THE TURKISH JOURNAL OF
PEDIATRICS
A HACETTEPE BULLETIN VOLUME 12 / Nos. 3-4 / JULY-OCT. 1970

# Bone Development, Incidence of Hypoglycemia and Effect of Maternal and Fetal Factors in Low Birth Weight Infants

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Approximately two-thirds of infants weighing 2,500 gms. or less at birth are considered premature, according to gestational age. The remaining one-third born after the completion of about 40 weeks are called low birth weight infants.[1,2] Shortness in the length of these babies suggests that their epiphyseal development might also have been delayed. Having the possibility of this type of delay in mind, we have studied the epiphyseal development of the knees of 40 infants born within the term, but showing an under-weight condition at birth, (between 1,840 - 2,800 gms) during the first five days of life. We have investigated the presence of a relationship between the intrauterine malnutrition, fetal and maternal factors (such as parity, age, socio-economic trends, complications of pregnancy) to discover the clinical conditions leading to intrauterine malnutrition. A study by Cornblath et al[3] showed that the incidence of toxemia in mothers of infants with symptomatic hypoglycemia was high, but Neligan et al[4] has not disclosed a similar association. The malnourished infants were also observed for the incidence of hypoglycemia and the correlation between hypoglycemia and complications of pregnancy such as toxemia was checked.

## *Material and Methods*

Forty infants with a full term gestation period (40 wks), low birth weight (2,500 gms. and under) or intrauterine malnutrition (between

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2,500 - 2,800 gms.) who were all born at the maternity ward of the Hacettepe University Hospital were included in the study group without any other preference. The gestational age was calculated from the first day of the last menstrual period. The prenatal care of the mothers was provided by the obstetrics staff of the maternity department. Records pertaining to the mothers were employed in the preparation of this study. In addition, mothers were interviewed by our staff members during their postpartum hospital stay for other necessary data.

The lowest birth weight in the group was 1,840 gms. and the highest 2,800, but most of the babies weighed around 2,500 gms. To determine the epiphyseal development at the knee, the following X-Ray technique was used : the child's knee was exposed for 100 MA, 0.006 second with the tube target distance being 90 - 100 cms. X-Rays of all infants were obtained within the first three days of life.

Determination of the blood sugar was done routinely for all infants around 24 hours of age. When the blood sugar level was found to be between 30-40 mg.% the blood sugar tests were repeated at six hour intervals in order to observe falling blood sugar levels. If the infants showed symptoms of hypoglycemia (such as tremors, cyanosis, apathy, convulsions, apnea, respiratory distress, weak or high pitched cry, eye rolling, etc.), within 24 hours of age, immediate blood sugar tests were done to be able to make a diagnosis of hypoglycemia and, if this proved to be the case, then proper treatment was started. A blood sugar level under 20 mg.% was accepted to be adequate for the diagnosis of hypoglycemia.

Infants who did not show any of the above-mentioned symptoms were given two feedings of 5% glucose in water starting 12 hours after birth and were breastfed thereafter. Hypoglycemic infants received earlier intravenous therapy and, as soon as the clinical condition permitted oral feeding, a formula was started.

Twenty normally developed full term infants who formed the control group were studied in the same manner for bone development.

