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Umbilical Cord TSH Levels in Term Small for Gestational Age Neonates

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ABSTRACT

Background: Small for gestational age (SGA) neonates are born as a result of Intrauterine Growth Retardation (IUGR). Thyroid hormones are critical for growth and development of the fetus. This may permanently influence the endocrine system by affecting its programming during development. In the present study, we have investigated the endocrine adaptation by the fetus to overcome the growth disadvantage. Objectives: The present study was a prospective cross-sectional cohort study, designed to assess Umbilical cord Thyroid Stimulating Hormone (TSH) levels in small for gestational age neonates. Material and Methods: A group of term babies delivered to eu-thyroid mothers was selected from our hospital. It was subdivided into cases(SGA neonates with birth weight ≤ 2.499 kg, n=58) and control (Average for gestational age neonates (AGA) with birth weight ≥ 2.5 kg, n=66). Umbilical cord TSH levels were measured by chemiluminescence immunoassay. Results: There was statistically significant rise in cord TSH levels in SGA neonates as compared to AGA (P=0.001). Conclusions: We found significantly higher levels of TSH in SGA neonates. However a larger survey with an appropriate follow-up is required to evaluate the prevalence and degree of thyroid dysfunction in children born SGA.

Keywords : Small for Gestational Age, Intra Uterine Growth Retardation, Thyroid Stimulating Hormone

Introduction:

Babies with a birth weight and/or length below the 10th percentile of a population of the same gestational age are defined small-for-gestational-age (SGA).[1] Small for gestational age (SGA) neonates are born due to failure to achieve the expected birth weight appropriate for the gestational week. This results due to Intra uterine Growth Retardation (IUGR). There may be many causes of intrauterine growth retardation and birth of SGA babies. Various pathophysiological mechanisms and endocrine-metabolic alterations characterize this condition. IUGR results due to complex factors of fetal, placental and maternal origin.[2,3] IUGR leads to a state of chronic fetal stress. This may lead to prolonged activation of hypothalamic-pituitary adrenal (HPA) axis. Due to these alterations SGA neonates are more prone for development of thyroid disorders, CVDs, metabolic syndrome in adult life these alterations may affect neonatal adaptation and future health in infancy and adulthood: indeed, higher incidences of pathologies such as cardiovascular events, metabolic syndrome, hypertension and obesity have been demonstrated.[4]

Thyroid hormones are fundamental for growth and neurocognitive development. A relationship between hormone alterations, growth retardation and related conditions has yet to be established, in particular whether alterations in thyroid function may be a cause or consequence of growth retardation. Few studies have compared thyroid function in SGA and appropriate-for-gestational-age (AGA) newborns.[2,3]

The present study was designed to assess umbilical cord Thyroid Stimulating Hormone (TSH) levels in term Small for Gestational Age Neonates.

Material and Methods:

Present study was a non randomized cohort study conducted in university medical college with tertiary care hospital. Study group included one hundred and twenty four (124) term babies delivered to uncomplicated primi or multipara mothers by normal vaginal delivery of both the genders.

Study Group consists of One hundred and twenty four term babies. It was subdivided into cases and controls as follows:

A) Cases: SGA Birth weight (kg) < 2.499 .n= 58 ,
B) Control: AGA Birth weight (kg) ≥ 2.500 Sample size n= 66

Mothers with thyroid diseases, DM, Respiratory diseases, CVDs, preeclampsia, incorrect expected date of delivery. Neonates with RDS, congenital diseases, babies seeking NICU admission were excluded from the study One ml of cord blood sample was collected from umbilical artery before clamping in plain vacutainer within 5 minutes of delivery in labor room. Serum was separated by centrifugation at 2500 RPM for 10 minutes. Separated serum was free from hemolysis. It was subjected for estimation of Thyroid Stimulating Hormone (TSH) by using automated chemiluminescence immunoassay system; (CLIA)Alpha Prime LS, France using commercially available kits of Acculite Monobind Inc (USA).

Principle of estimation of TSH was non-competitive immunoassay. Quality control was done by Bio-Rad immunoassay controls. Sensitivity of the assays was 98% with lowest detection limit up to 0.03 µIU/ml.

