

Normal Levels of Insulin, Growth Hormone and Cortisol Levels in Venous Cord Blood of Healthy Full-Term Infants: Correlation with Birthweight and Placental Weight

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Objective: The aim of this study was to determine reference values for the venous cord blood insulin, growth hormone and cortisol levels and also find out the correlations of these three hormones with the birthweight and placental weight.

Method: One hundred and eightythree healthy mothers and their full-term neonates were included in the study. The placental weights and birthweights were measured by the same digital scale. Venous cord blood insulin, growth hormone and cortisol levels of infants were analysed using enzyme-immunological, immunoluminometric and radioimmunoassay methods, respectively.

Results : The mean insulin level was found 6.01 ± 3.67 $\mu\text{U/ml}$ (0.5-18), mean growth hormone level 20.07 ± 8.38 (8.6-40) ng/ml and mean cortisol level 13.6 ± 7.87 (2.4-40) $\mu\text{g/dl}$. We found that the venous cord blood insulin levels were in linear correlation with both birthweight and placental weight ($r=0.39$, $p<0.05$ and $r=0.35$, $p<0.05$ respectively) but such correlation did not exist when growth hormone or cortisol was concerned.

Conclusion: We consider the values we have obtained as data to be used for our own reference. Moreover, it was shown that cord blood insulin values were in linear correlation with birthweight and placental weight but such correlation did not exist for growth hormone and cortisol.

Key words: Cord blood, insulin, growth hormone, cortisol, birthweight, placental weight

For many endocrine and metabolic diseases of the newborn, normal values or relevant parameters should be known. The venous cord blood (VCB) values given in classical sources have been based upon studies made many years ago (1-4). Some authors have stated that their own data are not in agreement with classical values (5). Due to this disparity between data of different researchers, there is an urgent need to obtain reliable data that we can use in our department.

It has been known for a long time that the most important hormones in the development of fetus are insulin and insulin-like growth hormone (6). Insulin also influences the development of placenta (7). The effects of growth hormone on development of fetus in intrauterine period are not known clearly, however it is a common belief

that it is ineffective (3). In our study, we also investigated relationship of cortisol with birthweight and placental weight. The effects of these hormones on intrauterine development of the fetus have also been discussed.

Material and Method

The study was carried out on the neonates born in the Hospital of Yüzüncü Yıl University Medical Faculty between January 1997 and January 2000. One hundred and eighty three healthy mothers and their full-term (38-42 weeks) neonates were included in the study. The gestational ages were calculated according to last menstrual period of mothers. The mothers and infants who developed complications (hemorrhage, infection, preeclampsia, eclampsia, intrauterine asphyxia, maternal diabetes etc.) that can negatively influence the placenta and fetus in pregnancy period were excluded. The ages and placental weights of mothers were recorded. Birthweights and VCB insulin, growth hormone and cortisol values of infants were measured.

Placenta was weighed with a digital scale approximately 1 hour after cord was severed. The cases whose placentas were removed in pieces were excluded. The weights of infants were measured with the same digital scale in the maternity room after the cord was clamped with a plastic clamp and severed. SGA (small for gestational age) and LGA (large for gestational age) infants were excluded from the study in accordance with the Lubchenco curve.

After the cord detached from the mother the part remained on the baby was clamped from a distance of 2-3 cm. VCB was taken with an injector from the remaining part of the cord, and its serum was separated and it was kept in a deep freezer at -20°C . The insulin level was measured with a kit (Boehringer Mannheim, Germany) using enzyme-immunological method. Growth hormone level was measured by immunoluminometric method (Pharmacia, Sweden) and cortisol level by Cortisol radioimmunoassay (Clonesystem, Italy).

The data were analysed using SPSS[®] statistical package program. The significancy between the groups were studied by Mann-Whitney U-test and the correlation

by Spearman's rank correlation test. $P < 0.05$ was considered significant. Informed consent was obtained from the mothers.

Results

One hundred eighty three mothers and their infants were included in the study. There were 102 males and 81 females. Characteristics of the mothers and the infants are shown in Table I. The normal distribution of VCB insulin, growth hormone and cortisol levels of 183 infants investigated in the study are given in Figs. 1,2 and 3, respectively. The relationship between these hormones and placenta and birthweights were searched in this study. A moderate and significant correlation was found out between placental weight and insulin ($r=0.35$, $p=0.001$), and as the insulin level increased, the placental weight also increased (Fig. 4). No significant and linear correlation could be found between placental weights and levels of growth hormone or cortisol ($r=0.02$, $p=0.77$ and $r=0.11$, $p=0.12$ respectively).

The correlations between birthweight and insulin, growth hormone or cortisol levels were investigated. Similar to the placental weight, a linear and significant correlation was determined between insulin levels and birthweights of infants ($r=0.39$, $p=0.0001$), that is, as the insulin level increased the birthweight also increased (Fig. 5). No significant and linear correlation was found between the growth hormone and cortisol levels ($r=-0.11$, $p=0.13$ and $r=-0.03$, $p=0.67$ respectively).