## *Findings*

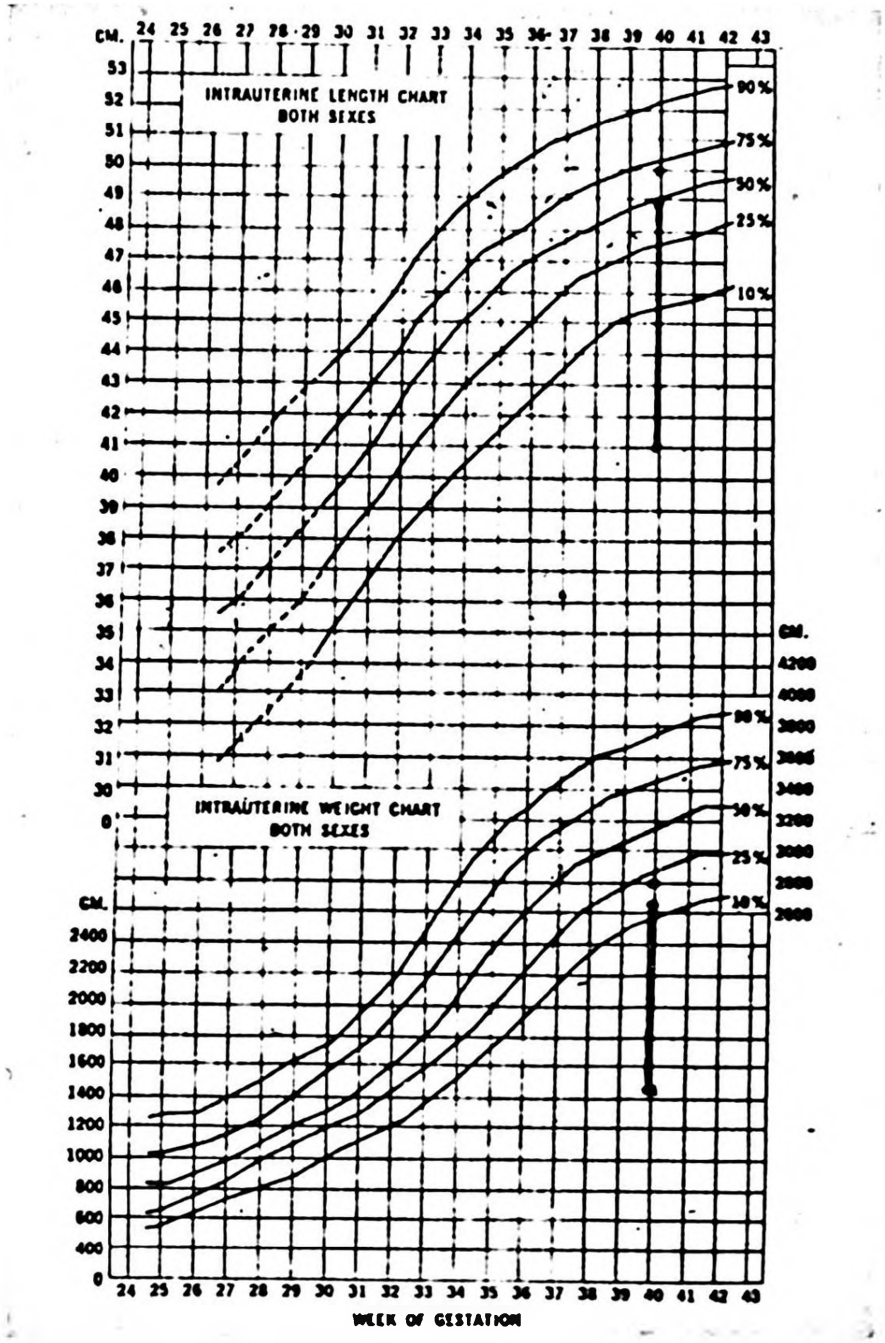
Findings encountered in this study can best be analyzed in five basic groups.

### 1. Intrauterine growth

As can be seen in Table 1, which was prepared using the Colorado Intrauterine Growth Chart 5, the majority of the infants were under

TABLE I

LOW BIRTH WEIGHT AND INTRAUTERINE LENGTH OF CASES PRESENTED IN THIS PAPER IN RELATION TO INTRAUTERINE GROWTH CURVES OF LUBCHENCO ET AL, 1963.




the 10 per cent range in weight. The length of the infants, although less affected than the weight were still under the 50th percentile.

