**DISCUSSION**

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The present study was carried out to evaluate the cord serum Ig M levels of 24 fullterm intrauterine growth retarded babies and their respective mothers. The study was conducted at M.L.B. Medical College, Jhansi, in the Department of Paediatrics from May, 1990 to June, 1991. The primary aim of the study was to evaluate the value of cord serum Ig M as a screening investigation for perinatal infection in IUGR babies who have no obvious cause of growth retardation. Further, an attempt was made to establish a relationship between cord serum Ig M level and birth weight in IUGR babies. The characteristics viz. height, head circumference and chest circumference of IUGR babies were also compared with control group.

Besides evaluating serum Ig M level a thorough physical examination of the newborn was done. The gestational age was calculated by counting the number of completed weeks from the first day of last menstrual period till the date of delivery, and also by using a scoring system for the assessment, which is based on certain morphological and neurological characteristics present in the newborn (Dubowitz et al 1970). Statistical analysis was done to derive mean ± SD values of Ig M, birth weight and other anthropometric measurements.
Values obtained in IUGR and control group of babies were compared by using student's 't' test and the significance of the difference ('p' values) was noted from the 't' distribution table. Based on observations depicted in (Table 1-9), various inferences have been drawn which are discussed.

**BIRTH WEIGHT AND GESTATIONAL AGE DISTRIBUTION:**

A total of 34 cases were examined in this study. All the cases were fullterm as confirmed by the gestational age. Considering the weight for age status as suggested by Singh et al (1974), the cases were further grouped as small-for-gestational-age (SGA) and appropriate-for-gestational-age (AGA) (Table- 1). The study group comprised of SGA (IUGR) and 10 AGA (Normal) babies. Chaturvedi et al (1989) had also grouped their cases into appropriate-for gestational-age and small-for-gestational-age groups following the criteria laid down by Singh et al (1974).

**SEX DISTRIBUTION:**

The sex of the child was given due consideration and accordingly the study group comprised of 12 (50.00%) male and 12 female (50.00%) cases (Table- 2). Control group comprised of 2 (20%) male and 8 (80%) female cases. An effort was made to observe the difference, if any, between the two groups, regarding the Ig M level. The Ig M values in male and female babies of the study group were almost the
same i.e. 32.83 ± 12.99 mg/dl in male and 37.91 ± 12.16 mg/dl in female. Although, the corresponding values in control group were 14.00 ± 0.00 and 20.50 ± 8.47 mg/dl, yet on statistical analysis, the difference between these values proved to be non-significant (70.05). It was thus, inferred that sex of the child had no contribution towards changes in cord Ig M. Chaturvedi et al (1989) found no significant difference between the male and female babies in IUGR and control groups. Also, Lars et al (1978) did not find significant difference in the Ig M values of male and female babies when individuals in both the sex groups had suffered from intrapartum asphyxia and metabolic acidosis.

DISTRIBUTION OF CASES ACCORDING TO BIRTH WEIGHT

CENTILE POSITION

Considering the criteria of birth-weight-for-gestational-age as suggested by Singh et al (1978), cases were further grouped into mild IUGR (babies whose birth weight fell between 3rd and 10th percentile of the standard) numbering 16 (66.66%) and severe IUGR (babies whose birth weight fell below 2 SD or 3rd percentile of the standard) numbering 3 (12.51%). The third group comprised of 5 (20.83%) cases whose birth weight was more than 10th percentile of the standard (Table-4). Chaturvedi et al (1989) had also grouped their cases into mild IUGR and severe IUGR following the
criteria laid down by Singh et al (1978). In the present study the predominant group was mild IUGR consisting of 16 (66.66%) cases. Chaturvedi et al found that the predominant group in their sample had birth weight more than 10th percentile.

