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Original Research Article

A STUDY ON MEAN TSH LEVELS AND VARIOUS PERINATAL FACTORS AFFECTING TSH LEVEL IN CORD BLOOD OF NEWBORN

Raguvaran R[1], Ezhil Vanan NR[2], Kuzhali S[3], Gowtham V[4]

[1]Assistant Professor, Department of Paediatrics, Government Thiruvarur Medical College, Tamil Nadu, India.
[2]Assistant Professor, Department of Paediatrics, Government Thiruvarur Medical College, Tamil Nadu, India.
[3]Assistant Professor, Department of Community Medicine, Government Thiruvarur Medical College, Tamil Nadu, India.
[4]Assistant Professor, Department of Community Medicine, Government Thiruvarur Medical College, Tamil Nadu, India.

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Corresponding Author:
Dr. Gowtham V,
Email: doc.gowthampkm@gmail.com

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Abstract

Background: Congenital hypothyroidism is the most common preventable cause of mental retardation. Clinical diagnosis is difficult at birth and the time of initiation of therapy is critical in the determinant of outcome. Cord blood TSH has high sensitivity but with a high false positive values and a wide range of values causes high recall rates. Various maternal and perinatal factors are known to affect cord blood TSH levels. **Objectives:** To evaluate the mean TSH levels and various perinatal factors affecting TSH levels in cord blood of newborn. **Materials and Methods:** This is a descriptive cross sectional study which was performed in Govt Thiruvarur Medical College during a period of 6 months period and 110 newborn cord blood sample was collected and analysed. The data collected was entered in Excel and analysed using SPSS software. Appropriate descriptive and inferential statistics were used. **Results:** On evaluating the relationship between cord blood TSH levels and the categorical variables there is significant relationship between emergency LSCS and cord blood TSH level (p value <0.001), resuscitation and cord blood TSH(P value 0.0292) and low APGAR value and cord blood TSH (p value< 0.0259). The other variables considered in the study which includes gender, parity of mother, birth weight, weight appropriate for gestation, gestational age does not have significant p values and are considered as statistically insignificant. **Conclusion:** Neonatal screening for congenital hypothyroidism is very essential using TSH levels either in cord blood or heel prick sample. Cord blood TSH level hence an accepted tool for screening. The cord blood TSH have high sensitivity but with high false positive values due to confounding factors. In our study emergency LSCS, low APGAR score and requirement of resuscitation affects cord blood TSH levels.

INTRODUCTION

Thyroid is a small endocrine gland, which is brownish red in colour, located anteriorly in the lower neck extending from the level of fifth cervical vertebra to the first thoracic vertebra. It utilizes iodine to synthesise thyroid hormones. These thyroid hormones are essential for normal growth, development and various metabolic regulations in the body. Therefore, the thyroid hormone deficiency results in short stature, cretinism, intellectual disability, mutism etc.

Congenital hypothyroidism is the most common preventable cause of mental retardation. The worldwide incidence is 1:3000 – 1:4000.[1] The estimated incidence in India is 1:2500 – 1:2800 live birth. Clinical diagnosis is difficult at birth and the time of initiation of therapy is critical in the determinant of outcome.

Neonatal screening methods measure either cord blood TSH level or heel prick sample at 3 to 5 days of life. Therefore Cord blood TSH is an accepted screening tool for congenital hypothyroidism. Cord blood TSH has high sensitivity but with a high false positive values and a wide range of values causes high recall rates requiring evaluation for confounding factors contributing to increase in TSH values. Postnatal surge in TSH levels common to all newborns is considered to be mediated through alpha adrenergic stimulation following cold stress. Also various maternal and perinatal factors are known to affect cord blood TSH levels. In the

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present study nine factors included are 1)parity of mother 2) gestational diabetes mellitus 3)mode of delivery 5)birth weight 6)gestational age 7)sex 8)weight appropriate for gestation 9)requirement of resuscitation 9) APGAR score

Herbstman et al.[2] study on perinatal factors affecting cord blood TSH levels among 300 newborns reveals that several perinatal factors such as maternal age, gestational diabetes, pregnancy induced hypertension ,gestational age, alcohol use during pregnancy can affect thyroid hormone status in the cord blood.

Eun young Kim et al (Korea).[3] ,study on 130 neonates revealed that cord blood TSH levels is affected by perinatal stress events .

Fuse et al., (Japan).[4], study on 124 healthy newborns with different types of delivery including normal vaginal delivery, cesarean and vacuum extractor revealed that there is no statistically significant difference in cord blood TSH among study group.

Franklin et al.[5] ,in his study on 229 newborns revealed that perinatal factors such as birth weight and mode of delivery significantly affect cord blood TSH.

Gupta et.al.,(India).[6] study on perinatal factors affecting cord blood TSH levels among 952 indian live newborn showed that fetal distress, mode of delivery and requirement of resuscitation significantly affect cord blood TSH levels.