Table I. Characteristics of mothers and their infants, and values of insulin, growth hormone and cortisol obtained from VCB (n=183).

	Mean ± SD	Range
		Range
Mother's age (years)	23.34 ± 4.80	16 – 39
Placental weight (gr)	546 ± 150	303 – 900
Birthweight (gr)	3252 ± 428	2500 – 4500
Insulin (µU/ml)	6.01 ± 3.67	0.5 – 18
Growth hormone (ng/ml)	20.07 ± 8.38	8.6 – 40
Cortisol (µgr/dl)	13.6 ± 7.87	2.4 - 40

Discussion

The cord blood provides very important data towards to problems pertaining the fetus and the newborn. For the validity of cord blood levels in diagnosis, it is first required to determine the reference values. The values given in classical sources have been based upon studies made abroad many years ago (1-4). Therefore VCB of 183 healthy full-term newborns were obtained and compared with the literature to determine our own insulin, growth hormone and cortisol level charts.

The insulin level is reported to be 3-20 µU/ml in

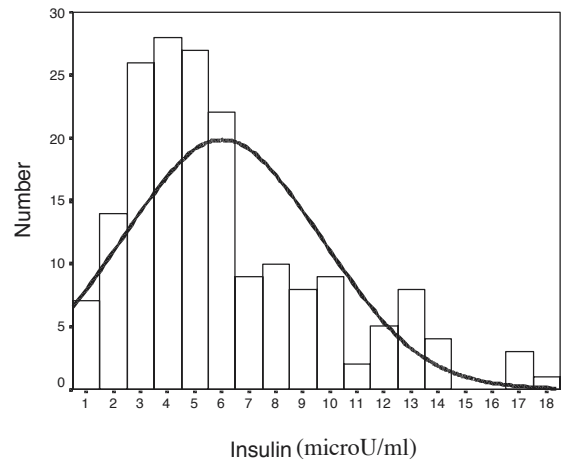


Figure 1. The normal distribution of VCB insulin levels.

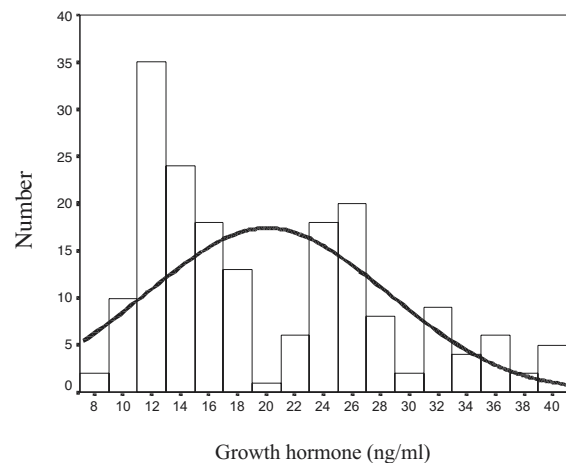


Figure 2. The normal distribution of VCB growth hormone levels.

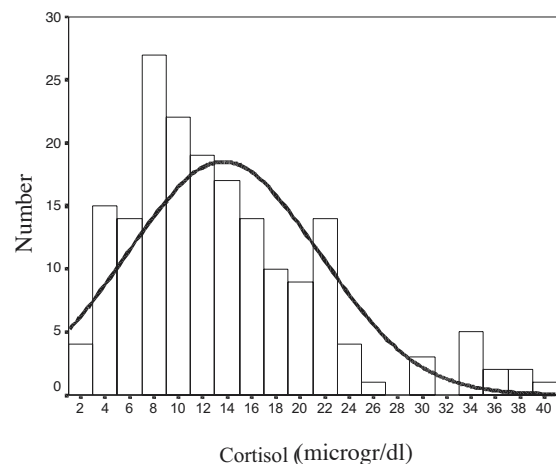


Figure 3. The normal distribution of VCB cortisol levels.

classical textbooks (1,6). This level was reported as 14.6±7.2 µU/ml in one study and as 8.6 µU/ml, 9.2µU/ml and 7.1µU/ml for various race groups in another study (8,9). At the latter reference, it is claimed that VCB insulin values are different among races. In our study the VCB

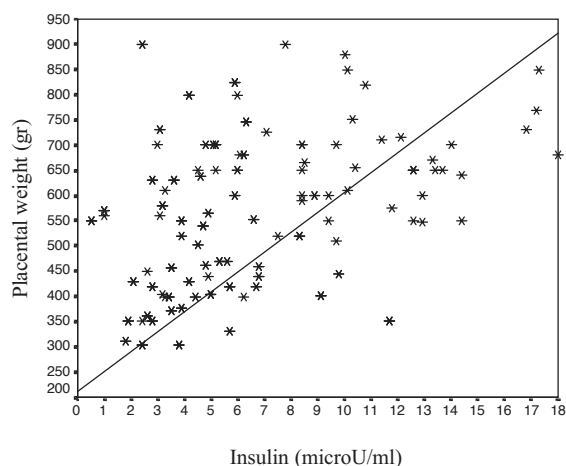


Figure 4. Linear correlation between placental weight and VCB insulin levels ($r = 0.35$, $p = 0.001$).