ANTHROPOMETRIC PROFILE OF CASES:

An effort was made to establish relationship between the anthropometric characteristics of control and study groups. On statistical analysis (Table - 5) it was seen that IUGR group of infants in comparison to control cases were lighter in weight, had shorter length and presented with smaller head and chest circumferences. The mean birth weight of IUGR group of babies was 2.2 kg whereas it was 3.1 kg in control cases. The difference between IUGR infants and control cases was statistically significant (p \( \leq 0.001 \)) in all the anthropometric measurements. These results are consistent with the findings of Low et al (1978).

PERINATAL STRESS FACTORS:

Some of the deliveries pass off uneventfully, while others are affected by perinatal stress factors and these exert their deleterious effect on the fetus in one way or the other. In 67 (73.63%) affected newborns of the present study, perinatal stress factors were known while in
24 (26.37%) affected newborns no stress factor could be recognised. The perinatal stress factors which could be identified in the present study were maternal hypertension and pre-eclamptic toxemia (54.94%), ante-partum hemorrhage (14.29%), severe anaemia and heart problem (4.40%). All those cases presenting with manifest perinatal stress were rejected from the present study. Only 24 (26.37%) cases of IUGR who had no manifest perinatal stress factors operating, were considered for the present study (Table-6).

The probable cause of growth retardation of fetus in these cases was intrauterine infection. In 21 out of 24 IUGR cases, Ig M level was raised with a mean of 35.37 ± 13.03 mg/dl, while the control group had mean Ig M level of 19.20± 8.00 mg/dl (Table-8). Hardy et al (1969) had found raised Ig M (≥ 30 mg/dl) in 132 cases who had perinatal infections while control group had low Ig M value (20 mg/dl). The observations of this study are in close proximity to the present study.

**COMPARISON OF Ig M WITH DIFFERENT GROUPS:**

The observations were further separated into 4 groups, according to the level of cord serum Ig M (Table-7). Chandra et al (1972) established a normal range of 4-22 mg/dl for cord blood Ig M with a mean of 6.80 ± 3.90 mg/dl. Levels above 20 mg/dl were designated as elevated by Steihm et al
(1975). Taking this as the criterion, it was observed that 87.10% of the babies in the study group had levels exceeding 20 mg/dl, while only 40% in the control group had levels above 20 mg/dl. When the criterion for elevated cord Ig M was taken as ≥ 30 mg/dl (Hardy et al, 1969), it was seen that 54.17% of the babies in the study group had levels exceeding 30 mg/dl and none in the control group had levels above 30 mg/dl. Chaturvedi et al (1989) observed the value of Ig M above 30 mg/dl in 22.80% in the study group and none in the control group.

The mean maternal serum Ig M level was 170.66 ± 62.39 mg/dl in the study group as compared to 98.88 ± 21.43 mg/dl in the control group, the difference was statistically significant (p < 0.01) (Table 8). Barring Group IV cases it is evident from Table 7 that the cord Ig M levels increased with the rise in mean maternal Ig M level in the study group while the control group did not follow the same trend. Raghvan et al (1976) found Ig M levels in cord blood and maternal blood as 11.38 ± 6.76 IU/ml and 366.70 ± 226.60 IU/ml respectively in normal babies. They found high cord Ig M only in one case and 3 maternal sera showed Ig M above 900 IU/ml. Excluding these cases, there was no correlation between Ig M levels of cord and maternal sera. That supports the present study. Chaturvedi et al (1989) had observed maternal serum
Ig M level of 142.42 ± 60.96 mg/dl in the study group as compared to 100.2 ± 33.63 mg/dl in the control group; the difference was statistically significant (p < 0.01). They found that in 1 case alone, the cord Ig M level did not rise with the rise in maternal Ig M level.

