MATERNAL AND CORD SERUM IMMUNOGLOBULINS IN FOUR MALAYSIAN RACES

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SYNOPSIS

Immunoglobulin G, A and M levels were determined in paired maternal and cord sera of premature, full term and postmature newborns of urban dwelling Chinese, Indian, Malay and full term newborn of the forest dwelling Orang Asli (Malaysian aborigines).

The mean serum IgC level in the full term Orang Asli newborns (1254±441 mg per 100 ml) is comparable to that of the Indians (1211±282 mg per 100 ml) and Malays (1169±286 mg per 100 ml) but these levels are higher than those of the Chinese newborns (1092±270 mg per 100 ml). Statistical analysis indicates a significant dependence of cord serum IgG level on maternal serum IgG level in the Chinese, Indians and Malays. In addition, in Indians the cord serum IgG was significantly dependent at 5% level on the gestation age. The fetomaternal serum IgG level ratios at term were equal to or just less than one. The cord serum IgM levels of the Chinese, Indian, Malay and Orang Asli newborns at term were 11.6 ± 6.5, 12.5 ± 7.3, 10.9 ± 5.8 and 16.7 ± 6.9 mg per 100 ml respectively. Statistical analysis showed absence of correlation between cord serum IgM level and birthweight, gestation age or maternal serum IgM level in Chinese and Malays. In Indians the cord sera IgM level showed a dependence on the birthweight.

Immunoglobulin A was present in 34.6%, 40.5%, 31.6% and 62.5% of full term Chinese, Indian, Malay and Orang Asli newborns respectively.

These observations are discussed in relation to the immunoglobulin levels observed in populations residing in temperate and other tropical regions.

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INTRODUCTION

In newborns the preponderant immunoglobulin is IgG which is chiefly derived from the mother; some IgM and IgA is often present in cord sera but these are synthesized by the fetus[37]; IgD and IgE appear in the circulation after birth. It is postulated that specific Fc receptors on the trophoblastic membrane assist in the transmission of maternal IgG molecule across the placenta and that Fc receptors for immunoglobulin A, M, D and E are absent[6,40]. The level of the immunoglobulins in the newborn varies with several factors which may include gestation age, mothers' health and congenital infections. The IgG levels increase in the fetal circulation with progression of pregnancy, and at term the IgG level in the corm serum may, in some instances, exceed the maternal level[13,14,19]. The immune protection provided by maternal antibody lasts in the infant for over six months but protection is against organisms to which the mother is immune and there is no protection to microorganisms like *Coxsackie viruses, Bordetella pertussis, E. coli, staphylococcus* and *streptococcus*- because these organisms evoke chiefly IgM antibody[43]. Thus, a relationship has been shown between low cord IgG levels and adverse fetal outcome. Furthermore high levels of cord sera IgM and IgA are often associated with congenital infections[1,20].

There are very few studies on the cord serum immunoglobulins of tropical populations outside the African region[33,15,30]. The aim of this work was to provide the basic information on the immunoglobulins of newborns in the four Malaysian races. Malaysia is situated in the tropical zone and the population is subject to regular incidence of protozoal and helminth infections similar to those described for other tropical countries[4].

MATERIALS & METHODS

Maternal and cord sera:

Blood samples for the three Malaysian races (Malays, Chinese and Indians) were obtained from the Department of Obstetrics and Gynaecology at the University Hospital. Maternal blood was taken by antecubital venipuncture one to two weeks prior to delivery. Cord blood was withdrawn from the placental side of the umblical cord within a few minutes of delivery. Blood samples were taken only from healthy mothers and newborns who underwent an uneventful gestation and normal birth. The gestation age was known for the cases studied and ranged from 35 to 43 weeks.

The Orang Asli (Malaysian Aborigines) cord and maternal sera from normal full term deliveries were obtained from the Gombak Orang Asli Hospital. In most cases the gestation age was not known and was estimated from measurements of the fundus height in pregnant females[22].

The blood samples were kept at 4°C overnight after which the serum was separated by centrifugation, and stored at -20°C.

Quantitative determination of Immunoglobulins:

Immunoglobulins A, G and M and specific antisera to them were prepared using previously published procedures[16,45]. The L-chain activity was removed from the immunoglobulins A and M by addition of rabbit anti-IgG immunoadsorbents[3] before preparation of antisera in New Zealand white rabbits. The immunoglobulin was given subcutaneously at 6 to 8 sites on the dorsum, initially in complete and later in incomplete fruend's adjuvant (Difco, Detroit).

Anti-IgG rabbit sera was made specific to the heavy chain by treatment with crude preparations of IgM and IgA. The precipitate formed after maintaining the reaction at 4°C overnight was removed by centrifugation. The procedure was repeated until the anti-IgG sera did not cross react with IgM or IgA on agar.

Anti-IgA and anti-IgM rabbit sera was made specific for the heavy chain by removing contaminants with pooled cord serum immunoadsorbents low in IgM and IgA.

The antibody-agar diffusion plate were prepared and the immunoglobulins quantitated by the radial immunodiffusion technique of Mancini *et al*[27]. The anti-IgG agar plates were incubated for 3 days while the anti-IgM and anti-IgA agar plates were incubated for 5 days before measurement of the diameters of the precipitin rings. Immunoglobulin standards, from Meloy Laboratories, U.S.A. and from W.H.O. were used. The results are expressed in mg per 100 ml serum for comparison with published works and also in International Units per ml (I.U./ml).

The accuracy of the Mancini's method in our hands was estimated by applying a standard serum sample to antibody-agar plates prepared on different days using different batches of antisera. The Coefficient of Variation (C.V.) was calculated from:

$$\left(\frac{\text{Standard deviation}}{\text{mean}} \times 100\right).$$

The C.V. for the assay of IgG, IgA and IgM were 3.5%, 6% and 6.8% respectively. Thus the day to day variation in our tests was small.

