Perinatal mortality in different ethnic groups

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SUMMARY   We have analysed the cause of perinatal deaths in four hospitals in the North West Thames region over a six year period commencing January 1980. The Pakistani population had a significantly greater perinatal mortality rate (15·7/1000 births) than the Europeans (11·3/1000 births). This was due to an increased incidence of macerated stillbirths and lethal malformations, the latter resulting from a significantly higher incidence of autosomal recessive disorders, neural tube defects, and renal malformations.

Several studies have shown that there is a higher perinatal mortality rate in the Asian subgroup of the British population.[1-3] This has been attributed to a higher incidence of stillbirths of low birth weight and in deaths due to congenital malformations.[3 4] It has been suggested that greater maternal age, higher parity, lower social class, and a high incidence of consanguineous marriage in the Asian population are aetiological factors in the higher perinatal mortality rate.[1 2] The aims of this study were to assess the contribution of lethal congenital malformations to perinatal mortality in different ethnic groups, to investigate the incidence of definite and probable autosomal recessive syndromes, and to estimate the possible effect of consanguinity.

Patients and methods

The population studied included all babies born from January 1980 until the end of December 1985 at four hospitals in the North West Thames region. These hospitals were selected because they notified births by ethnic group, which enabled accurate definition of ethnic perinatal mortality rates. The groups studied were Europeans, Pakistanis, and Asians from India. Other groups notified included Asians from Africa and Bangladesh, Chinese, Arabs, Africans, and Vietnamese, but these have not been further subdivided as numbers were too small to permit meaningful analysis.

Perinatal deaths were identified by inspection of the labour ward registers of births (to ascertain all stillbirths) and the neonatal intensive care registers, which recorded all neonatal deaths and transfers to other units. Where babies had been transferred to units not included in the study information regard-

ing their outcome was sought from the receiving hospital. Where possible ascertainment of perinatal deaths was checked against other sources of information such as necropsy files and perinatal mortality meeting records. Maternal and neonatal case records were examined to determine the circumstances of death, necropsy details, karyotype, maternal ethnic group, religion, consanguinity, age, parity, and medical, obstetric, and family history. The genetic case records were examined in cases that had been referred for genetic opinion. Deaths were then classified by cause or mode of death as described by Wigglesworth.[5] This permits classification based on simplified pathological subgroupings to which most perinatal deaths can be provisionally assigned even if necropsy is not done and provides groups with implications for aetiology (table 1). Statistical analysis was performed using Fisher's exact two tailed test and confidence intervals were calculated as described by Morris and Gardner.[6]

Results

There were 63 442 births in the six year period: 50 164 Europeans (79·0%), 3507 Pakistanis (5·5%), 3367 Indian Asians (5·3%), and 6404 others (10·2%). There was a total of 803 perinatal deaths giving an overall perinatal mortality rate of 12·6/1000 births. The distribution of deaths between the different pathological subgroups is shown in table 1. Four of the babies classified as macerated stillbirths had minor malformations not thought severe enough to cause death. These were mild bilateral hydronephrosis, a small ventricular septal defect, an isolated cleft palate, and a small meningocoele. In 13 (1·6%) cases it was not possible to classify the

Table 1 *Perinatal deaths in different ethnic groups (per 1000 births)*

Pathological subgroup	European	Pakistani	Indian	Total* (%)
Macerated stillbirths	142 (2·8)	17 (4·8)†	10 (3·0)	200 (24·9)
Congenital malformations	151 (3·0)	24 (6·8)†	11 (3·3)	209 (26·0)
Conditions associated with immaturity	141 (2·8)	7 (2·0)	13 (3·9)	204 (25·4)
Conditions associated with birth asphyxia	110 (2·2)	5 (1·4)	8 (2·4)	147 (18·3)
Other‡	21 (0·4)	2 (0·6)	1 (0·3)	30 (3·8)
Unclassified	—	—	—	13 (1·6)
Total	565	55	43	803
Perinatal mortality rate/1000 births	11·3	15·7†	12·8	12·6

*Includes perinatal deaths from all ethnic groups.
†Compared with Europeans $p<0.05$.
‡Rhesus disease, non-immune hydrops, metabolic disorders, etc.

deaths because the notes were unobtainable and insufficient information was available from the labour ward and neonatal registers. A total of 543 (67·6%) babies had undergone postmortem examination.

PERINATAL MORTALITY BY ETHNIC GROUP
The Pakistanis had a significantly higher perinatal mortality rate (15·7/1000 births) than the Europeans (11·3/1000 births) (odds ratio 1·39, 95% confidence interval 1·05 to 1·82, $p<0.05$). The Indian rate (12·8/1000 births) was not significantly different from that of either of the other groups.

