Indian J Pediatr 1991; 58 : 415-419

The Prematurity Paradox of the Small Indian Baby

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The low birthweight Indian baby has remained a perinatal enigma. It is estimated that 13-14 million babies in South East Asia are born at term with growth retardation and low birthweight.[1] The proportion of babies with a birthweight of less than 2500 gm varies widely in different communities. In India it may account for nearly 28% of births. Communities with a high proportion of low birthweight babies born at term also have high stillbirth rates. Differences in the ethnic composition within each country could lead to variation which is not evident when the total population is considered. In these countries the proportion of preterm babies that are growth retarded is high in certain ethnic groups (for instance, in the Indian babies born in Singapore). In the developing world the most important contributing factors are poor socio-economic status with maternal undernutrition resulting in poor nutrition transfer, placental insufficiency and growth retardation. In Singapore and France the correction of these has not resulted in improved median birthweight in the Indian and Malay baby in Singapore nor in those babies born to the mothers of French mixed ancestry or of African origin in France.[1,2] Ethnic variations of the duration of gestation and of perinatal mortality arising from short gestation has been a major concern in Singapore and the region.[3] In Singapore the high mortality was in Indian and Malays whose gestations were significantly shorter than those of the Chinese (Indian 38.8 weeks, Malay 38.7 and Chinese 39.1) (Table 1). In a study in France, (Fig. 1) Papiernik[2] compared the duration of gestation in three groups of patients attending the Antoine Beclere Maternity Clinic. Group A consisted of French women of European ancestry, group B consisted of mothers born in the French Antilles of mixed ancestry and group C mothers were black Africans. The high mortality in the black Africans could not be explained by socio-economic variables alone. When compared to group A within each socio-economic group, groups B and C had shorter gestational periods. Socio-economic differences can modify the distribution of gestational age at delivery of different groups. It was also shown that within equivalent age groups black babies are more mature with mature pulmonary function and fewer cases of hyaline membrane disease.[4,5] There is even earlier maturation of the lecithin/sphingomyelin ratio[6] by one week. Socio-economic differences in the Indians and Malays in Singapore and black races in France were thought to be the

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TABLE 1. Significant Difference in Gestational Age of Delivery Between Chinese, Malay and Indian

	Singapore		
	Gestational age distribution		
	Chinese	Malay	Indian
	N = 6515	N = 1643	N = 771
Gestational age (weeks)	39.09	38.66 ****	38.82 ***
Mean (SD)	(2.04)	(2.4)	(2.1)
% Deliveries before (37, weeks)	6.83	12.7 ****	7.3
% Deliveries 37-42 (weeks)	90.6	84.3	90.7
% Deliveries	2.61	3.10	2.08

Difference from Chinese group ***P < 001; **** P < 0.0005

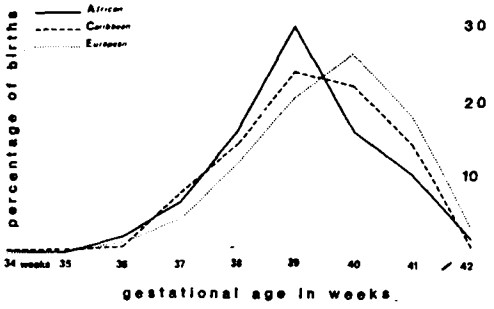

Fig. 1. Gestational age comparison in the three ethnic groups in France : A : Black Africans; B : French women of European ancestry; C : Caribben women of mixed ancestry.

major cause of the shorter pregnancy duration and the higher mortality. It is seen (Table 2) that in the low birthweight group in Singapore, the Malays and the Indians have double the stillbirth rate compared to their Chinese sisters (9.9, 9.7 and 5.1 per thousand respectively), whereas the neonatal mortality for all three races for low birthweight is similar.[7] Within equivalent gestational age groups the Indian babies appear to have matured earlier (Table 3).

In India, the lowest neonatal mortality reported by various authors[8] from different urban and rural populations is in the weight group 2000-2500 gm. Bhargava *et al*[9] conclude that the striking decline in morbidity and mortality in birthweight group 2000-25000 gm has prompted several investigators to suggest 2000 grams as the limit more appropriate for defining low birthweight in India. What is intriguing is that most of these babies are born before 38 weeks of gestation. In a large cohort of patients in India, Bhargava *et al*[10] have shown that in the birthweight group 1501-2000 gm, 30-45% are preterm, the rest being term or post-term.