Statistics

Comparison of data was performed by analysis of variance and Student's t-test. A multiple regression analysis of the cord serum IgG and IgM on the birth weight and gestation age of the newborns, and the IgG and IgM levels in the maternal serum was carried out using the following mathmatical computation:

$$Y_i = \mu + b_1x_1 + b_3x_3 + E$$

Where Y_i = the immunoglobulin level in the cord serum in mg/100 ml

μ = the common mean

b_1 = regression coefficient of cord immunoglobulin on birth weight

b_2 = regression coefficient of cord immunoglobulin on gestation age.

b_3 = regression coefficient of cord immunoglobulin on the maternal immunoglobulin level

x_1 = birth weight of the newborn in grams

x_2 = gestation age of the newborn in weeks

x_3 = maternal immunoglobulin level in mg per 100 ml serum

E = random error associated with the regression analysis

RESULTS

IgG levels in cord and maternal sera

Chinese: In newborns with gestation age 35 to 43 weeks the mean cord serum IgG concentration ranges from 750 ± 55 to 1270 ± 232 mg/100 ml (Fig. 1). Normal term babies have significantly higher ($p < 0.01$) mean cord serum IgG level than premature ones and the IgG level in normal term babies is of equal magnitude to that in postmature babies (Table 1).

The serum IgG concentration of mothers who delivered after 35 to 43 weeks of gestation, range from 1062 ± 155 to 1463 ± 88 mg/100 ml. The mean serum IgG value of mothers with normal gestation is similar in magnitude to the serum IgG level of mothers with premature gestation and is significantly lower ($p < 0.05$) than the serum IgG level of mothers with postmature gestation (Table 1).

A multiple regression analysis with the serum IgG concentration of the newborn as the dependent variable, and the gestation age, the birth weight and the serum IgG concentration of the mother as independent variables shows that a significant positive correlation exists between the serum IgG level of the newborn with that of the serum IgG level of the mother ($r = 0.38$, $p < 0.01$). There was no correlation between the serum IgG value of the newborn and the birthweight or the gestational age ($r = 0.073$, 0.096 respectively, $p > 0.05$)

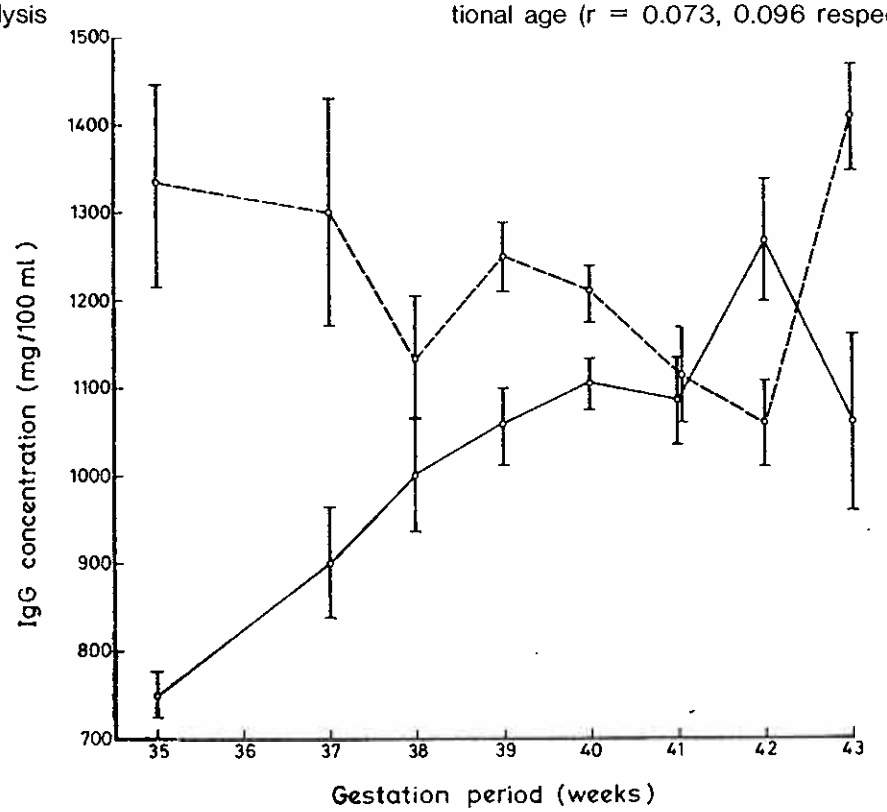

Fig. 1. Fetal ( ) and maternal ( ) serum IgG levels at various gestation periods in Chinese. Bars indicate standard error of the mean.

TABLE 1: Paired maternal and cord serum immunoglobulins levels in premature, full term and postmature newborns of four races

Race	Malay			Indian			Chinese			Orang Asli		
Immuno-globulin / Maturity of newborn (week)	G Cord mother	M Cord mother	A Cord mother	G Cord mother	M Cord mother	A Cord mother	G Cord mother	M Cord mother	A Cord mother	G Cord mother	M Cord mother	A Cord mother
Premature infants 35—37 weeks	1040* 1306 ±298 ±184 (9) (9)	8.8 186 ±5.2 ±77 (17) (17)	248 NO ±93 (17)	935** 1269 ±216 ±287 (23) (23)	9.8** 160 ±4.5 ±57 (34) (34)	238 NO ±78 (32)	845** 1311 ±175 ±345 (14) (14)	11.7 178 ±5 1 ±72 (17) (17)	256 ND ±128 (17)	ND	NO	NO
Full term infants 38—42 weeks	1169*1257 ±286 ±321 (165) (165)	10 9 160 ±5 8 ±65 (161) (161)	37* 270 (1 35 ±84 (25/79) (154)	1211 1310 ±282 ±270 (210) (210)	12.5 168 ±7 3 ±61 (202) (202)	3.1* 230 (1.35 ±73 —17) (32/79) (196)	1092 1181 ±270 ±293 (168) (168)	11 6 177 ±6 3 ±60 (183) (183)	2 9* 286 (1.35 ±105 —10) (27/79) (175)	1254 1256 ±441 ±321 (44) (44)	16.7 268 ±6 9 ±137 (43) (43)	3 1* 263 (1.35 ±114 —17) (30/48) (40)
Postmature infants 43 weeks	1267 1543 ±272 ±423 (3) (3)	8.4 143 ±2.1 ±17 (2) (2)	311 ±45 NO (2)	1217 1217 ±346 ±313 (9) (9)	15.1 162 ±8 7 ±72 (8) (8)	255 ±90 ND (7)	1060 1463* ±140 ±88 (2) (2)	9.3 184 ±4 0 ±66 (7) (7)	261 NO ±61 (6)	ND	ND	ND
Total 35—43 weeks	1190 1264 ±289 ±320 (177) (177)	10.10 163 (170) (170)	268.3 ±84.9 (173)	1164 1300 ±289 ±317 (242) (242)	12 0 166 ±7 0 ±60 (244) (244)	231 ±74 (235)	1072 1194 ±273 ±299 (184) (184)	11.5 177 ±5 8 ±64 (207) (207)	282 ±106 (198)	1254 1256 ±441 ±321 (44) (44)	16.7 268 ±6.9 ±137 (43) (43)	263 ±114 (40)