ETHNIC DIFFERENCES IN PATHOLOGICAL SUBGROUP
There was no significant difference between groups in deaths due to immaturity, birth asphyxial conditions, and other specific causes (table 1). The increased perinatal mortality rate in Pakistanis when compared with Europeans was entirely accounted for by significantly higher incidences of macerated stillbirths (odds ratio 1·67, 95% confidence interval 1·02 to 2·78, $p<0.05$) and lethal congenital malformations (odds ratio 2·33, 95% confidence interval 1·49 to 3·57, $p<0.01$). The Indians had slightly higher rates than Europeans in all categories but these did not reach significance.

ANALYSIS OF LETHAL MALFORMATIONS
During the period of the study 209 babies died as a result of congenital malformations. Postmortem examination had been performed in 150 cases and successful chromosome analysis in 52 cases. Seventy two of these babies were stillborn and 137 died in the neonatal period as a result of their malformations. Table 2 shows the incidence of malformations by system subdivided into ethnic groups. There were significantly higher incidences of neural tube

Table 2 *Malformations divided by system in different ethnic groups and the potential for prenatal detection*[7]

	No in study (incidence/1000 births)			No (%) detectable by prenatal ultrasound
	European	Pakistani	Indian	
Central nervous system	3 (0·06)	2 (0·57)	0	1 (20)
Neural tube defects	37 (0·73)	7 (1·99)*	2 (0·59)	46 (100)
Cardiovascular	24 (0·48)	2 (0·57)	2 (0·59)	12 (43)
Renal	16 (0·32)	5 (1·43)**	2 (0·59)	12 (52)
Pulmonary	7 (0·14)	1 (0·29)	0	0
Gastrointestinal	4 (0·08)	0	1 (0·29)	4 (80)
Musculoskeletal	12 (0·24)	0	1 (0·29)	5 (38)
Recognised syndromes	13 (0·26)	1 (0·29)	1 (0·29)	11 (73)
Multiple malformations	16 (0·32)	4 (1·14)*	2 (0·59)	14 (64)
Chromosomal	19 (0·38)	2 (0·57)	0	5 (24)
Total	151	24	11	110 (59)

Compared with Europeans *$p<0.05$, **$p<0.01$.

defects, renal malformations, and multiple malformations (which were mainly recessive) in the Pakistani population compared with the Europeans, but no significant differences in the incidence of malformations occurring in other systems.

Central nervous system and neural tube defects
In 32 of the total of 49 babies in the study with a neural tube defect the diagnosis was made on clinical grounds alone. Three of the babies dying with hydrocephalus had no postmortem examination, destructive procedures having been performed at the time of delivery. In the remaining cases necropsy confirmed the diagnosis. In three cases there had been an affected sibling with a neural tube defect. In one case the mother was an epileptic on phenytoin and phenobarbitone. The incidence of neural tube defects among perinatal deaths in the Pakistani population (2/1000 births) was significantly higher (odds ratio 2·7, 95% confidence interval 1·2 to 6·25, p<0·05) than among Europeans (0·74/1000 births) or Indians (0·6/1000 births).

Cardiovascular
In 21 of the 29 cardiac cases the diagnosis was confirmed by postmortem examination. In three cases where necropsy was not performed the diagnosis was based on the results of catheterisation or echocardiography. The remaining five babies had been transferred and died at the receiving hospital and insufficient information was available to establish accurately the nature of the cardiac lesion. In two cases there had been a previous affected sibling with congenital heart disease.

Renal
Twenty six babies died as a result of renal disorders. The diagnosis was confirmed at necropsy in 20 cases and in the remainder it was made on the basis of the clinical features, antenatal ultrasound findings, or postnatal radiographs and ultrasound. In three cases there was a history of renal malformations in previous siblings. One baby with cystic dysplastic kidneys had a sibling who died in the neonatal period with Potter's syndrome. The histology was reviewed and confirmed cystic dysplasia. One of the babies with prune-belly syndrome was born to a consanguineous couple who already had a child with only one kidney. A consanguineous Pakistani couple had the child with Finnish congenital nephrotic syndrome having had a similarly affected child and another child who was stillborn with cystic dysplastic kidneys. A woman who was an insulin dependent diabetic gave birth to one of the babies with renal agenesis. There was a significantly higher incidence of lethal renal disorders in the Pakistani

population compared with the Europeans (odds ratio 4·76, 95% confidence interval 1·72 to 12·5, p<0·01).

Pulmonary
The diagnosis was confirmed by necropsy in all cases reported here; there was no relevant family history in any of these babies.