RELATION OF Ig M WITH BIRTH WEIGHT:

When the babies with IUGR were re-distributed according to birth weight (Table-9) into different centiles groups (Singh et al., 1974), it was seen that 3 babies had birth weight below 3rd percentile (Group A). These babies had mean cord and mean maternal Ig M levels of 38.00 ± 9.93 mg/dl and 134.66 ± 32.42 mg/dl respectively. The mean serum Ig M levels of cord and maternal blood in a similar group of cases was observed as 11.30 ± 15.95 mg/dl and 83.20 ± 85.98 mg/dl by Chaturvedi et al (1989).

Group B (birth weight between 3rd and 10th percentile) consisted of 16 IUGR babies in the present study. These had mean Ig M levels of 33.06 ± 12.66 and 162.25 ± 63.96 mg/dl in cord serum and mothers serum respectively. In this group of cases cord serum Ig M level was slightly lower than that seen in Group A cases. However, Chaturvedi et al (1989) found higher values of Ig M i.e. 25.70 ± 36.96 mg/dl and 156.90 ± 76.50 mg/dl in babies and mothers serum respectively in a similar group of cases which were higher than those observed in group A babies of their series.
Group C consisted of 5 cases with cord and maternal serum levels of 41.20 ± 12.81, 219.20 ± 43.66 mg/dl respectively. Barring cord serum values in Group B, it was observed that cord serum Ig M level increased with the increase in birth weight, (Table-9). The mean maternal serum Ig M level did, however, follow a clear rising trend with the increase in birth weight. Since cord Ig M values could be influenced by gestational age and duration of infection, these factors were controlled in the present study by excluding preterm babies and those born to mothers with obvious history or findings on examination, suggestive of infection in the last trimester of pregnancy.

Growth retarded babies had mean cord serum Ig M levels (35.37 ± 13.03 mg/dl) almost double that of the control group (19.20 ± 8.00 mg/dl) (Table-8). Bharadwaj et al (1987) has reported a similar finding. These observations are also in conformity with those of Chaturvedi et al (1989) who obtained significantly higher levels of cord serum Ig M in full term IUGR babies (26.80 ± 29.35 mg/dl) in comparison to full term normal babies (13.70 ± 5.40 mg/dl). Recently Sharma et al (1991) has observed high mean Ig M values both in full term IUGR and full term normal babies i.e. 46.00 ± 7.11 mg/dl and 34.00 ± 15.14 mg/dl respectively. This may possibly be attributed to an increased incidence of sub-clinical intrauterine infection in their cases.
The mean cord serum Ig M level of the control group (19.20 ± 8.00 mg/dl) of the present study compares well with that of Singh et al (1978) with mean cord Ig M (18.71 ± 12.75 mg/dl). These findings are further comparable to those (11.38 ± 6.76 mg/dl) reported by Raghvan et al (1976).

In the present study, only 40% neonates of the control group had raised Ig M values (< 20 mg%). The high level of Ig M in the cord blood of control group baby was found to be 5% by Stiehm et al (1966). Hardy et al (1969) found raised Ig M level (< 20 mg%) in 5-20% caucasion and 8-11% Negro full term normal babies. Bharadwaj et al (1987) found raised level in 4.44% control cases.

The highest mean cord Ig M in control cases observed in the present study was 30 mg/dl, while Sharma et al (1991) observed a high mean value of 34.00 ± 15.14 mg/dl Ig M in term appropriate for gestational age babies. The high value could be explained on the basis of intrauterine infection.

The overall incidence of elevated cord serum Ig M (< 20 mg/dl) in consecutively born babies varied from 0.2 to 6.3% in some of the earlier studies (Alford, 1971 and Lechtig et al, 1971, 1978), while it was much higher 87.50% in the present study (Table- 7). The reason being that the present study included a very selective group of high risk babies. Chaturvedi et al (1989) found an incidence of 51.40%
in which Ig M level was $\geq 20$ mg/dl. In contrast to earlier studies, Lechtig et al (1971, 1978) found 47.80% neonates to have elevated cord serum Ig M levels ($\geq 20$ mg/dl) in a random selection of babies from poor income group in a rural area of one developing country (Guatemala).