a = Mean ± Standard deviation in mg per 100 ml; to convert to I.U /ml multiply value by 0 12 for IgG, 1 43 for IgM and 0.66 for IgA. Parenthesis indicates number of observations

b = Mean and range. Parenthesis indicates the ratio of samples with detectable levels over number tested in full term infants

Significant different from the full term newborn value at $^{*}p < 0.05$ or at $^{**}p < 0.01$.

TABLE 2: Multiple Regression analysis of cord serum IgG concentration on the birthweight, gestation age and maternal serum IgG level of newborns of Chinese, Indian & Malay origin

	Chinese				Indians				Malays			
	Y	X_1	X_2	X_3	Y	X_1	X_2	X_3	Y	X_1	X_2	X_3
Mean	1072.3	3021.9	39.5	1193.8	1189.6	3089.8	39.7	1299.6	1164 0	3135.4	39.6	1264.0
Standard deviation	272.9	335.4	3.3	299.0	288.9	356.5	1.6	316.7	289.1	313.0	1.4	320.0
Standard error of mean	20.1	25.2	0.25	22.5	18.5	16.4	0.1	20.3	21.65	23.54	0.11	50.03
Correlation X_i vs Y (r)	—	0.074	0.087	0.388**	—	0.079	0.176	0.380**	—	0.080	0.108	0.234
Regression coefficient	—	0.068	9.04	0.37	—	0.075	26.88	0.372	—	0.079	15.86	0.1015
Standard error of reg. coeff	—	0.056	5.722	0.062	—	0.049	10.926	0.053	—	0.069	15.17	0.032
T value	—	1.218	1.579	5.882	—	1.535	2.463	6.96	—	1.152	1.045	3.170

Y = cord IgG level in newborns in mg%
X_1 = weight of newborns in grams
X_2 = gestation age in weeks
X_3 = IgG levels of maternal serum in mg%

TABLE 3: Multiple regression analysis of cord serum IgM concentration on the birthweight, gestation age and maternal serum IgM concentration of newborns of Chinese, Indian and Malay origin

	Chinese				Indian				Malays			
	Y	X_1	X_2	X_3	Y	X_1	X_2	X_3	Y	X_1	X_2	X_3
	11.51	3195.0	39.45	176.62	12.28	3103.78	39 36	165.70	10.76	3104.6	39.36	162.62
Standard deviation	5.88	334.59	1.49	64.0	6.99	368.18	1.60	60.24	5.66	349.01	1.44	66.50
Standard error of mean	0.41	23.23	0.10	4.440	0.44	23.60	0.10	3.85	0.42	26.04	0.11	4.96
Correlation X_i vs Y (r)	—	0.0703	0.025	0.008	—	0.1753	0.1419	0.1109	—	0.0381	0.0137	0.0822
Regression coefficient	—	0.0012	0.0543	0.0016	—	0.0029	0.4891	0.0127	—	0.0006	0.0672	0.0071
Standard error of reg. coeff.	—	0.0013	0.2810	0.0065	—	0.0012	0.2905	0.0073	—	0.0012	0.3021	0.0064
T values	—	0.9767	0.1937	0.2428	—	2.3432	1.7437	1.7446	—	0.4758	0.2222	1.1202

Y = cord IgM level of newborns in mg%
X_1 = weight of newborns in grams
X_2 = gestation age in weeks
X_3 = IgG levels of maternal serum in mg%

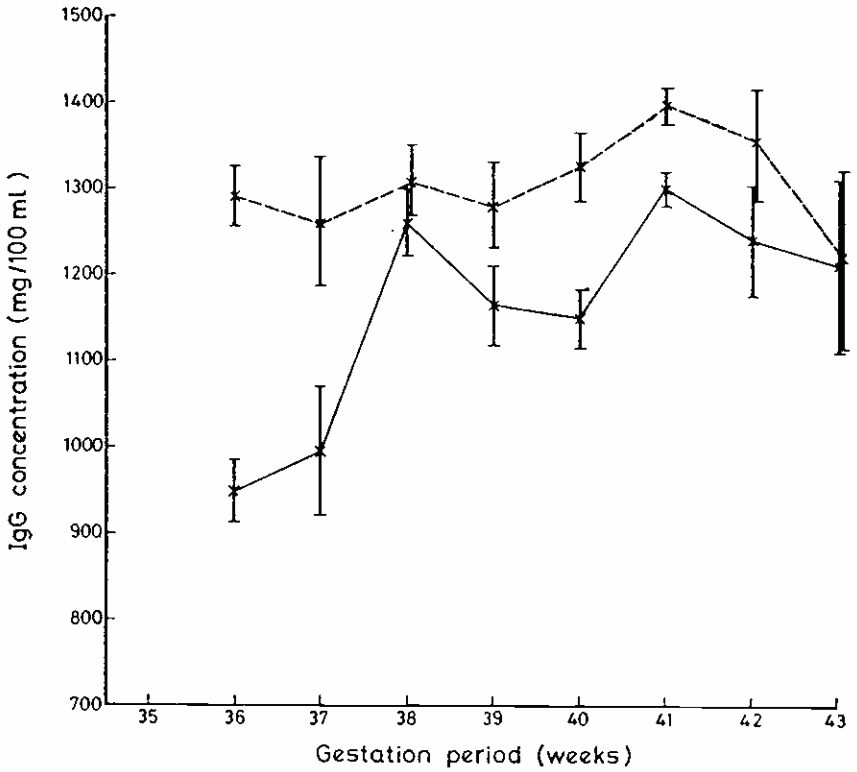

Fig. 2. Fetal ( ) and maternal ( ) serum IgG levels at various gestation periods in Indians. Bars indicate standard error of the mean.