## 2. Bone growth

Following our observations of the degrees of bone development in 40 infants we divided the cases into four groups :

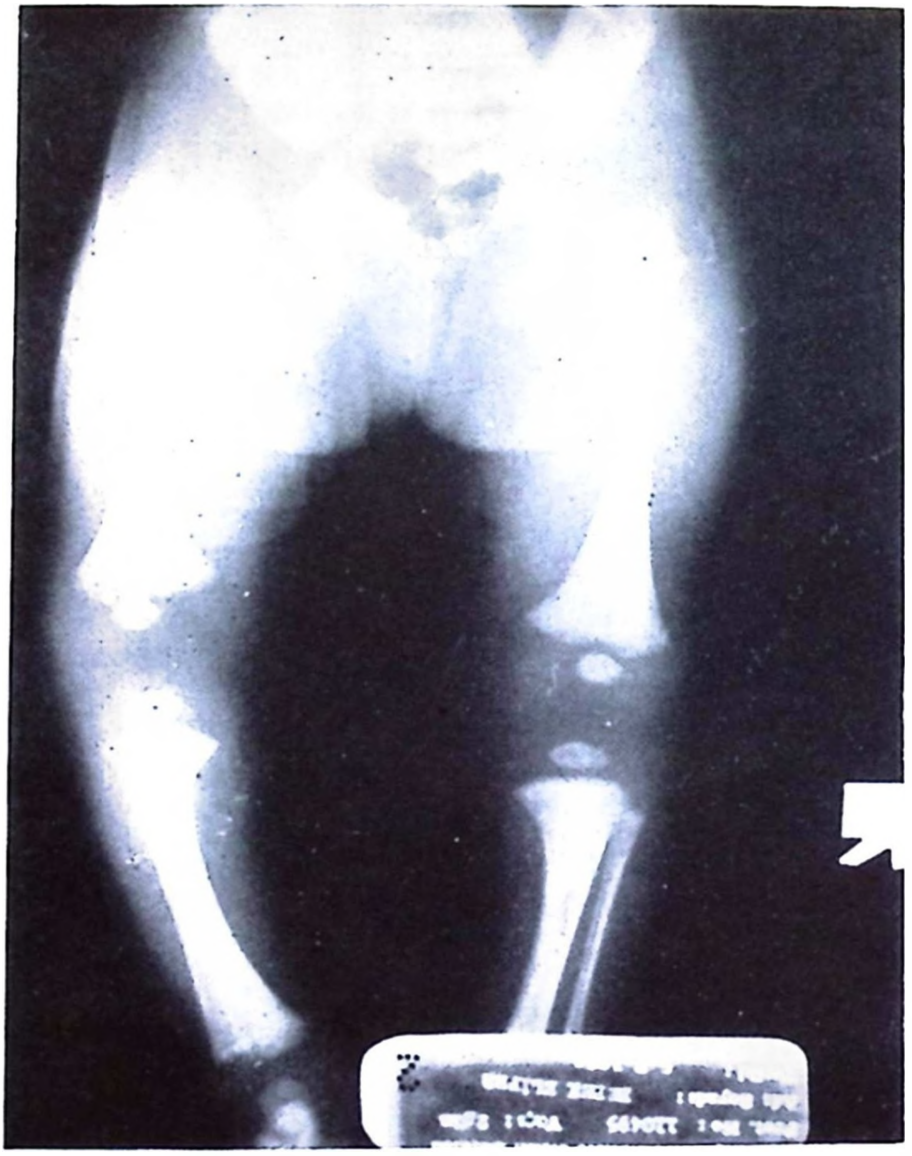


**Figure 1**
Sample case of Group A.

*Group A.* Cases in which both ephiphysical centers are present. The diameter of the distal femoral epiphysis in this group should be 6 mm or more, and proximal tibial epiphysis 4 mm or more (Figure 1).

*Group B.* Cases in which both epiphyses are present, smaller in diameter than those in Group A. In this group the diameter of the distal femoral epiphysis is 5 mm or less and proximal tibial epiphysis 4 mm or less (Figure 2).

*Group C.* Cases in which only distal femoral epiphysis is present (Figure 3).