Miyamato N et.al.[7] study on influence of mode of delivery on pituitary- thyroid axis among 922 newborns showed that the cord bood TSH level reflects delivery stress and an elevated level does not influence the TSH screening test for congenital hypothyroidism in which blood is obtained at five days of life.

Armenian et al.[8] (Isfahan,Iran),in a study of perinatal factors influencing cord blood TSH in Isfahan Iran in 2012 involving 440 newborns revealed that mode of delivery significantly affect. cord blood TSH.

Chan LY,leung TN et.al.[9], study on 24,892 babies showed that cord blood TSH levels reflects fetal response to perinatal factors.

Sunil raj et al.[10] (India) study on cord blood TSH level variations in newborn- Experience from rural southern india revealed that the mode of delivery significantly affects cord blood TSH.

Turan S et.al.[11] study of effect of mode of delivery on neonatal thyroid function among 638 newborns reveals that there is significant correlation between mode of delivery and cord blood TSH levels.

Objectives

To evaluate the mean TSH levels and various perinatal factors affecting TSH levels in cord blood of newborn.

MATERIALS AND METHODS

This is a descriptive cross sectional study which was performed in Govt Thiruvarur Medical College during a period of 6 months period and 110 newborn cord blood sample was collected and analysed.

Blood samples were drawn from maternal end of cord immediately after the cord is being cut and about 2ml of blood is collected. The sample thus collected was kept at room temperature of around 250C and transported to laboratory within 4 hour and then sample analyzed with electro-chemiluminence assay.

The data of each child will be collected in the specific proforma which includes the newborn name, gestational age, sex, birth weight, requirement of resuscitation, APGAR score, weight appropriate for gestation, parity of mother, gestational diabetes mellitus and mode of delivery.

Cord blood TSH levels are measured using electro-chemi-luminescence immunoassay. The mean TSH levels are calculated and effect of perinatal factors on cord blood TSH levels are analysed statistically. All neonates who had TSH level above the cut off values are repeated TSH levels in venous sample on 5th day of life.

All consecutive live births delivered in hospital during study period(6 months) with informed parental consent were included in the study. Those neonates whose mothers were on any known antithyroid drugs and those with antenatal detected CNS malformations and major life threatening malformation were excluded.

The data collected was entered in Excel and analysed using SPSS software. Appropriate descriptive and inferential statistics were used to describe the results. Institutional ethics committee approval obtained to conduct the study.

RESULTS

Among 110 cord sample, 40 samples are from nulliparous women and 70 samples are from multiparous women. About 95 samples are from non GDM mother and 15 from GDM mothers. About 74 samples are from term babies and 36 samples from preterm babies. About 96 samples are from AGA babies and 14 samples from SGA babies. About 13 babies born from emergency LSCS delivery and 97 from other mode of deliveries (Vaginal, Elective LSCS, Vacuum assisted).

About 85 from babies are above 2.5kgs and 25 are low birth weight babies(<2.5kgs). About 65 samples are from male babies and 45 from female babies. About 100 samples are from babies with APGAR score more than 7 and 10 babies with APGAR scores <6. Nearly 102 babies do not require resuscitation and 8 babies require resuscitation.

The mean TSH among multiparous women is found to be 10.3068 and for nulliparous it is 10.049. The difference is not statistically significant. The mean

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TSH value is 11.093 among GDM mothers and 10.074 among non GDM mothers. The difference is not statistically significant.

The mean TSH value among the preterm babies is 10.0798 and among 74 term babies it is 10.2778. The difference is not statistically significant. The mean TSH value among SGA babies is found to be 5.08706 and is 5.6807 among AGA babies. The difference is not statistically significant.

The mean TSH value is found to be 17.977 among those delivered by Emergency LSCS and 9.172 among those delivered by other modes of delivery including Vaginal, Elective LSCS and Vacuum delivery. The difference is statistically significant. The mean TSH value is 5.791 among female babies and 5.5031 among male babies. The difference is not statistically significant.

The mean TSH value is 15.702 among babies whose APGAR score less than 7. Among those with APGAR scores above 7 the mean TSH is 5.0611. The difference is statistically significant. The mean TSH value among babies who required resuscitation is 8.6866 and for babies without resuscitation, it is 4.8971. The difference is statistically significant.

On evaluating the relationship between cord blood TSH levels and the categorical variables there is significant relationship between emergency lscs and cord blood TSH level (p value <0.001) , resuscitation and cord blood TSH(P value 0.0292) and low APGAR value and cord blood TSH (p value< 0.0259). The other variables considered in the study which includes gender, parity of mother, birth weight, weight appropriate for gestation, gestational age does not have significant p values and are considered as statistically insignificant. (Table 1).