(Table 2). A partial regression coefficient analysis of the cord serum IgG concentration on the birthweight gestation age and the serum IgG level of the mother confirmed that the cord serum IgG value is significantly ($p < 0.01$) dependent on the maternal serum IgG concentration.

The multiple regression equation is given by the following equation:

$$Y = 62 + 0.07\,X_1 + 9.04\,X_2 + 0.037\,X_3$$

Where Y is the cord IgG concentration in mg/100 ml and X_1, X_3 and X_3 are the birthweight in grams, gestation age in weeks and the maternal serum IgG level in mg/100 ml, respectively.

Indians: The serum mean IgG concentration of newborns with gestation age 36 to 43 weeks ranges from 950 ± 35 mg/100 ml to 1297 ± 294 mg/100 (Fig. 2). Table 1 shows that the mean serum IgG level of the premature babies is significantly lower ($p < 0.05$) than the mean level of full term babies and the mean IgG level of postmature infants.

The mean serum IgG levels of mothers who delivered after 36 to 43 weeks gestation ranges from 1217 + 313 to 1394 + mg/100 ml. The mean IgG levels of maternal sera in premature, full term and postmature gestation do not differ significantly from each other (Table 1).

There was no correlation between the cord serum IgG concentration and birth weight, but a small positive correlation ($r = 0.17$, $p < 0.05 > 0.01$) exists between the cord serum IgG concentration and the gestation age. A significant positive correlation ($r = 0.399$, $p < 0.01$) was observed between the cord serum IgG level and the maternal serum IgG level. The partial regression coefficient of cord serum IgG concentration on the birthweight, gestation age and maternal serum IgG level show that the IgG level is significantly dependent on the gestation age ($p < 0.05 > 0.01$) and on the maternal serum IgG level ($p < 0.01$) (Table 2).

The multiple regression equation relating the change in cord serum IgG concentration (Y), with birthweight (X_1), gestation age (X_2) and maternal serum IgG level (X_3) is given as follows:

$$Y = (-570) + 0.07\,X_1 + 26.88\,X_2 + 0.37\,X_3$$

Malays: The mean serum IgG concentration of newborns of 36 to 43 week gestation ranges from 841 ± 30 to 1266 ± 272 mg/100 ml (Fig. 3). The mean cord serum IgG concentration of full term infants is not significantly different from the mean cord serum IgG level of premature or postmature infants.

The serum IgG concentration of mothers who delivered after 36 to 43 weeks gestation range from 1217 to 1543 ± 423 mg/100 ml. The maternal IgG concentration at premature, normal full term or postmature gestation do not differ significantly from each

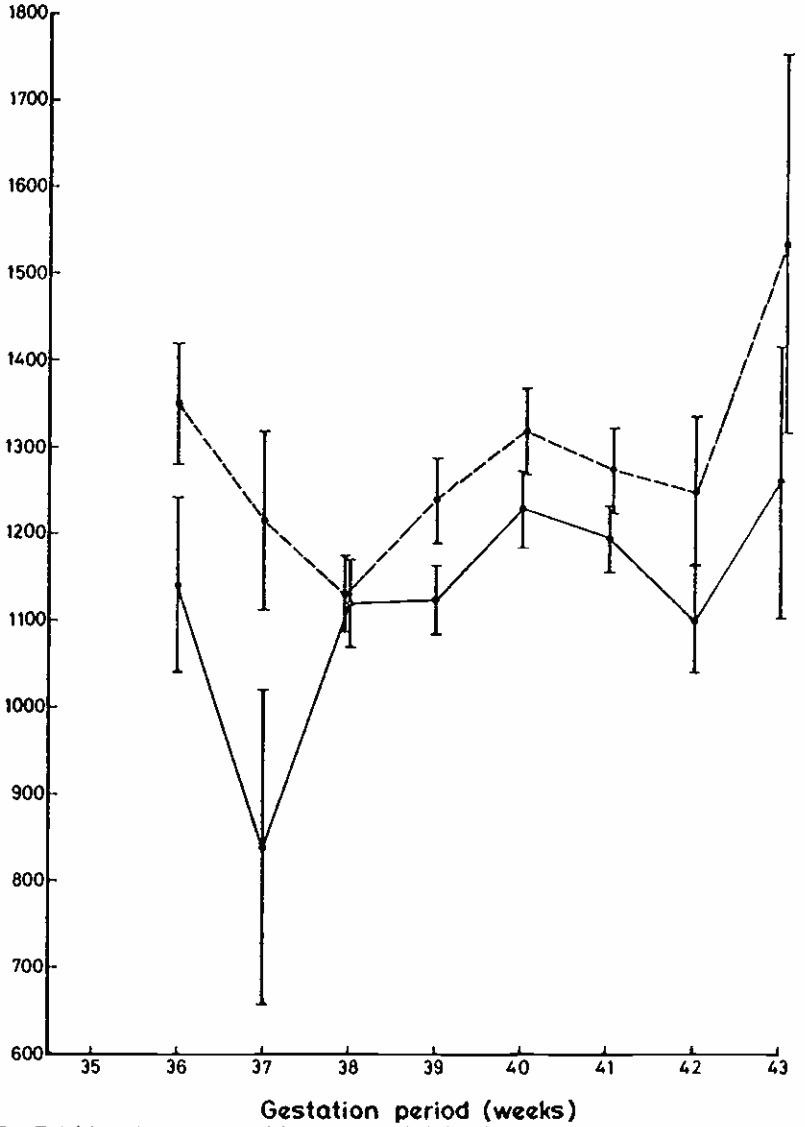

Fig. 3. Fetal ( ) and maternal ( ) serum IgG levels at various gestation periods in Malays. Bars indicate standard error of the mean.