*Group D.* Cases in which none of the two epiphyses is present (Figure 4).

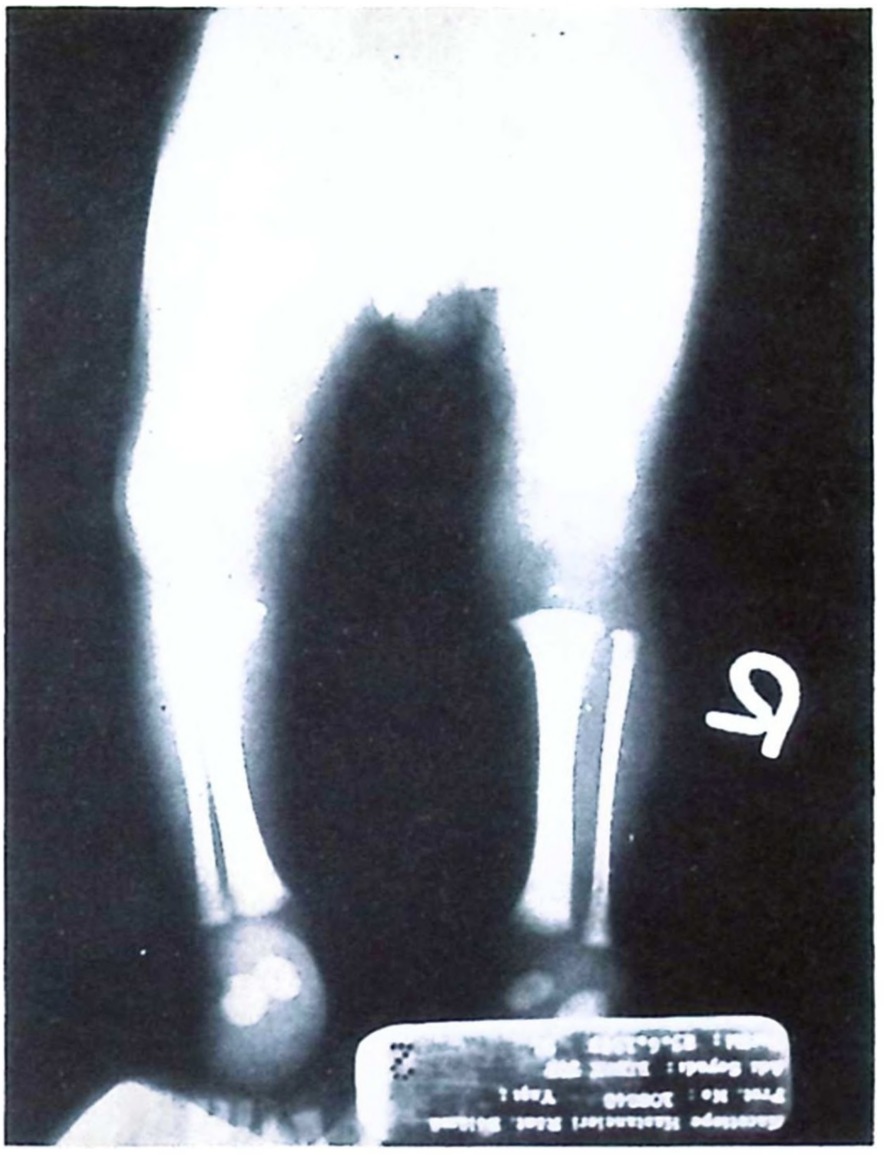


**Figure 2**
Sample case of Group B.

Significant bone growth retardation is present in the intrauterine malnourished infant (p. 0.001, Table II).

TABLE II

DISTRIBUTION OF 40 CASES ACCORDING TO THE DEGREE OF BONE DEVELOPMENT

| | Group I | Group II | Group III | Group IV | TOTAL |
|---|---|---|---|---|---|
| Study Group | 7 | 9 | 15 | 9 | 40 |
| Control Group | 16 | 3 | 1 | 0 | 20 |
| | | | | p 0.001 | |

Eleven of the forty infants who weighed less than 2,500 gms had more severe delayed bone growth than babies weighing between 2,500-2,800 gms (p 0.001). This is shown in Table III.