Gastrointestinal
Postmortem examination had been carried out in all cases. A baby who died with oesophageal atresia was one of twins, the other twin was live born with no abnormalities.

Musculoskeletal
In all cases the diagnosis had been confirmed by necropsy and, where relevant, the radiographs and histology had been reviewed by experts. Three of the cases of congenital muscular dystrophy occurred in the same European family. The baby with Pena Shokeir syndrome was born to a consanguineous couple with a previously affected child. A woman known to have myotonica dystrophica had the baby who died with congenital myotonic dystrophy.

Recognisable syndromes and multiple malformations
There was no difference in the incidence of recognisable syndromes in the different ethnic groups. There was, however, a significantly higher incidence of multiple malformations with no recognisable syndrome in the Pakistani population when compared with the Europeans (odds ratio 3·57, 95% confidence interval 1·19 to 11·1, p<0·05). In three of the four cases which occurred in Pakistanis these were probably recessive syndromes as there had been a previously affected sibling and these cases occurred in consanguineous couples.

Chromosomal abnormalities
Abnormal karyotypes were obtained in 16 of the cases described here. A presumptive diagnosis was made in the remaining five cases on the basis of the clinical features (trisomy 13, trisomy 18, two cases of trisomy 21, and triploidy). There was no difference between ethnic groups in the incidence of abnormal karyotypes.

ANALYSIS OF AUTOSOMAL RECESSIVE CONDITIONS (TABLE 3)
There were seven perinatal deaths due to autosomal recessive conditions among the European population (0·14/1000 births). Of these, three babies with congenital muscular dystrophy were born to one couple and there were two siblings that died from megacystis megaduodenum. In the Pakistani

Table 3 *Lethal autosomal recessive conditions*

	Consan-guinity	Race
Megacystis megaduodenum[8]	Yes	European (n=2)
Pena Shokeir[9]	Yes	European
Cystic fibrosis	No	European
Congenital muscular dystrophy	No	European (n=3)
Congenital muscular dystrophy	No	Indian
Neu-Laxova[10]	Yes	Pakistani
Finnish congenital nephrosis	Yes	Pakistani
I cell disease[11]	Yes	Pakistani
Multiple abnormalities	Yes	Pakistani (n=3)

population there were six deaths due to autosomal recessive syndromes. The three multiple abnormalities with no recognisable syndrome occurred in two different but consanguineous couples. One couple had had a previous affected child (delivered outside the study period) with similar clinical features. The other two lethal multiple malformations were still-born twins born to a couple who had had a previous stillborn child with similar features. The incidence of deaths due to recessive conditions in Pakistanis (1·71/1000 births) was significantly higher than the European rate of 0·14/1000 births (odds ratio 12·5, 95% confidence interval 4·17 to 33·3, p<0·0001). In the Indian population the rate of 0·29/1000 births was not significantly different from the other groups.

CORRECTED PERINATAL MORTALITY RATES
When corrected for deaths due to autosomal recessive syndromes the Pakistani perinatal mortality rate was 13·7/1000 births as compared with 11·1/1000 in Europeans (odds ratio 1·25, 95% confidence interval 0·94 to 1·67, p>0·05). The excess deaths were largely due to malformations and were explained by the higher incidence of neural tube defects in the Pakistani population. The perinatal mortality rates per 1000 births corrected for both neural tube defects and autosomal recessive conditions in the different groups were then 10·4 for Europeans, 11·9 for Pakistanis, and 11·9 for Indians. There was no significant difference between the groups. The higher rate of macerated stillbirths in Pakistanis accounted for the remaining excess in perinatal mortality.

POTENTIAL FOR PREVENTION
Many of these lethal malformations are amenable to detection in the second trimester either by consideration of the family or medical history followed by appropriate investigations or by routine prenatal ultrasound examination. In 11 cases there was a relevant family history and in six of these

referral for expert ultrasound examination should have resulted in prenatal detection. In two cases the mother was an insulin dependent diabetic and in one an epileptic on medication and thus they were at increased risk of having a child with a malformation. There was one baby with trisomy 18 whose mother was 38 years old and this would have been detected had she undergone amniocentesis. Review of the remaining lethal malformations shows that a further 59% could be detected by careful routine prenatal ultrasound performed at 18–20 weeks' gestation (table 2).[7] In the cases reported here only two cases were detected in the second trimester. One was a neural tube defect where the parents elected to continue with the pregnancy and the other was extrophy of the cloaca in one triplet in an in vitro fertilisation pregnancy. It must be remembered, however, that prenatal ultrasound is considerably more sophisticated now in 1989 than it was in the period of the study.