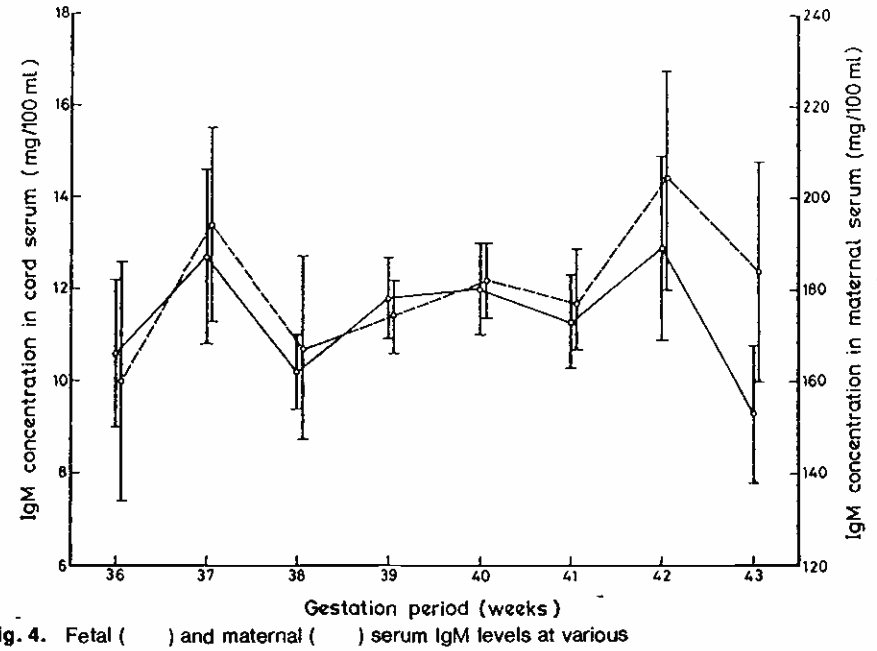

Fig. 4. Fetal ( ) and maternal ( ) serum IgM levels at various gestation periods in Chinese. Bars indicate standard error of the mean.

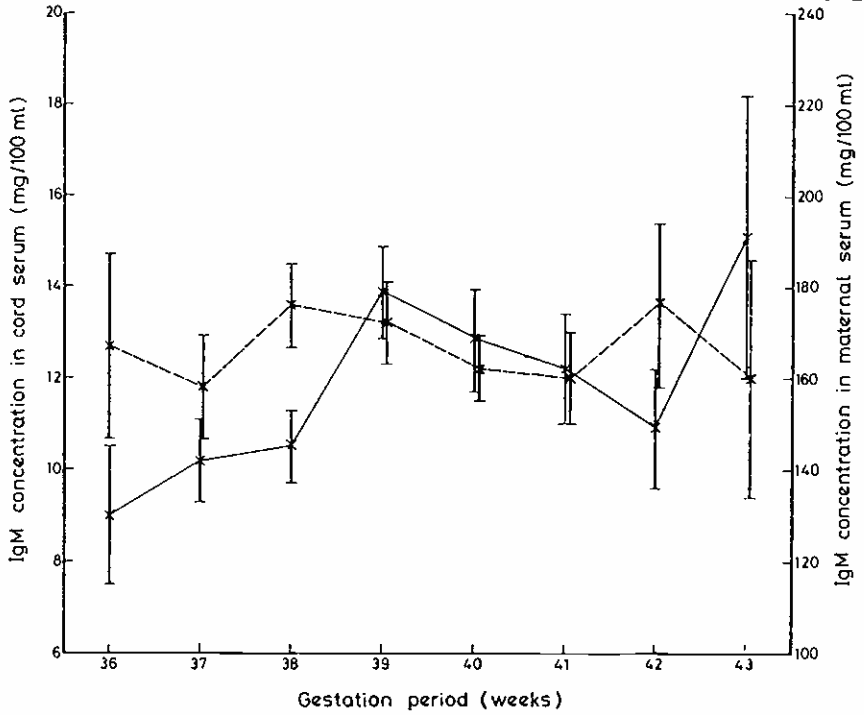

Fig. 5. Fetal ( ) and maternal ( ) serum IgM levels in Indians at various gestation periods. Bars indicate standard error of the mean.

other (Table 1).

There is no correlation between the cord serum IgG level and the birthweight or the gestation age ($r = 0.05$ or 0.107 respectively $p > 0.05$) but there is a significant positive correlation ($r = 0.234$, $p < 0.01$) between the cord serum IgG concentration and the maternal serum IgG concentration (Table 2).

Analysis of the partial regression coefficient of cord serum IgG concentration on birthweight gestation age and the maternal serum IgG level, shows a significant dependence ($r = 0.1015$, $p < 0.05$) of cord serum IgG level on maternal serum IgG level. The multiple regression equation relating cord serum IgG level (Y) to birthweight (X_1), gestation age (X_2) and maternal serum (X_3) is given as follows:

$$Y = 153 + 0.08\,X_1 + 15.9\,X_2 + 0.1\,X_3$$

IgM levels in cord and maternal sera

Chinese: The mean serum IgM levels of newborns of gestation age 36 to 43 weeks range from 9.3 ± 4.0 to 12.9 ± 6.5 mg/100 ml (Fig. 4). The cord serum IgM concentration in full term newborn is similar in magnitude to levels in premature and postmature babies (Table 3).

The mean serum IgM levels of mothers who delivered after 36 to 43 weeks of gestation, range from 160 ± 75 to 205 ± 77 mg/100 ml. The serum IgM concentration of mothers with premature, full term and postmature gestation do not differ significantly from one another (Table 5).

The correlation coefficients of a multiple regression analysis indicates that there is no significant correlation between the cord serum IgM concentration with the gestation age, the birthweight or the maternal serum IgM concentration ($r = 0.0703$, 0.025 and 0.00082 respectively) (Table 3).

Indians: The mean cord serum IgM concentration in newborns aged 36 to 43 weeks gestation, range from 9.0 ± 15.1 ± 8.7 mg/100 ml (Fig. 5). The mean cord serum IgM level of premature babies is significantly lower ($p < 0.01$) than the mean IgM level of full term and the postmature babies (Table 1).