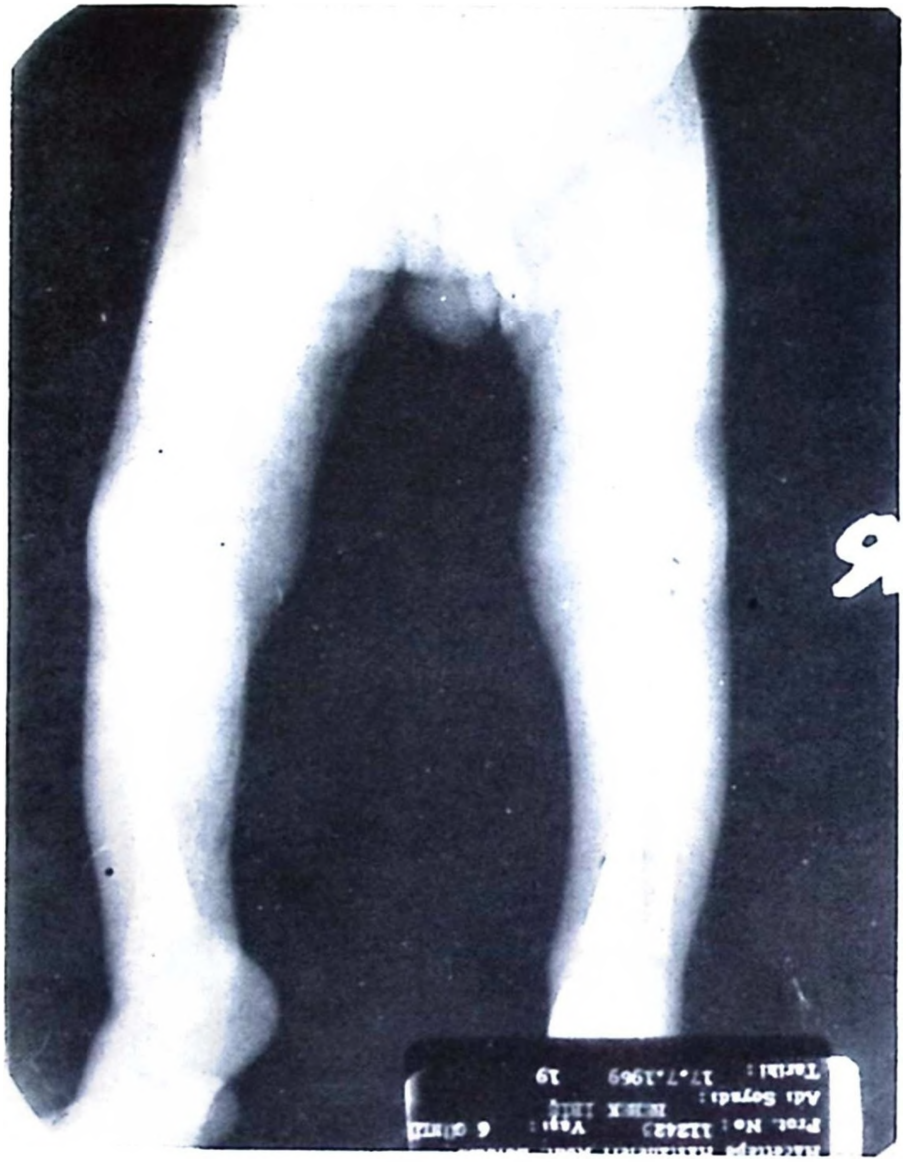


**Figure 3**
Sample case of Group C.

TABLE III

DISTRIBUTION OF ELEVEN CASES WITH A BIRTH WEIGHT OF 2,500 gms. AND LESS ACCORDING TO THE DEGREE OF BONE DEVELOPMENT

| | Group A | Group B | Group C | Group D | Total |
|---|---|---|---|---|---|
| Birth Weight less than 2,500 gm. | 3 | 0 | 4 | 4 | 11 |
| Birth Weight, 2,500-2,800 gm. | 4 | 9 | 11 | 5 | 29 |
| | | | | p 0.001 | |

### 3. Fetal factors

The relationship between these factors and intrauterine malnutrition was studied by observing the sex differences and the Apgar scores in these infants.

