features, partly, the rare incidence of such tumors makes it a potentially difficult diagnosis and a diagnostic pitfall.[1,2] Conversely, the straightforward? diagnosis of extramedullary plasmacytoma with or without associated amyloid deposition, requires primarily the presence of a rather uniform preparation of invariably large number of discohesive plasma cells of stages of maturation and sizes, with an associated background of lymphoglandular bodies as well as occasional lymphocytes, and as minimal as possible stromal cells.[3] It is such, that without these constituent cells, one cannot make the diagnosis of extramedullary plasmacytoma. Other factors that also interfere in the diagnosis of plasmacytoma includes; 1. The degree of differentiation of plasma cells 2. Relative frequency and proportion of distribution of the accompanying inflammatory/ reactionary and stromal cells 3. Demonstrating unequivocal monoclonality in the examined cells.[3] On the other end of the "neoplastic spectrum", one should also consider other neoplasms, whose constituent discohesive neoplastic cells greatly mimic plasma cells in various other neoplasms, when the later assumes other shapes or grades of differentiation that may mimic plasma cells. Amelanotic melanoma, or aggressive non-Hodgkin's lymphoma is such examples, and it depends on how the cytopathologist can easily make the distinction between these cell types sometimes; that will most likely require immunohistochemical staining.[3] In one of the largest studies on FNAB of extramedullary plasma cell tumors, there was no emphasis made on the role of the giant cell as a cellular component of these neoplasms, especially with special reference to its close association and relationship to the amyloid deposition. Similarly, intracytoplasmic amyloid observed within the cytoplasm of the giant cells did not receive any emphasis.[3] The presence of a certain proportion of a giant cells in lytic bone lesions will primarily aid in the separation of a main giant cell tumor of bone from "reactionary" presence of giant cells in primary bone lesions; the combination of clinical, radiological, and the complete cellular composition alongside with giant cells help in the final distinction. With reference to the small cell variant of osteogenic sarcoma, especially if the needle passes into a zone of minimal osteoid formation, or other sarcoma composed mainly of small cells, can still pose a problem in the differential diagnosis. Amyloid can sometimes be confused (especially in scanty amounts and if the cytologic setting is right), with osteoid.[4,5]

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From the Division of Hematopathology, Department of Pathology, Riyadh Military Hospital, Riyadh, Kingdom of Saudi Arabia. Address correspondence and reprint requests to: Dr. Ibrahim S. Tillawi, Division of Hematopathology, Department of Pathology, Riyadh Military Hospital, Riyadh 11154, Kingdom of Saudi Arabia. E-mail: ibrahimtellawi@hotmail.com

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Maternal and fetal thyroid stimulating hormones and the fetal indices of maturation, growth, and development

Oluwole O. Adedeji, *D.PHIL,*
George K. Oyakhire, *FRCOG.*

The thyroid stimulating hormone (TSH) occupies a central position in the hypothalamic-pituitary-thyroid axis, which regulates and controls the secretion of thyroid hormones.[1] The developing fetus depends on the thyroid hormones for neurological maturation, growth, and development.[2,3] Thyroid hormones are supplied by the mothers to the fetus through transplacental transfer until mid-gestation when the fetus begins to produce the hormones.[3] The placenta is permeable to thyrotropin releasing hormone, tetra-iodothyronine (T_4), and tri-iodothyronine (T_3), however, TSH does not cross the placenta. In fact, the fetal hypothalamic-pituitary-thyroid axis develops relatively independent of maternal influence,[4] and TSH production is determined by the thyroid hormone status. The maturation of negative feedback of thyroid hormone synthesis occurs by approximately mid-gestation, and elevated TSH concentrations were observed in infants as early as 2 weeks.[3] An abnormal TSH is usually the first indication of thyroid dysfunction. Hence, TSH screening for thyroid diseases has been recommended.[1,3] There is a growing interest in relative influence of maternal and fetal TSH on the growing fetus. Therefore, the objective of this study was to determine the correlation between maternal and fetal

thyroid stimulating hormones and the fetal indices of maturation, growth, and development.