The serum IgM levels of mothers who delivered at 36 to 43 weeks gestation range from 158 ± 511 to 177 ± 62 mg/100 ml. The maternal serum IgM levels in premature, full term and postmature gestation are not significantly different from each other (Table 1).

The correlation coefficients show that there is small positive correlation ($p < 0.05 > 0.01$) between the IgM level of the newborn with the birthweight ($r = 0.17$) and gestation age ($r = 0.14$). No correlation ($r = 0.11$, $p > 0.05$) was noted between cord serum IgM level with that of maternal serum IgM concentration (Table 3).

The partial regression coefficient of cord serum IgM concentration on birthweight, gestation age and maternal serum IgM levels are 0.0029, 0.4891 and 0.0127 respectively and indicate that cord serum IgM level is essentially dependent ($p < 0.05$) on the birthweight and not on the toher two parameters. The

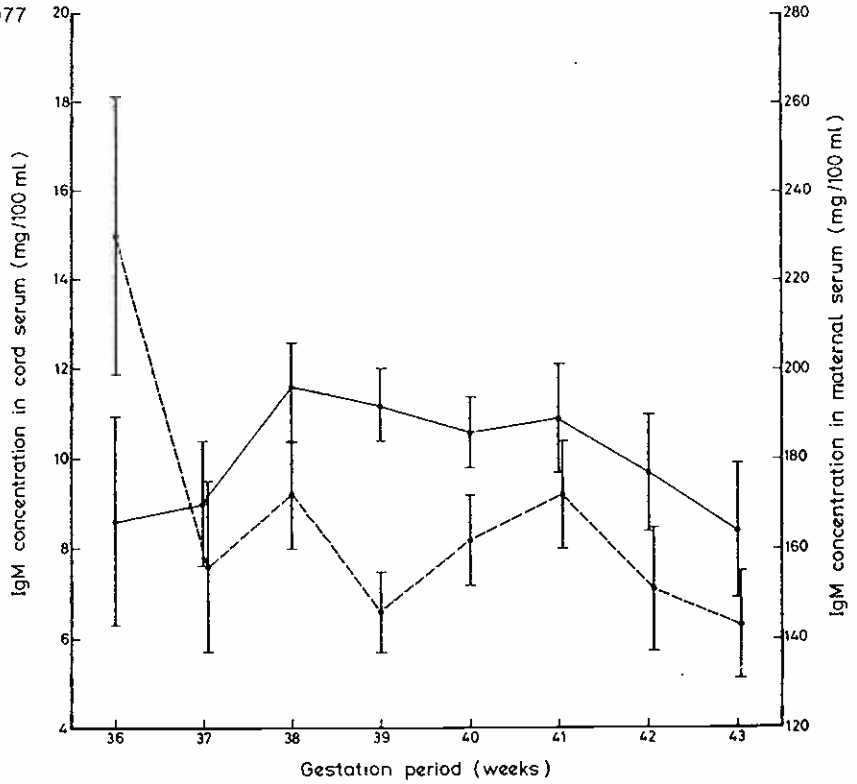

Fig. 6. Fetal ( ) and maternal ( ) serum IgM levels in Malays at various gestation periods. Bars indicate standard error of the mean.

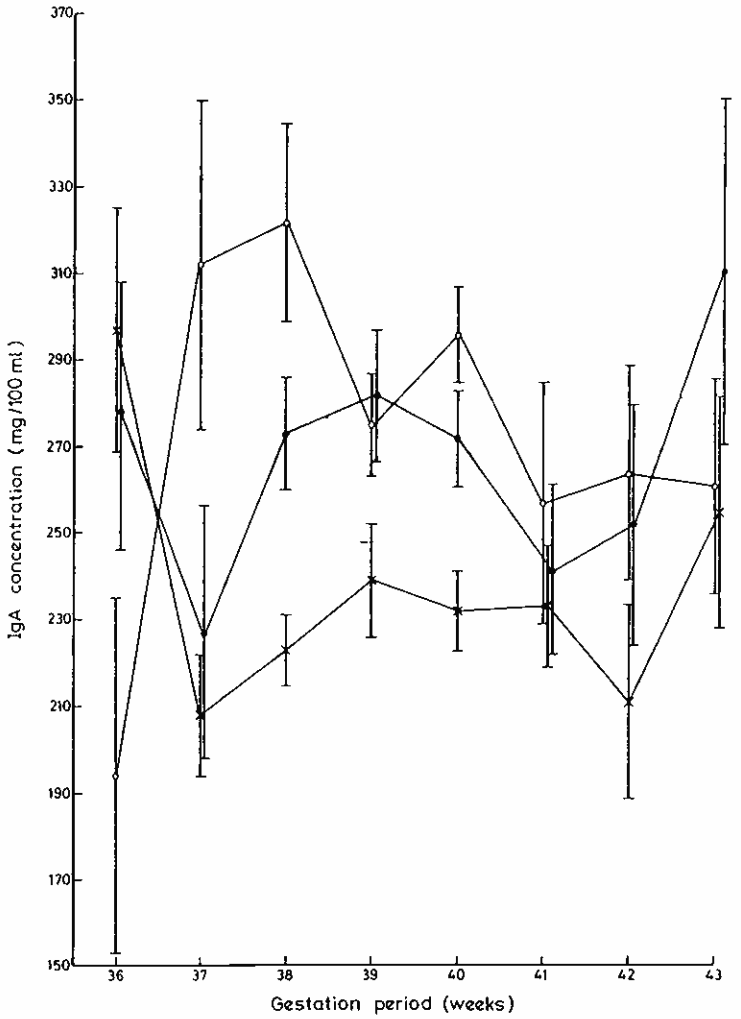

Fig. 7. Maternal serum IgA levels in Chinese (0—0), Indians (x—x) and Malays (0—0) at various gestation periods. Bars indicate standard error of the mean.

multiple regression equation is

$$Y = (-17.8) + 0.0029\,X_1 + 0.4891\,X_2 + 0.012\,X_3$$

Malays: The mean serum IgM levels of the newborns from 36 to 43 weeks gestation range from 8.0 ± 6.0 to 11.6 ± 6.6 mg/100 ml (Fig. 6). The mean cord serum IgM concentration of premature full term and post-mature newborns (8.4 + 2.1 mg/100 ml) do not differ significantly ($p > 0.05$) from one another (Table 1).