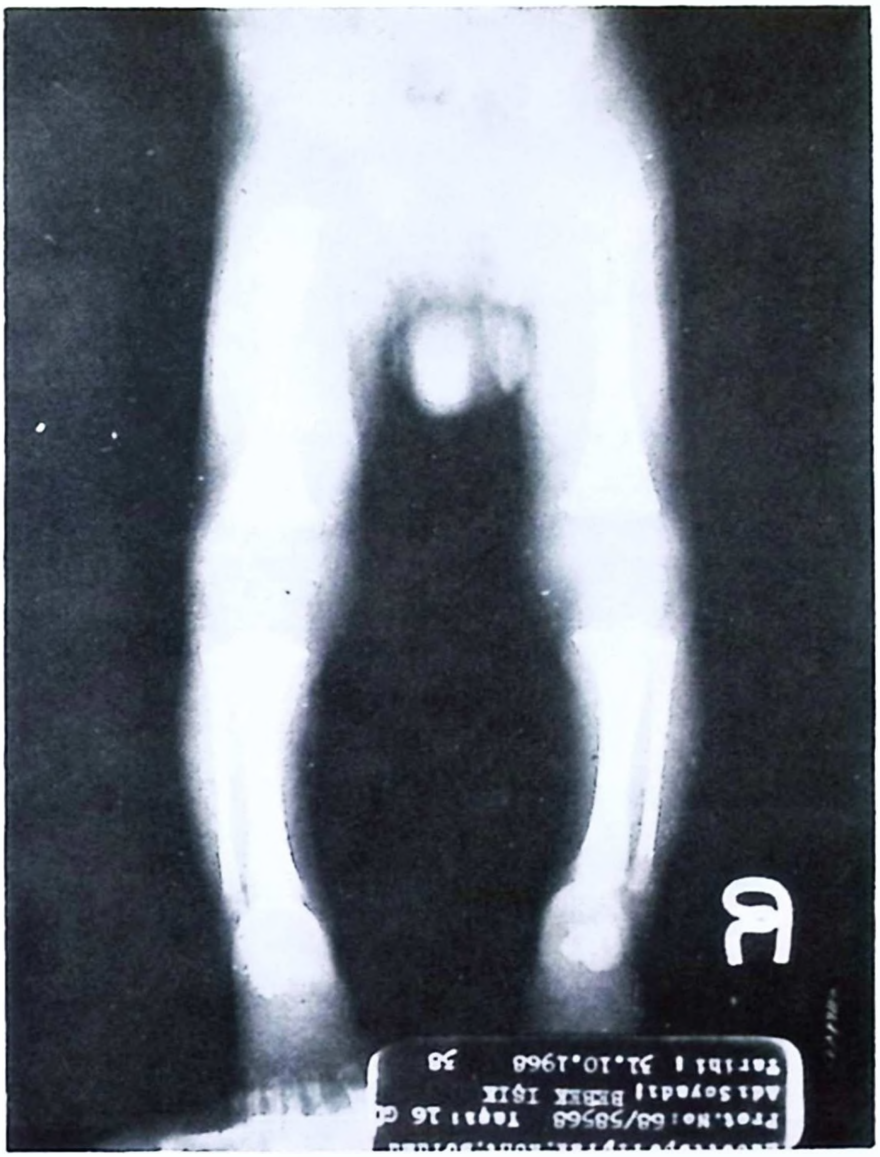


**Figure 4**
Sample case of Group D.

*A. Sex*

The 19 male and 21 female infants in the groups showed no significant sex preponderence.

