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# Transient Tyrosinemia of the Newborn

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Transient tyrosinemia was first described by Levin in 1939.[1,2] Increased serum tyrosine level in the neonates is due to a temporary inactivity of p-hydroxyphenyl pyruvic acid (p-HPPA) oxidase in the liver.[1-7] The disorder is common among premature infants but relatively rare among full-term infants. Its prevalence varies from country to country.

This study was carried out to investigate the prevalance of neonatal tyrosinemia which might be expected to be lower than in the other countries due to the nutritional factors in Turkey.

## *Materials and Methods*

One hundred fifty full-term infants whose birth weights ranged between 2700 and 4950 g and fifty premature infants weighing between 900 and 2500 g were studied. 85 of full-term infants were boys and 21 girls. They were breastfed. The gestational ages of the premature infants were between 28 and 37 weeks, of them 29 were boys and 21 girls Table I. These infants were fed with 8-10 ml/SMA-S26/kg of body weight for the first few days and it reached 150 ml/kg of body weight/day at the end of the first week.

Capillary blood samples were obtained by heel puncture on the 4th or 5th day from full-term infants. In premature infants serial blood samples were obtained at two day intervals until the 8th day of the life with the same technique. 50 mg ascorbate was given to every premature infant in the second week and serum tyrosine was determined again.

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Serum tyrosine levels were measured by the fluorometric method.[8] The values above 7.5 mg/dl were considered to be high. The other blood aminoacids also were investigated using one dimentional paper chromatography.[9]

*Results*

Four (2.6 %) out of 150 full-term infants had tyrosine levels above 7.5 mg/dl. After one month serum tyrosine levels could be determined again in three of them and were found to be normal. No differences were observed between the serum tyrosine levels of boys and girls ($p < 0.05$) The tyrosine levels were not correlated with serum bilirubin levels either.

Nineteen (38 %) out of 50 premature infants had high tyrosine levels. The highest levels were observed on the 7 th day of the life. With 50 mg ascorbate administration serum tyrosine levels fell into normal limits within few days. There were significant differences between the mean of tyrosine levels of full-term and premature infants especially between 4th and 7th days ($p < 0.001$) Table I, Figure 1) Serum aminoacids other than tyrosine were found to be normal in all cases.

TABLE I

STUDY GROUPS AND MEAN SERUM TYROSINE LEVELS

| Groups | No. of infants | Girls | Boys | Mean-serum tyrosine levels of groups (mg/dl) | No. of infants with high tyrosine level |
|---|---|---|---|---|---|
| Full-term | 150 | 67 (44.6%) | 83 (55.3%) | 4.56±1.75 | 4 (2.6%) |
| Premature | 50 | 21 (42%) | 29 (58%) | 6.06±2.28-7.16±3.14 | 19 (38%) |

*Discussion*

Transient tyrosinemia is caused by temporary inactivity of p-HPPA oxidase.[3, 5, 6, 10, 11, 12] There are three interrelated causes for hypertyrosinemia in the newborn. Diminished amounts of p-HPPA oxidase apoenzyme in the liver, high dietary intake of tyrosine, low ascorbate content of the unsupplemented postnatal diet. Unless ascorbic acid is added to the high protein diet, the high level of tyrosine may persist for weeks even for months.[6]