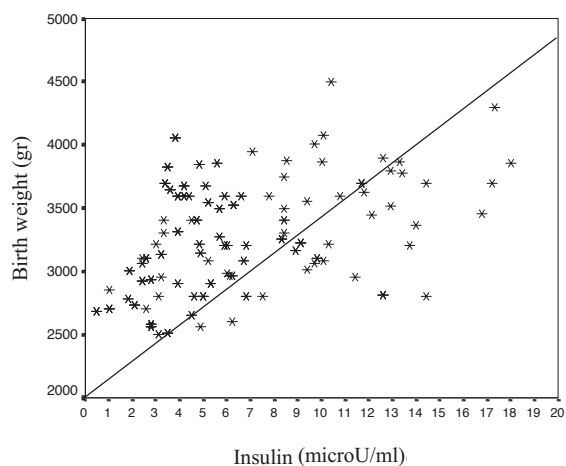


Figure 5. Linear correlation between birthweight and VCB insulin levels ($r = 0.39$, $p = 0.0001$).

insulin level was found to be $6.01 \pm 3.67 \mu\text{U/ml}$ (0.5-18) which is quite different from that of the study mentioned above and similar to the average of European ethnical group in the latter reference.

As a reference, growth hormone level was given in a wide range as 5-53 ng/ml (1). Mirlesse et al. have reported that the placental growth hormone remained at the same level after the 35 weeks of pregnancy and it was 27.5 ± 3.4 ng/ml on the average at birth (10). In other two studies, the venous cord growth hormone levels of healthy full-term infants were reported to be 20.6 ± 8.5 ng/ml and 23.4 ± 10.2 ng/ml respectively (11,12). While Brinsmead et al. reported the venous cord growth hormone level of 71 healthy full-term infants to be 20.5 ± 4.4 ng/ml, Hintz et al. reported it 41.7 ± 3.6 ng/ml for 52 healthy full-term infants (13,14). Ayhan et al. investigated the VCB growth hormone values of SGA, LGA and AGA (appropriate for gestational age) infants and reported the level for AGA

infants as 43.5 ± 4.8 ng/ml (15). As understood from the above mentioned studies, a common value of VCB growth hormone level has not been determined yet. In our study this value was found to be 20.07 ± 8.38 (8.6-40) ng/ml.

Different values of VCB cortisol level of full-term infants were reported in the literature. Kauppila et al. reported it $17.4 \pm 3.4 \mu\text{g/dl}$, Murphy $20.1 \mu\text{g/dl}$, Sybulski et al. $7.43 \pm 0.29 \mu\text{g/dl}$ (4,16,17). In Turkey, Orhaner et al. also compared different delivery types and found the cord blood cortisol values $23.44 \pm 11.93 \mu\text{g/dl}$. In elective cesarean sections cortisol levels were found to be lower (18). The values obtained in our study are quite different from those mentioned in the literature and are 13.6 ± 7.87 (2.4-40) $\mu\text{g/dl}$.

In this study, the relationships of these three hormones with placenta and birthweights were also investigated. The role of insulin in intrauterin development has been known for a long time (6). Simmons has shown in his study that cord blood insulin is in accordance with birthweights (9). Insulin also influences the placental weight. There are limited numbers of studies on this subject which shows that insulin positively influences the placental weight (7,19). Our results are in agreement with the studies mentioned above. We found a linear correlation between insulin levels and weights of birth and placenta ($r=0.39$, $p=0.0001$ and $r=0.35$, $p=0.001$ respectively). As the insulin level increased the placental weight and birthweight increased as well. (Figs. 4,5).

Although the growth hormone is the major hormone that ensures development in the postnatal life, it has a very little effect in intrauterine life (6). In many studies, it has been shown that this hormone does not affect the birthweight of the baby and it is not in accordance with the cord blood hormone levels (3,5,6). Besides, the relationship between the growth hormone and placental weight has not been suggested in the literature. As for our data, the growth hormone is not in correlation with either the birthweight or placental weight ($r=-0.11$ and $r=-0.02$). This result is valuable, since it shows that similar to birthweight, the growth hormone does not have any effect on the placental weight either. In the intrauterine life, the cortisol level does not increase until the 34th to 35th week. At the last trimester cortisol level increases with the rapid development of the fetus. However this is a situation which takes place in parallel to the development of the baby, because no direct effect of cortisol on the weight of the baby was reported (16,17,20,21). In our study, no relationship was shown between cortisol and birthweight or cortisol and placental weight ($r=-0.03$, $r=0.11$).

As a result, the normal distribution of VCB insulin, growth hormone and cortisol values of healthy full-term infants are shown in the first section of this study. We believe that these values can be used as our own reference values. In the second section, it is shown that cord blood insulin values are in linear correlation with the weights of baby and placenta yet such a correlation is not encountered for growth hormone and cortisol levels.

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