*B. Apgar score*

Apgar scores were available for analysis in 35 of the 40 infants. The lowest Apgar score, which was 4, was found in two cases. Two cases had Apgar scores of 6 and the rest of the infants had scores which were above 7. In conclusion, we can say that no significant correlation existed between low Apgar scores and intrauterine malnutrition.

**4. Maternal factors**

The maternal factors influencing intrauterine growth was observed by taking into consideration the age of the mother, the parity, complications of pregnancy and socio-economic factors.

*a. Maternal age*

The mothers' age distribution is shown in Table IV. Almost half of the infants were born from mothers aged between 21-25 years, the best child bearing period. Twenty nine mothers were below 25 years of age. There was no significant correlation between elderly mother's infant and intrauterine malnutrition.

TABLE IV

MATERNAL AGE DISTRIBUTION

| Maternal Age | 15-20 yrs | 21-25 | 26-30 | 31-35 | 35 + |
|---|---|---|---|---|---|
| No. of Cases | 10 | 19 | 5 | 2 | 4 |

*b. Parity*

Twenty three of the forty mothers were primigravida. The remaining number was not enough to give a conclusive result.

TABLE V

GRAVIDA DISTRIBUTION

| Gravida | G.1 | G.2 | G.3 | G.4 | G.5 | G.6 | G.7 |
|---|---|---|---|---|---|---|---|
| No. of Cases | 23 | 8 | 4 | 2 | 2 | 0 | 1 |

*c. Complications of pregnancy*

1. Toxemia : Five mothers had toxemia of pregnancy, one of them was praeeclamtic. Babies of the three out of five toxemic mothers developed hypoglycemia.

2. Other complications : One mother's pregnancy was complicated by bleeding during the first trimester, another had pyelonephritis and one suffered from Tetralogy of Fallot.

*d. Socio-economic factors*

Eleven mothers belonged to above average or high socio-economic level families, and 29 mothers came from low socio-economic fami-

lies. The results of comparison were significant, pointing to intrauterine malnutrition in mothers from low socio-economic families.

### 5. Incidence of hypoglycemia in infants with intrauterine malnutrition

Seven infants in the study group had hypoglycemia. (under 20 mg.%), five of them being symptomatic. One asymptomatic baby was diagnosed because of severe intrauterine malnutrition on routine blood sugar determination. This infant's blood sugar was found to be 10 mg.%, although the baby showed no symptoms. One baby had hyperglycemia (blood sugar 710 mg. %), diagnosed as transient neonatal diabetes mellitus. On follow-up the blood sugar was found to be 20 mg % without any symptoms suggesting hypoglycemia. This baby did not receive insulin therapy for hyperglycemia. Clinical courses of seven hypoglycemic infants are shown in Table VI.

## *Conclusion and Comment*

From this study, the following conclusions can be made :

1. Infants with intrauterine malnutrition for their gestational age had delayed epiphyseal development.

2. This conclusion is important from the obstetrical viewpoint. Many obstetricians use the criteria of epiphyseal development of the knee to judge baby's maturation. This is true in cases where the baby's development is parallel to its gestational age. If the infant has intrauterine malnutrition, for its gestational age, bone development will be delayed. With a criteria such as the epiphyseal development of the knee a premature infant cannot possibly be differentiated from an infant with intrauterine malnutrition. The two previous reports support this conclusion.[6,7]

3. Young primigravida and mothers from low socio-economic families seem to be more likely to have a child with intrauterine malnutrition.