The subjects were 101 consecutive female patients (mean age 26.78 ± 6.25) with no known thyroid abnormalities who gave birth at the King Abdullah Hospital, Bisha, Saudi Arabia and their corresponding neonates. The preterm neonates were babies delivered after 20 weeks and before 37 weeks of completed gestation. After obtaining consent from the mothers, blood samples were collected from the mothers and the umbilical cords immediately after delivery into plain tubes for TSH and heparinized tubes for biochemical analytes. The TSH levels of maternal and cord blood were determined, since humans have homochondrial placentas consisting exclusively of fetal tissue. Moreover, the fetal physiological indices, which included gestational age, weight, and Apgar scores at one and 5 minutes, as well as the biochemical indices such as, glucose, calcium, total protein, albumin, and albumin/globulin (A/G) ratio were measured. These indices reflect fetal maturation, growth, and development. The TSH was measured using DELFIA (Perkin Elmer Inc., Finland) hTSH ultra assay, a solid phase 2 site fluoroimmunometric assay, based on direct sandwich technique, in which 3 monoclonal antibodies are directed against separate antigenic determinants on the human thyroid-stimulating hormone (hTSH) molecule. Biochemical analyses were carried out on Hitachi 912 chemistry autoanalyzer using Roche reagents.

The Statistical Package for Social Sciences Version 10.0 was used for the analysis of data. Student's t-test and Pearson's correlation coefficients were determined. The p value of <0.05 was considered as a significant difference, while R=1.0 represented absolute positive correlation between the parameters. **Table 1** shows that the maternal TSH level (4.01 ± 0.36 mU/L) was significantly lower than the fetal TSH level (8.16 ± 0.51 mU/L) (p<0.05). These values were within the normal ranges for the mothers and fetuses at the time of delivery. There was no significant difference between the mean TSH levels of preterm and term neonates (p>0.05). In addition, the results showed that the mean fetal glucose and total protein concentrations were significantly lower than the levels for their mothers (p<0.05), while the mean fetal calcium level and A/G ratio were significantly higher than the values for their mothers (p<0.05). The mean fetal albumin concentration was higher than that of their mothers, although, the difference was not significant (p>0.05). The results showed some degrees of correlation, albeit low, between maternal and fetal TSH levels (R=0.08), fetal TSH and gestational age (R=0.08), fetal TSH and weight (R=0.20), maternal TSH and Apgar score at one minute (R=0.10), and fetal TSH and Apgar score at 5 minutes (R=0.20). There was no appreciable correlation between maternal TSH and neonatal weight (R=0.04), maternal TSH and Apgar scores at 5 minutes (R=0.01), and fetal TSH and Apgar scores at one minute (R=0.03). Finally, both maternal and fetal TSH levels were appreciably correlated to the mean fetal glucose, calcium, total protein, albumin, and A/G ratio.

Table 1 - Correlations between maternal and fetal thyroid stimulating hormone levels and the fetal indices.

Parameters	Maternal (Mean ± SEM)	Fetal (Mean ± SEM)	*P*-value
Maternal parameters (n=101)			
TSH* (n=101) (mU/L)	4.01 ± 0.36	8.16 ± 0.51	0.000
Glucose (mmol/L)	5.05 ± 0.23	3.51 ± 0.26	0.001
Albumin (g/dl)	30.4 ± 0.68	33.40 ± 0.42	0.521
Total protein (g/dl)	59.10 ± 1.26	52.62 ± 1.10	0.000
Calcium mmol/L	2.26 ± 0.02	2.70 ± 0.02	0.000
Albumin/glucose ratio	1.08 ± 0.02	1.78 ± 0.04	0.005
Fetal parameters (n=101)	**Maternal TSH R = value**		**Fetal TSH R = value**
TSH	0.08		1.0
Gestation age	-		0.08
Weight	0.04		
Apgar Score			0.20
1 minute	0.10		0.03
5 minutes	0.01		0.20
Glucose	0.46		0.28
Calcium	0.96		0.40
Total protein	0.59		0.61
Albumin	0.78		0.88
Albumin/glucose ratio	0.64		0.47

*Preterm (25) (<30 weeks), thyroid stimulating hormones (6.38 ± 0.90), term (75), TSH - thyroid stimulating hormones (6.39 ± 0.79) (p=0.996)