About 54.17% IUGR babies in the present study had cord serum Ig M levels above 30 mg/dl and none in the control group achieved a level above 30 mg/dl (Table- 7). Chaturvedi et al (1989) had found raised value ($\geq 30$ mg/dl) in nearly 25% of babies of IUGR group and none in the control group. Hardy et al (1975) observed only 5% of neonates achieving Ig M values above 30 mg/dl. Hence, the findings in a selective group of cases in the present study are significant.

Alford (1969) detected specific intrauterine infection in 39% babies with raised cord Ig M levels, suggesting that roughly 1/3 babies with elevated Ig M levels in cord blood may actually have had perinatal infection. However, this could not be substantiate from the present study.

A positive relationship was seen between cord serum Ig M and the birth weight (Table- 9). Present study consisted of 16 babies who had mild IUGR (Group B). These babies had mean cord serum Ig M values of $33.06 \pm 12.66$ mg/dl, while Singh et al (1978) found considerably lower levels of Ig M ($16.00 \pm 7.71$ mg/dl). The mean levels of Ig M in cord blood
have been estimated to be 46.00 ± 7.11 mg/dl (Sharma et al., 1991) in a similar groups of cases. These observations are in close proximity to those obtained in the present study. Severe IUGR cases (Group A) whose birth weight fell below 3rd percentile had mean cord Ig M 38.00 ± 9.93 mg/dl while Singh et al (1978) obtained 20.00 ± 19.35 mg/dl Ig M values in the cord blood of a comparable group of cases. In contrast to it, Chaturvedi et al (1989) and Sharma et al (1991) got mean cord Ig M values of 11.30 ± 15.95 mg/dl and 10.00 ± 10.00 mg/dl respectively in a similar group of cases which are lower than those obtained in the present study. A higher mean Ig M value was obtained in severe IUGR babies (Group A) in the present study while lower values were obtained in mild IUGR (Group B) cases. Chaturvedi et al (1989) and Sharma et al (1991) have obtained an opposite pattern. This could be explained on the basis that low birth weight babies with severe IUGR at a greater risk to develop infection. More severe the infection, more would be the insult in the form of growth retardation and higher will be the Ig M value, while Chaturvedi et al (1989) has explained the phenomenon on the basis that a better immunological responsiveness would be present in babies with a higher birth weight when they face intrauterine antigenic challenge.
Chandra et al (1970) demonstrated significantly higher levels of Ig M in premature neonates weighing less than 2.5 kg as against the level in full term babies. Raghavan et al (1976) got higher values (11.90 ± 8.90mg/dl) of Ig M in the premature than in full term babies (11.30 ± 6.76 mg%). Prasad et al (1971) suggested that the premature neonates are certainly immunologically different but in no way immunologically incompetent.

A significant increase in mean maternal serum Ig M levels in case of growth retarded babies has also been reported by Bharadwaj et al (1987). The level of Ig M observed by author (253.19 mg/dl) is close to that obtained in the present study (134.7 ± 32.42 mg/dl) in Group A, 162.3 ± 63.96 mg/dl in Group B and 219.2 ± 43.66 mg/dl in Group C babies. Asymptomatic infection in the mother of IUGR babies could be the possible reason for the elevated maternal Ig M levels. This was also borne out by the finding of higher mean cord serum Ig M levels 35.37 ± 13.03 mg/dl in IUGR neonates as compared to controls 19.20 ± 8.00 mg/dl.

It is, thus inferred that cord Ig M levels are raised (possibly ≥ 20 mg/dl and certainly ≥ 30 mg/dl) in a higher percentage of IUGR neonates who have no obvious clinical cause for growth retardation; suggesting accelerated Ig M synthesis in utero brought about by intrauterine antigenic challenge (possibly intrauterine infection). The mean maternal serum Ig M was also increased in the IUGR group of babies, probably due to subclinical infection in pregnancy.