Nutrition not only of the mother but the grandparents also-affect fetal weight. In developing countries like India immediate corrections of these factors by emigration has not resulted in change of mean birthweight in the same generation.[11] However, anaemia and preeclampsia do influence fetal weight and growth. The placenta is an important element in the maternal fetal unit. Experimental studies[12] show that fetus can enter a state of "Metabolic Nirvana" wasting away and giving its amino acids and glucose to the placenta. A recent study[13] show a close relation between intrauterine weight and placental volume. Economides and Nicolaides[14] from cordocentesis provide

TABLE 2. Perinatal and Stillbirth Rates in the Three Ethnic Groups

Mortality in relation to low birth weight Kandang Kerbau Hospital 1982-1986

	Chinese	Malay	Indian
PNMR	10.2	16.6*	16.6*
SBR	5.1	9.7*	9.9*
< 2.5 kg	6.3	7.9*	8.4*
< 2.27 kg	3.40	4.62*	4.78*
< 1.5 kg	0.59	0.77	0.90

* Significant

TABLE 3. Neonatal Mortality in the Three Races in Low Birthweight Babies

	Neonatal mortality (1982-1986)		
	Chinese	Malay	Indian
< 2.5 kg	7.5	6.1	7.1
< 1.5 kg	42.5	41.0	35.6

data that the reduced glucose supply as a reason for reduced growth and show lower fetal insulin/glucose ratio with elevated fetal glycine/valine ratio in SGA fetuses with fetal hypertriglyceridemia. The figure (Fig. 2) illustrates a model of the starved Indian baby. There are several possible sites of intervention within the realms of advancing technology from simple measures of improving maternal nutrition to hyperalimentation by cordocentesis.

Leela Raman[15] has demonstrated a constant association between hypoglycaemia in the mother and prematurity. Nathienielz[16] and co-workers have shown increased uterine activity in hypoglycaemic pregnant monkeys. This could be a perfect model for the preterm growth retarded infant of South East Asia.

We have to understand how a 3 gm fertilized ovum over 40 weeks becomes a 3000gm infant. 1500gm of that weight develops in the first 30 weeks and in these there is 50gm of fat. The balance 1500gm develops in the next 10 weeks where the remaining 500gm of fat is deposited. This fat seems to be lacking in the low birthweight infant of developing countries. The growing human fetus deflected from its own predetermined growth has an astonishing capacity to return to normal. Intervention measures using glucose, oxygen and aspirin are yet experimental.[12] The crux of the problem is early diagnosis and for this intrauterine growth curves have to be drawn for different ethnic groups. Cross-sectional studies hitherto performed are not of much value as our own studies seem to indicate that the velocity of growth is different in the differing ethnic groups.[15] (Figure 2)

The factors influencing and controlling intrauterine growth are complex. Embryogenesis has its control centre within the genome directing cell division and differentiation. The South Indian fetus has low growth potential which can be adversely affected by environmental factors like nutrition and anemia. In the last trimester of pregnancy the fetus can make metabolic and endocrine responses as if it were an individual receiving parenteral nutrition via the placental conduit. It is the neuronal endocrinological control of fetal tissues and the firing off of signals from the neurosecretory mechanisms that are exciting. Gluckman and colleagues[18] studying insulin somatamedin and somatostatin in metabolism have paved the way to better understanding of the small baby. It is not clear

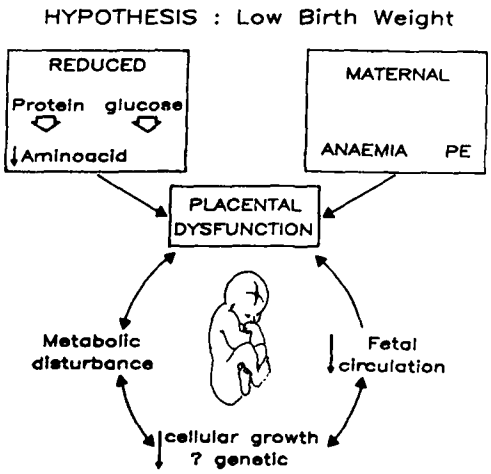

Fig. 2. Model of interacting factors in the low birthweight Indian baby.

whether pulse generators exist in the human as in the sheep model.

A hypothesis is therefore proposed that in some ethnic groups the higher stillbirth rates and perinatal mortality may be related to different intrauterine maturation patterns leading to a postterm or rather "post mature" state in utero. Our preliminary investigations suggest ethnic prediliction to early maturity and this may predispose to a vulnerability to even mild asphyxial insults resulting in perinatal anoxia and mortality. Our observations reveal that fetal distress and meconium release may develop in these racial groups (Black and Indian) before 40 weeks. The clinical importance for the Obstetrician could be that we should increase antenatal surveillance in these groups and deliver them before 40 weeks. The higher stillbirth rate and perinatal mortality may be related to different intrauterine maturation patterns leading to a post term (post mature state) before the accepted standard of 40 weeks. It may therefore become apparent that what has been accepted as the norm will have to be modified in these races. Knowledge is deficient of human fetal growth in different ethnic groups. Genetic factors seem to overwhelm those of social and medical origin. It would seem that there are ethnic groups like the Indians in whom the evidence is accumulating that the velocity of growth is different and in the vast majority of cases low birthweight is due to abnormal growth and shortened gestation. The mortality of the Indian baby is not confined to the perinatal period. Indians are well known to have a higher prediliction to ishaemic heart disease.[19] David Baker[20] has shown a remarkable correlation between weight at birth and the probability of such death to be inversely related. Perinatal and adult medicine are closely related and such mortality can be at last understood by experimental science. The first prospective study on ethnicity, fetal growth and gestation in South-East Asia is under way and will provide clinicians the necessary normograms for improved antenatal care.

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