmol/l, with raised liver enzymes after excluding other liver diseases. This is done by detailed physical examination, biochemical investigations, and ultrasound of the hepatobiliary system. We use ursodeoxycholic acid for treatment. There is a strict policy of monitoring maternal and fetal condition by serial doppler and growth scans and serial biochemistry, and of induction of labour before term.

RESULTS

Between April 1995 and March 1997, a total of 73 women who delivered at the Birmingham Women's Hospital and who lived in the defined area were diagnosed with obstetric cholestasis of pregnancy. The deliveries from the South Birmingham area for the period were 10 335, giving an overall incidence of 0.7%.

Forty-two of the women were white Caucasian in origin, giving a prevalence rate of 0.62%. Twenty-three of the women were Asians of Pakistani origin, resulting in a prevalence of 1.46% (Table 1). Seven of the women were Asians of Indian origin, thus giving a prevalence rate of 1.24%. Only one Bangladeshi woman was diagnosed with the condition, resulting in a prevalence of 0.43%. We did not detect the condition in any woman of Afro-Caribbean or Far Eastern origin.

We found a significantly higher incidence of obstetric cholestasis of pregnancy in Asian women of Pakistani origin as compared with the white population with an odds ratio (OR) of 2.38 [confidence interval (CI) = 1.43–3.97], $p = 0.0009$. Similarly, Asian women of Indian origin were also found to have a significantly higher incidence of obstetric cholestasis, the OR being 2.02 (CI = 0.90–4.5), $p = 0.087$. An overall OR of 2.13 (CI = 1.34–3.40), was worked out for the Asian population from the Indian subcontinent, giving rise to a statistically significant difference in the occurrence of the condition compared with the white population, $p = 0.0015$.

DISCUSSION

The object of this study was to find out the true incidence of obstetric cholestasis in our population. We found 0.7% of our population suffering from the condition. An interesting finding, however, is the significantly higher incidence of pregnancy-induced intrahepatic cholestasis in the Asian population of the region. The Indian and Pakistani populations had an incidence twice that of the white population.

The only parallels found in the literature were the papers by Reyes *et al.*,[6] which described the prevalence of the condition in the inhabitants of Chile and Bolivia. It was noted that women of Araucanian descent were more susceptible to the condition than Caucasoids. The condition is also more frequent in Sweden and Finland[4] as compared to other European countries.

A genetic susceptibility has been postulated,[8] along with some environmental factors. A mendelian dominant type of inheritance is most likely along with certain histocompatibility antigen haplotypes shared amongst affected family members. It was noted that the consumption of rapeseed oil containing erucic acid, a long-chain monosaturated fatty acid (*cis*-13-docosenoic, 22:1 $n = 9$) was higher in both Sweden and Chile. However, an experimental study did not detect hepatic morphological or functional abnormalities in pregnant and non-pregnant rats fed rapeseed oil with a high erucic acid content. Though it may be a possibility that metabolic responses to this dietary oil could be different in humans than in rodents, how this theory applies to people form the Indian subcontinent is difficult to say without an in-depth study of their dietary habits.

Obstetric cholestasis has only recently begun to be taken seriously as a disease entity which may do considerable harm to both mother and baby. Our study highlights the need for awareness of this disease entity among obstetricians and more importantly among family practitioners taking care of the pregnant woman in the community. Though it affects a small percentage of the pregnant population, the potential costs in terms of fetal morbidity and mortality are high.

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