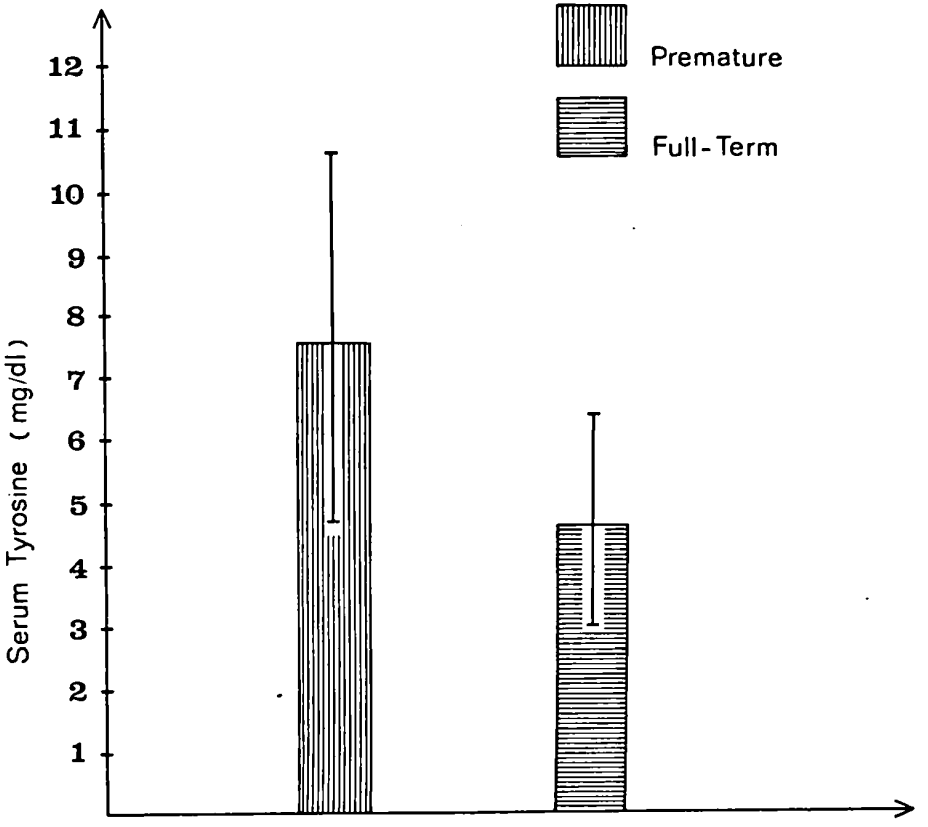


**Figure 1**
The Comparison of Mean Serum Tyrosine Levels of Full Term and Premature Infants

Transient tyrosinemia has been detected in 0.5-5 % of the full-term infants.[1, 2, 6, 13] The prevalance of transient tyrosinemia among the prematures has been found to be between 30 and 89 %.[1, 2, 5, 14, 15] In this study 4 (2.6 %) out of 150 full-term and 19 (38 %) out of 50 premature infants were found to have high serum tyrosine levels. If ascorbic-acid had not been given to the premature infants we could probably have seen that some normal tyrosine values might have become elevated during the second week and thus the frequency of transient tyrosinemia would have been higher. Transient tyrosinemia has been observed more frequently in the infants weighing less than 2000 g. (Table I) Almost half (44 %) of our premature cases had the birth weights above 2000 g. This also would account for the low frequency of transient tyrosinemia in prematures.

It has been shown that elevation of serum tyrosine level has most commonly been observed in the 7th and 8 th days in the prematures.[3] We have also found the highest tyrosine levels in premature infants on the 7th day of the life. The difference between serum tyrosine levels was statistically significant after the 4th day of life in the two study groups ($p<0.001$). (Figure 1) This finding can be attributed for the very low protein intake in the prematures for the first few days and the gradual increase of protein intake towards the end of the first week.

The fact that there was no relationship between tyrosine levels and bilirubin values in our cases and no difference existed between males and females which is compatible with other reports in the literature.[3]

Transient tyrosinemia should be differentiated from hereditary tyrosinemia which is an autosomal recessive disease associated with permanent inactivity of p-HPPA oxidase and impairment in hepatocellular and renal functions. Besides higher plasma tyrosine level, presence of alpha ketoacids, and generalized aminoaciduria are the other main laboratory findings.[16] If the newborn does not respond to ascorbic acid then hereditary tyrosinemia should be considered.

The effects of transient tyrosinemia on the growth and development of the infant have been discussed. Menkes and Avery[3] observed that weight gain of the prematures slowed down in neonatal tyrosinemia while Partington and Mathews[17] have shown no differences between the weight in normal infants and infants with transient tyrosinemia.

Dank and et al[18] ascribed the metabolic acidosis of a 20 week old infant to transient tyrosinemia and observed that acidosis improved with diet containing low phenylalanine and tyrosine.

It has been reported that high serum tyrosine level gives rise to certain neurological symptoms. Menkes et al,[19, 20] presented an infant with neonatal tyrosinemia who had convulsions, spasticity and growth retardation. In the premature infants with high level of tyrosine decrease in motor activity was observed in the first month.[20] However, some investigators,[19] followed up the prematures with transient tyrosinemia for 7-8 years and no impairment in mental and motor development had been found.[21, 22]

Our conclusion is that administration of vitamin C beginning from early days will be useful in premature infants. On the other hand there is no need for the early administration of vitamin C in full term infants since in Turkey they are generally breastfed and breastmilk contains appropriate amount of protein and thus prevents the occurrence of transient tyrosinemia.

*Summary*

The serum tyrosine levels of 50 premature and 150 full-term infants have been assessed in order to find out the prevalence of transient tyrosinemia. 2.6 % of full-term infants and 38 % of premature infants were observed to have increased serum tyrosine levels.

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