The serum IgM levels of mother who delivered at 36 to 43 weeks gestation range from 143 ± 17 to 230± 81 mg/100 ml. The maternal serum IgM levels in premature, full term and postmature gestation are not significantly different from each other (Table 5).

The correlation coefficients show an absence of correlation between cord serum IgM concentration with gestation age ($r = 0.038$), birthweight ($r = 0.0137$) or maternal IgM concentration ($r = 0.0822$) (Table 3). The partial regression coefficient of cord serum IgM concentration on the above three independent variables are 0.006, 0.0671 and 0.0071 respectively, and confirm that there is no correlation between cord serum IgM level and the three parameters. The multiple regression equation is

$$Y = 5.1 + 0.0006\,X_1 + 0.0671\,X_2 + 0.0071\,X_3$$

Racial variations

Cord serum IgG levels of Indians, Malay, and Orang Asli newborn of gestation 35 to 43 weeks are of similar magnitude and their levels are significantly higher ($p < 0.01$) than the cord serum IgG concentrations of Chinese (Table 1).

The total serum IgG levels of Indian and Malay mothers do not differ significantly but the serum IgG levels of Indian ($p < 0.01$) and Malay ($p < 0.05 > 0.01$) differ significantly from the levels observed in Chinese mothers. The mean maternal IgG concentration of the Orang Asli mothers is similar in magnitude to the levels observed in Chinese, Indian and Malay mothers.

The total mean cord serum IgM levels of newborns of gestation age 35 to 43 weeks for Chinese, Malay and Indian is of similar magnitude. The serum IgM level in Orang Asli newborn is significantly higher ($p < 0.01$) than the levels observed in the other races. The total mean serum IgM levels of mothers of the 3 races are of similar magnitude but their levels are significantly lower than those observed in the Orang Asli mothers.

It was noted that 34.6 percent of 79 Chinese, 40.5 percent of 79 Indians, 31.6 percent of 79 Malays and 62.5 percent of 48 Orang Asli possessed detetable IgA levels in the cord sera (Table 1) and the mean cord serum IgA levels ranged from 2.9 to 3.7 in the four races. Figure 7 illustrates that there is no difference in the maternal serum IgA level at mature, full term or post-mature gestation in the Chinese, Indians and Malays.

The maternal serum IgA level of Orang Asli with full term gestation is of equal magnitude to the mean serum IgA levels observed in Chinese, Indian or Malay mothers with normal term gestation (Table 1).

Levels in Pregnant and Non-pregnant females:

A comparison of the serum IgG levels of non-pregnant and all pregnant females show that the serum IgG levels (a) remained unchanged in Malays, (b) were significantly lower ($p < 0.05$) in pregnant Chinese, (c) were significantly higher ($p < 0.05$) in pregnant Indians, and (d) were significantly reduced ($p < 0.01$) in the Orang Asli (Table 4).

The maternal serum IgM levels when compared to serum levels non-pregnant females are significantly lower in Chinese, Indians and Malays, while the levels

TABLE 4: Immunoglobulin G, M and A levels in pregnant and non-pregnant females

Race	IgG		IgM		IgA	
	Pregnant females	Non-pregnant females	Pregnant females	Non-pregnant females	Pregnant females	Non-pregnant females
Chinese	1194 ± 299[a] (184)	1268 ± 266 (23)	176 ± 64 (207)	202 ± 63* (42)	281 ± 110* (98)	225 ± 70 (26)
Indian	1300 ± 317* (242)	1206 ± 163 (17)	166 ± 60 (244)	227 ± 80* (32)	235 ± 74* (234)	199 ± 57 (31)
Malay	1264 ± 320 (177)	1265 ± 184 (45)	162 ± 67 (180)	215 ± 70*** (36)	268 ± 85** (173)	197 ± 90 (19)
Orang Asli	1256 ± 321*** (44)	1845 ± 440 (46)	268 ± 137 (43)	263 ± 64 (43)	264 ± 114 (40)	412 ± 112*** (42)

[a]mean = standard deviation in mg/100 ml; to convert to IU/ml multiply by 0.12 for IgG, 1.43 for IgM and 0.66 for IgA. Parenthesis shows number of observations T test between values of pregnant and non-pregnant female.
* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

are unchanged in the Orang Asli.

Table 4 shows that the maternal serum IgA levels relative to non-pregnant females are reduced ($p < 0.01$) in Orang Asli and elevated in Chinese ($p < 0.01$), Malays ($p < 0.01$) and Indians ($p < 0.05 > 0.01$).

Fetal-Maternal Ratios:

The IgG Fetal-Maternal ratio is lower in premature than in normal term and postmature gestation in the 3 races studied. With the exception of 42 weeks in the Chinese, the fetal maternal ratio is less than one in all instances in the 3 races. Only in the full term Orang Asli newborns and the postmature Indians the ratio is practically equal to one (Table 5).

TABLE 5: Fetal-maternal ratio of serum IgG concentration in premature, full term and postmature gestation periods

Maturity (weeks)	Race			
	Malay	Indian	Chinese	Orang Asli
Premature (35—38 weeks)	0.80	0.78	0.64	—
Full term (38—42 weeks)	0.93	0.92	0.93	0.998
Postmature (43 weeks)	0.82	0.999	0.72	—

DISCUSSION

Immunoglobulin levels in fetal and maternal sera

Immunoglobulin G: The immunoglobulin increases in the fetus from the first few weeks of life and at term reaches levels equal to or at times, greater than the serum IgG level of the mother[7]. The biologicalsignificance of the variable transmission of serum IgG to the young in different populations is not clear. In Malaysians feto-maternal ratio in four races was equal to or lower than one. Our findings are in agreement with the observations on the Taiwanese[47], and Africans[15,30] but are at variance with those of Kohler & Farr[26] and Cochrane & Good[12] who reported that the feto-maternal ratios in Caucasians with normal deliveries were greater than one. The serum IgG are significantly higher than maternal serum concentrations in vaginal delivery as opposed to elective Caesarian birth[11, 25]. These authors suggest that maternal IgG transfer occurs passively in the fetus and that at parturition the contractions of labour are physiologically instrumental in causing further materno-fetal transfer of IgG resulting in significant elevation of cord over maternal IgG level. However, other reports suggest that the differences between maternal and fetal IgG levels may be produced by an active transport mechanism[26], possibly one of pinocytosis[7] specific for IgG. Both these hypothesis do not help to explain the variable, particularly the lower-than-one feto-maternal ratios in different Afro-asian populations. A possible explanation for these differences among the temperate and the tropical residing populations may be that the maternally derived fetal serum IgG and catabolically eliminated faster in the tropics[36], but this aspect requires further study.