Discussion

This study has confirmed the higher perinatal mortality rate and shown the significant contribution of lethal malformations in the Pakistani population as reported by others.[2 3] The pattern of malformations found in the three ethnic groups (table 2) confirms an increase in the number of multiple malformations as described by Terry *et al.*[3] We differ, however, in finding of similar rates of chromosomal abnormalities and, in keeping with Gillies *et al*,[2] a significantly higher incidence of neural tube defects in Pakistanis.

Many neural tube defects in this country are now detected by antenatal screening programmes based on routine ultrasound examination in the second trimester or on maternal serum α fetoprotein concentrations. Many women opt for termination of pregnancy when found to have an affected fetus. Lumb *et al* showed that Asian women tended to book later for their antenatal care with 60·7% of them booking after 26 weeks.[1] If this is true of Asian women in other areas it may account for the high contribution of neural tube defects to perinatal mortality as second trimester screening and termination would be available to a relatively smaller proportion of Pakistani women. Furthermore, they may find termination of pregnancy unacceptable on religious grounds.[12] We are currently investigating these hypotheses by examining the ultrasound department records of one of our study hospitals where details of prenatal diagnosis of neural tube defects have been kept and by reviewing the maternal case notes of women who had affected babies.

We have shown the significant contribution of autosomal recessive syndromes to perinatal mortality in the Pakistani population. It is of note that all the autosomal recessive disorders occurring in this group were in babies born to consanguineous couples, as indeed were half of those in the European population. In Bradford, Gillies *et al* showed that 48% of Pakistani marriages were between first cousins compared with 8% of Indian marriages and 0·5% of non-Asians.[2] A similar pattern has been reported in Birmingham.[3] In our study we have incomplete ascertainment of consanguinity rates because only one of the four hospitals routinely made direct enquiry of consanguinity. The others only recorded it as a positive finding. Accurate information was also available from those couples who had received genetic counselling. Our findings with regard to consanguinity are shown in table 4, which confirms the trend found in Bradford and Birmingham. These observations indicate that consanguinity has an important influence on the excess perinatal mortality in Pakistanis, but a prospective study with complete ascertainment of consanguinity rates in all ethnic groups is required before this can be proved.

After correction of perinatal mortality rates for autosomal recessive syndromes and neural tube defects there still remains an excess of perinatal deaths in the Pakistani population compared with Europeans. This is largely due to a significantly higher incidence of normally formed macerated stillbirths. As more European (72%) than Pakistani (50%) perinatal deaths underwent postmortem examination, relatively more internal malformations may have been missed in the latter group. Furthermore the Pakistani population may have been subject to influences such as higher parity, shorter pregnancy interval, and greater maternal age as described by Lumb *et al,*[1] and to which a higher perinatal mortality may be attributed.[13]

While this study confirmed the higher perinatal mortality rate in the Pakistani population it failed to show a similar significant trend in Indian Asians as reported by Terry *et al.*[14] Explanations for these different observations include differences in both social class and religion between the two Indian populations studied. Most Indians in Birmingham are Punjabi Sikhs in social class 4 and 5,[15] whereas in the study reported here they are mainly Hindu and fall into social class 2 and 3 (J Chapple, personal communication). The appreciable differences in cultural and social classification may partly explain the observed discrepancies between the two studies as there is an association between low social class and higher perinatal mortality rates,[13] and dietary differences may affect maternal nutritional status.[16]

What practical steps may taken to reduce the excess risk in the Pakistani population? It seems unlikely that structure of society and the incidence of consanguinity will change in the immediate future—indeed a recent study has suggested that there is an increasing rate of consanguineous marriage in Pakistanis in West Yorkshire.[17] We should therefore direct our attention towards measures such as vitamin supplementation for Asian women both before and during pregnancy as this may help reduce the contribution from neural tube defects.[18] Preconceptional and genetic counselling, and expert second trimester ultrasound, should be readily available for all Pakistani women. Their risk of having a baby die in the perinatal period as a result of a congenital malformation is one in 150, which is higher than the risk level at which screening for Down's syndrome is currently offered on the grounds of maternal age. Those women who have a consanguineous marriage appear to be at greater risk. In this study of the 14 perinatal deaths that occurred in consanguineous Pakistani families 10 were due to congenital malformations.

Finally we would urge that full assessment including photography, radiology, cytogenetics, and detailed necropsy of babies who die in the perinatal period should be undertaken to enable accurate diagnosis. This would ensure that parents are fully informed of the risks for future pregnancies and enable the relevant prophylactic and diagnostic facilities to be made available to them.

Table 4 *Consanguinity rates (%)*

	Consanguineous	*Non-consanguineous*	*Unknown*
European	1·2	16·9	81·9
Pakistani	25·9	3·7	70·4
Indian	0	23·3	76·7

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