The fetal TSH could be assumed to be produced solely by the fetal pituitary gland since maternal TSH does not cross placenta. The higher fetal TSH level could be explained either on the basis of enhanced TSH release or impaired TSH degradation, which might be due to immaturity of the hepatic glycoprotein metabolic clearance system.[3] Another reason might be the increase in fetal TSH late in the third trimester, which continues up to 24 hours postnatal period. Nevertheless, it is conceivable that there is some degree of maternal influence on the fetal TSH production due to transplacental passage of T_4 and T_3.[4] Hence, there was some degree of correlation between the maternal and fetal TSH levels. Thus, the fetus is not completely independent of maternal thyroid status in utero. The transplacental passage of T_4 has provided partial explanation for normal clinical appearance at birth of over 90% of infants with congenital hypothyroidism.[4] Also, it explains the prevention of the development of mental retardation by early treatment of affected neonates with adequate thyroxine.[4] The reasons for the absence of significant difference between preterm and term TSH levels could be explained by the matured gestational age of the preterm neonates in this study, with mean age of 35 weeks, and the probable error in the calculation of gestational age, which was based on maternal recollection that could be incorrect. Nevertheless, it has been reported that, although the preterms experience a transient hypothyroxinemia with a fall in serum FT_4, there is no TSH elevation.[3] This is associated with lack of maturity of the hypothalamic-pituitary-thyroid axis resulting without a TSH surge in response to the hypothyroxinemia.[3] This could create difficulty in detecting hypothyroidism, if TSH is used for screening premature neonates. The fetal thyroid status has been postulated to play a role in the weight of neonates and infants. It has been shown in utero studies that, fetuses with severe intrauterine growth restriction (IUGR) had significantly lower levels of FT_4, FT_3, and slight elevation of TSH.[3] Intrauterine growth restriction is associated with placental insufficiency. Low levels of thyroid hormones, may contribute to reduced oxygen consumption by peripheral tissue to maintain viability at the expense of disrupting neurological development.[4] The maternal TSH level showed appreciable positive correlations with Apgar scores at one minute, while the fetal TSH showed some correlation at 5 minutes. Both maternal and fetal thyroid status may be important in the fetal brain development. It has been suggested that some degree of compensation may occur if one or the other is lacking, but the differences in the neuropsychological development are still demonstrable in either case compared with euthyroidism.[3] Maternal hypothyroidism has been associated with poorer neuropsychological expression in off-springs. Thus, it was reported that in the Netherlands, mothers with low FT_4 levels at 12 weeks gestation gave birth to babies who at 19 months of age had scores below tenth percentile of psychomotor index.[4] Fetal glucose, which was used for growth and energy metabolism, is supplied partly from the mother, and partly by gluconeogenesis in the fetus. The lower fetal glucose level might be because the fetuses require less glucose for energy metabolism than their mothers. However, there were positive correlations between maternal and fetal TSH levels and the fetal glucose concentration. The higher value of the correlation coefficient between the maternal TSH and the fetal glucose could be a reflection of a greater maternal contribution to fetal glucose level. Thus, raised TSH level is associated with increased gluconeogenesis and glucose utilization,[5] whereas, hypoglycemia and heat intolerance are associated with neonatal hypothyroidism. The fetus derives its calcium supply from the mother. The fetal calcium level was 16% higher, which agrees with previous reports of 10-20% higher fetal calcium concentrations than corresponding maternal levels.[5] This could be due to the high turn over of calcium from bone development and modeling in the growing fetus. Also, the maternal and fetal TSH showed positive correlation with fetal calcium level, which reflects the important role of TSH in bone maturation and growth, and its involvement with calcium metabolism.[5] The fetus derives its total protein partly from the mother and partly by fetal protein synthesis. Total protein level is associated with the body mass per surface area, which is less in fetuses than their mothers. Hence, the fetal total protein level was less than the mean level for the mothers. There were positive correlations between maternal and fetal TSH and fetal total protein, which are indicative of the role of TSH in the fetal development, maturation, and growth. The lower albumin concentrations of the mothers could result from hemodilution due to fluid retention during pregnancy. Nevertheless, there were positive correlations between maternal and fetal TSH and the fetal albumin level, which is compatible to the relationships with total protein. Furthermore, similar associations were also found between the maternal and fetal TSH and A/G ratios. The fetal A/G ratio was higher than that of the mothers due to the higher fetal albumin concentration.

In conclusion, this study showed that the maternal and fetal thyroid stimulating hormones played significant influential roles, and complement each other during the growth, maturation, and development of the fetus. Hence, there were positive correlations

between the maternal and fetal TSH levels and the fetal physiological and biochemical indices.

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From the Department of Pathology, King Abdullah Hospital, Bisha, Kingdom of Saudi Arabia. Address correspondence and reprint requests to: Dr. Oluwole O. Adedeji, Department of Pathology, King Abdullah Hospital, PO Box 60, Bisha, Kingdom of Saudi Arabia. Tel. +966 (7) 6223333 Ext. 1149. E-mail: adedeji12us@yahoo.com

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