4. The incidence of hypoglycemia was found to be 17.5 % in our series of forty infants with intrauterine malnutrition. In one case severe hypoglycemia (blood sugar 10 mg %) was not associated with the symptoms. Griffiths[8] reported that in 44 cases where the blood sugar level was 20 mg and under, there were only 24 symptomatic cases of hypoglycemia. There have been many reports published[9-14] on the subject of hypoglycemia in the newborn. The relationship between hypoglycemia and toxemia has also been investigated. Their findings and our observations in this study emphasize, once more, the importance

## TABLE VI

### MEDICAL HISTORY AND CLINICAL COURSE OF SEVEN HYPOGLYCEMIC INFANTS

| Patient | Mother's History | Gestation | B.W. | Apgar Score | Sex | Symptoms of Hypoglycemia | Lowest Blood Sugar Mg. % | Intrauterine Growth Rate (Lubchenco) | Outcome at the Time of Discharge |
|---|---|---|---|---|---|---|---|---|---|
| 1 E | Tetralogy of Fallot | 40 | 1,840 | 8 | F | None | 10 | Below the 10th % percentile | Good |
| 2 I | Toxemia | 40 | 1,860 | 6 | M | Tremors Lethargy Bradycardy | 18 | Below the 10th % percentile | Good |
| 3 D | Toxemia Pyelonephritis | 40 | 2,710 | 6 | M | Tremors tachypnea Irregular Respirations | 15 | Above the 10th % percentile | Good |
| 4 I | Toxemia | 40 | 2,600 | 10 | M | Tremors | 23 | 10th percentile | Good |
| 5 M | Mild Edema | 40 | 2,000 | 8 | M | Tremors Lethargy Absence of suck | 14 | Below the 10th percentile | Good |
| 6 K | None | 40 | 2,650 | 8 | M | Tremors | 12 | 10th percentile | Good |
| 7 A | None | 40 | 1,570 | 7 | F | None | 20 | Below the 10th percentile | Good |

of neonatal care of hypoglycemic infants. The only way to overcome this problem is to check the infant for hypoglycemia and the clue to this is intrauterine malnutrition. It is well known that many asymptomatic hypoglycemia cases result in severe neurologic defects.[15,17]

In our series, seven symptomatic and asymptomatic hypoglycemic infants received immediate intravenous glucose and, where necessary, additional cortisone therapy as outlined by Cornblath and Schwartz.[18] On neurological examination at the time of discharge from the premature unit, none were found to be abnormal.

One interesting case of transient neonatal diabetes mellitus was found to be hypoglycemic during follow-up. Hyperglycemia and hypoglycemia in the same infant was first reported by Chance et al.[19] We had two cases (one in this study) where hypoglycemia developed after hyperglycemia. What the predisposing condition for both is, is still not understood. Probably the placenta is responsible, in most cases. Transient neonatal diabetes and symptomatic hypoglycemia both occur in infants with intrauterine malnutrition. It is possible that the same factor diminishing glucose transfer of the placenta causes intrauterine malnutrition, hyperglycemia and hypoglycemia. The explanation for this is as follows:

1. When the active glucose transfer of the placenta is diminished the glycogen reserve of the infant will also be diminished and the result will be hypoglycemia.

2. When the active glucose transfer of the placenta is diminished the infant will have low blood sugar during the intrauterine life and hyperglycemia will ensue as a result of diminished stimulation of the Beta Cell of the pancreas by the low blood sugar.

The proper way to care for these high risk infants is through diagnosing the difficulty before symptoms of hypoglycemia appear and instituting immediate treatment to prevent permanent brain damage.

## *Summary*

Forty infants with intrauterine malnutrition were studied for their bone development and incidence of hypoglycemia. Correlation between fetal and maternal factors and intrauterine malnutrition was investigated. Delayed development of the bone growth and a high incidence of hypoglycemia were found with intrauterine malnutrition. The importance of neonatal care for these infants is once more emphasized.

*Acknowledgment*

I wish to thank to Prof. Abdullah Kenanoğlu and his associates in the X-Ray Department and the residents of the Department of Pediatrics of Hacettepe University Hospital, and to Vural Türker, B.D., M. Ed., for editorial assistance, without whose help this work would not have been possible.

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