Table 1: Roc Curve for TSH Values with Respect to Following Variables

VARIABLE	SENSITIVITY	SPECIFICITY	AUC	CRITERION	P VALUE	SIG
RESUSCITATION	75	89.2	0.776348	>15.1	0.0292	YES
EMERGENCY LSCS	84.6	88.7	0.896511	>13.1	<0.0001	YES
APGAR	70	85	0.737500	>13.1	0.0259	YES
BIRTH WEIGHT	48	74.1	0.571765	>11.33	0.2463	NO
GDM	86.7	29.5	0.543860	>6.54	0.5940	NO
GES.AGE	63.89	56.76	0.559685	≤8.32	0.3341	NO
PARITY	34.29	85	0.513571	>11.9	0.8102	NO
WEIGHT APPROPRIATE	64.3	75	0.597842	>11.5	0.2577	NO
SEX	42.22	72.31	0.512137	>10.5	0.8338	NO

DISCUSSION

Our hypothesis is to evaluate the mean TSH levels and various perinatal factors affecting the TSH levels in the cord blood of newborn. There are many perinatal factors during the delivery affect the TSH levels but in our study emergency LSCS, resuscitation and APGAR score are the variables that have significant statistical relationship with cord blood TSH. The exact reason for this condition has not been found yet; but possibly can be explained by stress events during labour and pregnancy. From the previous tables we conclude that the variables such as emergency LSCS, low APGAR scores and babies who required resuscitation are having statistically significant elevated cord blood TSH levels.

The other perinatal variables such as gestational age, parity of mother, sex of the newborn, gestational diabetes mellitus, weight appropriate for gestation doesnot have significant TSH elevations and their P values remains insignificant. Furthermore to strengthen our hypothesis, the cross tables, ROC curves and cut off criterion of all perinatal outcome were identified and discussed in results.

It is found that the variables such as mother who had emergency LSCS, babies with low APGAR scores and baby who are resuscitated follows the same line of significant P values, area under curve, ROC cut off criterion. The other perinatal factors doesn't have statistically significant area under curve and P values.

The variables such as requirement of resuscitation, emergency LSCS and APGAR scores were having direct correlation with the elevation of TSH levels in cord blood. Then we have taken venous sample for newborn with TSH value more than 13.1 (cut off values from ROC curve) at 5th day of life. Then paired t test done for the initial and venous blood TSH values and finding out the statistical significance .It is found to be low and this falsely elevated TSH levels is due to perinatal stress factors which also supported by other previous journals done in different centres.

There are some studies which have been performed in this same field, in which some are supporting and some results are controversial. Herbstman et al., study performed in 300 newborns revealed that several factors such as maternal age, pregnancy induced hypertension, gestatational diabetes mellitus and mode of delivery can affect thyroid hormone status which is inconsistent with our study.

Kim et al., study of perinatal factors affecting cord blood TSH levels performed in 130 neonates in Korea revealed that perinatal stress events significantly affect cord blood TSH levels. Amit gupta et al., study revealed that there was no significant difference in cord blood TSH between male and female babies which is consistent with our study.

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Various studies are using different cut-offs for CBTSH levels ranging from 20-90 Miu/ml. We have used the cut-off value for cord blood TSH level as per ROC curve is 13.1u/ml. Devi AR and Noushad et al.[12] has taken the following range for comparison-CBTSH value <10uu/ml as normal,10-20uu/ml as borderline and >20uu/ml as abnormal. Gurjit kaur et al., from Chandigarh has taken 9uu/ml as the TSH cut off value. Ruth V Mikelsaar et al.[13] from Estonia has taken CBTSH cut off value of 12uu/ml which is lower cut off value when compared to our study.

In our study 20 cord samples among 110 samples are found to have CBTSH levels above the cut off value of 13.1 and repeat venous sampling done on 5th day of life. All venous samples TSH levels found to be lower than cut off TSH levels. This reveals that the high cord blood TSH levels are due to perinatal stress factors such as emergency LSCS, resuscitation and low APGAR score which has significant positive correlation as evidenced with P values in our study.

CONCLUSION

As we know that congenital hypothyroidism is the most common preventable cause for mental retardation with an incidence of 1:3000-1:4000 live births worldwide and about 1:2500-2800 in India. Therefore, neonatal screening for congenital hypothyroidism is very essential using TSH levels either in cord blood or heel prick sample. Cord blood TSH level hence an accepted tool for screening. But it is limited by the fact, that the cord blood TSH have high sensitivity but with high false positive values due to confounding factors. There are various perinatal factors affects cord blood TSH levels. In our study emergency LSCS, low APGAR score and requirement of resuscitation affects cord blood TSH levels.

Recommendations

As various perinatal factors influence cord blood TSH levels, knowledge about these factors helps in reliable interpretation of the results and any rise in TSH should be seen in the light of these factors. This helps in avoiding unnecessary repeat evaluation and hence this will save cost as well as the need to subject for invasive investigations.

Limitations

To have more conclusive evidence of our findings,

a. We have to evaluate large number of babies.
b. To include other maternal and perinatal factors in the analysis.

Conflict of Interest Nil

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