Observation and Results:

Mean Gestational age and Mean birth weight in SGA group is 39.1± 0.78 wks & 2263.34±110.13grams. For AGA mean

gestational age and mean birth weight is 39.5 ± 0.90 wks and 2942.69± 268.11 grams respectively.

We found that there was statistically significant difference in the levels of TSH among the two groups.

Table 1: Showing Cord TSH levels in SGA and AGA neonates

Group	Cord TSH µIU/ml	Normal Range of Term Cord TSH
Cases: Small for Gestational age (SGA)	6.23±0.87	1.0-17.4 µIU/ml
Control: Avarage for Gestational age (AGA)	4.49± 0.36	
p value	< 0.001	

Table 2: Showing TSH levels across various ranges of BW in SGA and AGA

	SGA with BW 1.500-1.999 Kg	SGA with BW 2.000-2.499 Kg
Number	3	55
TSH	6.41±3.85	4.30 ±1.60
p value	< 0.001	
	AGA with BW 2.500-2.999 Kg	AGA with BW 3.000-3.500 Kg
Number	4	62
TSH	4.51 ± 1.91	4.31 ± 1.36
p value	< 0.001	

Diagram 1: Showing decrease in Mean TSH levels from SGA to AGA across various ranges of Birth Weight.

Discussion:

Our findings of raised level of TSH in SGA neonates as compared to AGA indicates that there is no suppression of HPA axis though there is association of stress related to IUGR. This suggests that there may be intrauterine reprogramming of TSH sensitivity at the hypothalamic –pituitary level. Recent studies have shown that raised TSH might not result due to thyroid impairment due to reduced expression of thyroid receptors in IUGR.[5]

Studies of SGA newborns have been extended to infancy and the role of hormones such as insulin, glucagon, cortisol, ACTH and GH have been studied in depth.[6] The secretion of thyroid hormones in SGA subjects has been investigated to a lesser extent, especially in the neonatal period. To our knowledge, only six published studies have examined differences in secretion of thyroid hormones in AGA and SGA babies in the fetal period or the first week of life. Our results are in line with those of Setia et al[7] in cord blood and those of Thorpe-Beeston et al[8]. who used cordocentesis, finding higher concentrations of TSH and lower concentrations of T4 in SGA newborns. Our results are in contrast with those of Nieto-Diaz et al[9] and Brock Jacobsen et al[10] as far as TSH concentrations are concerned. Rashimi et al[11] and Mahajan et al[12] did not find any significant differences in plasma concentrations of thyroid hormones at birth between SGA and AGA newborns. Since differences in TSH between AGA and SGA babies are relatively small and can only emerge in a large population, the population examined by Nieto- Diaz et al[9] was presumably too small to detect statistically significant differences. Our data cannot be compared with that of Brock Jacobsen et al.[10] who examined babies after the first week of life .Our finding of higher TSH in SGA newborns indicates reduced fetal secretion of thyroid hormones. This reduced secretion could be due to retarded development of the gland, caused by the malnutrition typical of intrauterine growth retardation, and by any placental hypoxia.

Recent studies on populations of malnourished babies found T4 concentrations lower and TSH concentrations higher than in controls. Since fetal malnutrition is a typical aspect of intrauterine growth retardation, it seems likely that malnutrition has the same negative effects on the thyroid gland in the fetal period as in postnatal life.[13] The same seems likely for SGA newborns, who are typically undernourished babies. We interpret the finding of high plasma concentrations of TSH in our population of SGA newborns as a correct pituitary response to low levels of T4 in the fetal and neonatal periods, suggesting that the pituitary is not influenced by nutritional status.

This endocrine and metabolic state could be an advantage in conditions of poor nutrition or pathologies leading to growth retardation, because it is associated with reduced oxygen consumption. The fact that no SGA newborn had hypothyroidism and that hypothyroxinemia normalized spontaneously in the first months of life, suggests that adequate nutrition leads to recovery of thyroid function. [13]

However, it seems worthwhile enrolling these babies in follow-up protocols to monitor correct gland function, certainly in the first year of life and possibly in subsequent periods as well. Thus our results show higher levels of TSH in term SGA neonates as compared to term AGA.

Conclusion:

Longitudinal case control studies are required to establish whether the higher level of TSH in SGA children are associated with development of thyroid dysfunction or any other metabolic abnormalities in adulthood.

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