Since cord serum IgG is chiefly of maternal origin, a correlation between the IgG concentration in the mother and cord sera would be expected. We confirm in 3 Malaysian races the observations made in Americans [42, 2]; and Europeans[5], that a correlattion which was independent of the birthweight and gestation age existed between the maternal serum IgG level and the fetal serum IgG level. The dependence of cord serum IgG concentration on the maternal IgG level has been demonstrated in newborn who lack IgG of agammaglobulinaemic mothers[9]. Furthermore, the cord IgG level was elevated in mothers with hypergammaglobulinaemia[33].

The cord sera IgG was not correlated to the birthweight and gestation age in full term caucasian babies[41, 5] and our data for the Chinese and Malay supports these. However, in Indian the partial regression coefficient analysis showed a significant correlation at 5% level of cord serum IgG with the gestation age.

Premature newborns had lower cord serum IgG levels in contrast to full term Chinese and Indian newborns. This suggests a progressive increase of cord serum IgG concentration in growing fetuses. Similar observations have been made for the British[21], the Greek[34] and the Australians[23, 24]. In Malays, an unexplainable high IgG level at 36 weeks gestation obscured the difference in IgG level in the premature and mature infants. However, the IgG level at 37 weeks, did differ significantly when compared to IgG levels at other periods of gestation. The cord serum IgG levels of the Chinese newborns differ significantly with the Orang Asli newborns, but the Indian and Malay newborns had cord IgG levels similar in magnitude to those of the Orang Asli.

Immunoglobulin M: Since maternal IgM is not transmitted to the young[19] the cord serum IgM is entirely of fetal origin[18, 44]. Small amounts of IgM are usually synthesised by the fetus and thus variable levels may be detected in cord sera[44, 8, 32, 46]. The total mean cord serum IgM levels of the Chinese, Indian, Malay and Orang Asli newborns are 11.5 ± 5.9 (6.8% of adult

value), 12.3 ± 7.0 (7.4%), 10.8 ± 5.7 (6.6%), 16.7± 6.9 (6.3%) respectively. In other populations like Hawaiians[46] Taiwanese[47], Americans[44], cord serum IgM values range from 5 to 15 percent of the adult serum levels and the Malaysian values are well within this range. The relatively higher cord serum IgM levels in the Orang Asli in contrast to the other Malaysian races is suggestive of a greater fetal antigenic stimulation as a consequence of high rate of protozoal and helminth infections prevalent in this community[4].

Caucasian premature babies had lower cord sera IgM level than mature babies, but at term, the IgM levels were not dependent on the gestation age[23, 24, 41, 42]. In our study, the mean cord IgM levels of the premature, full term and postmature newborns of the Chinese and Malays were not significantly different. In Malay and Chinese newborns the cord IgM level was not dependent on the birthweight and gestation age or the maternal serum IgM level. In contrast, however, the premature Indian newborns had a mean cord serum IgM level which was significantly lower than the mean cord serum IgM level of full term and postmature infants. The newborn also showed a significant correlation between the cord serum IgM and the birthweight. The regulatory function involved in the production of fetal proteins including IgM is not well understood[36] and therefore we are unable to comment on these observations.

Variations in the maternal IgM level have no influence on the fetal serum IgM level[32], since IgM is not transmitted to the fetus[19]. In Malaysians, a correlation between the maternal and fetal IgM was not found in the four races. The cord sera IgM levels may depend on variable factors like the genetic capacity of the fetus to synthesise IgM and subclinical intrauterine antigenic stimulation.

Immunoglobulin A: The fetus in utero, although able to synthesise high levels of IgA under strong antigenic stimulation (Steihm et al, 1966) is usually born with very low serum IgA levels[38, 10, 47]. Using the Mancini's[27] immunoassay technique which has the minimum limit of sensitivity for IgA of 1.35 mg/100 ml, we found that 34.6, 40.6, 31.6 and 62.5 percent of the Chinese, Indians, Malays and Orang Asli full term newborns had demonstrable IgA levels. The absence of IgA in some cord sera may be due to lack of antigenic stimulation or transient IgA deficiency. These IgA values are within 1 to 2 percent of maternal IgA level[10, 38, 47]. However, Faulkner and Borella[17] using a sensitive radio-immunoassay method found low IgA levels in all the cord sera they analysed. Intra-uterine infections may raise the level of cord sera IgA and IgM substantially[20, 29, 39].

Immunoglobulins in pregnant and non-pregnant females

The IgA levels, during pregnancy were significantly lower in the Chinese, significantly higher in the Indians and unchanged in the Malays. The IgM levels were significantly lower, while the IgA levels were significantly higher in the pregnant females of the three races. The Orang Asli had greatly reduced IgG levels, significant lowering of IgA levels and unaltered IgM levels during pregnancy. Thus a clear pattern was not observed.

Variations in maternal serum immunoglobulin levels have been reported in Gambians[35], Nigerians[31] and Caucasians[28]. IgG levels were found to be decreased while the IgM and IgA vary with different populations.

No specific explanation has been provided for these variations. The increase in IgA levels in the pregnant Chinese, Indians and Malay females may be related to the altered physiology of the pregnant females of these races particularly by the mediation of pregnancy hormones on the antibody-synthesising mechanism.

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