REFERENCE INTERVAL OF THYROXINE AND THYROTROPIN OF HEALTHY TERM NIGERIAN NEWBORNS IN JOS UNIVERSITY OF TEACHING HOSPITAL

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Abstract

Objective

To establish a local Reference Interval of Serum Thyroxine (T4) and Serum Thyroid stimulating Hormone(TSH) of healthy Nigerian Newborns in Jos University Teaching Hospital Jos.

Materials and Methods:

One hundred and sixty healthy term Nigerian Newborns who fulfilled the criteria for inclusion were selected by simple random sampling.

Cord blood sample taken from the Newborns were analyzed for levels of T_4 and TSH (Thyroid stimulating hormone) using the Enzyme Link Immunosorbent assay (ELISA) method.

Reference intervals were determined by Rank Procedure of non- parametic method.

Results

TSH Mu/L Reference Interval

Lower reference limit 0.22 (0.21 – 0.23) mU/L

Upper reference limit 29.2 (21.8 – 29.2) mU/I

Reference Interval = 0.21 – 29.2 mU/L

TSH Mean = 3.31mU/L ±2.56

T4 nmol/L Reference Interval

Lower reference limit 63.0 (55.0 – 66.0)

Upper reference limit 201.2 (201.1 – 202.9)

Reference interval = 63.0 – 202.9

T_4 Mean = 143.5 ±136 nmol/L

Conclusion

This study revealed the serum values of T_4 and TSH in these healthy Nigerian Newborns. These values can be used to diagnose congenital hypothyroidism (CH) and ultimately used for screening for congenital hypothyroidism in this region of iodine deficiency disorder (IDD). This may form a basis for establishing a neonatal screening program in collaboration with pediatricians in this region as CH is one of the commonly screened inborn errors of metabolism.

KeyWords: Reference Interval, Thyroxine, TSH ,Congenital hypothyroidism

Introduction

The purpose of setting up of the reference interval is for the diagnosis, treatment, monitoring and evaluation of the patient. Reference intervals enable clinicians to evaluate thyroid function. Several pediatric reference intervals for thyroid function test have been published[1-4].

Newborn screening for congenital hypothyroidism (CH) in sub- Saharan Africa is still a mirage[5], Neonatal screening programs for detection of CH in neonatal period are wide spread in the developed countries in the last three decades [6] and fast gaining momentum in the developing world as well [7]. CH is associated with impaired physical and mental development.

Therefore, neonatal screening for T_4 and TSH has been established in the majority of developed countries to timely diagnose and treat CH in order to prevent severe mental retardation.[6,7]

Age – and method dependent plasma TSH reference intervals are essential for diagnoses and management of Ch[8].

TSH is accepted as the single indicator of thyroid

function because if its high sensitivity. Nevertheless free T_4 is indispensable to confirm these diagnoses since hormone production directly reflect hormone production by the thyroid gland

The IFCC has recommended a minimum of 120 subjects for non – parametric methods[9].

The method used and population are key factors in determining reference interval.

Accurate reference interval for plasma TSH have not been adequately defined due to the difficulties in obtaining samples from a healthy pediatric population.[9]

In a study the estimate method-dependent plasma TSH upper reference intervals was of great practical use to clinicians to diagnose and follow up infants found to have increased blood spot TSH concentrations identified by Newborn screening programme.[10]

It was observed by Adenira of Okolo studied in one hundred and fourteen apparently healthy term AGA neonates had their thyroid function analyzed[5].

More than 2 decades ago, Isichei *et al* studied Thyroid profile in cord blood of healthy Nigeria newborn in Jos[11]. In resetting the level of cord blood thyrotropic, Ogunkeye[12] et al in Rai Saudi discovered a TSH references interval of 2.0 – 16.8 mu/L in unaffected infants and a mean cord blood TSH concentration of 39.9mu/L.

In Germany[13], it was shown that dried blood spot has been widely use for TSH and T_4 analysis for diagnosis of CH.

High incidence rates for CH reported in a hospital based study suggests the need for screening programme for CH in Bahrain[14].

The aim of this study is to re-establish age – specific references for serum concentration of TSH and T_4 in healthy Nigerian Newborn. And to compare this result to previously published reference data the crucial role the clinical chemist depend on[15].

Materials and Methods
Research Design and Setting
This study was carried out at Jos University Teaching Hospital (JUTH) Nigeria between the months of June and August 2008.

One hundred and sixty women were randomly selected for counseling and consent was obtained from them.

Umbilical cord blood samples were obtained from these women who had just been delivered of the pregnancy at the labour ward in JUTH.

Excluded were women who were clinically hyperthyroid or hypothyroid or on any drug that may alter thyroid hormone levels e.g. propranolol, women with severe debilitating disease like chronic liver disease, diabetes, or hypertension and delivery by caesarian section were excluded.

Data Collection and Sample Analysis
Blood was obtained from the placental side of the cord before delivering the placenta. Cord blood (5ml) was collected into a plain vacuum container and transported to the laboratory. Cord blood samples collected were allowed to clot then centrifuged at 3000 r.p.m for 5mins. The serum stored at $2 - 8^0C$ until assayed. Sera were frozen at – 20^0C where assay was delayed longer than 24 hours. Assays were done in 4 batches each containing forty samples at different time intervals.

Cord blood TSH and T4 level were measured by the ELISA method, a second generation assay.

Results
The study had a total of 160 newborns in JUTH, and revealed reference values for TSH and T_4 at birth.

From table 1, the mean TSH was found to be 3.3 mU/L for female newborn and mean TSH was 3.72mU/L, and male mean TSH was found to be 2.82 mU/L and the reference interval is 0.21 – 29.2mU/L

From table 2,

We observed that the mean T_4 of the 160 newborn was 143.5 nmol/L for female newborn and 132.1 nmol/L for male newborn and the reference interval is 63.0 – 202.9nmol.

Figure 1 showed negatively skewed frequency distribution and bar chart of cord blood TSH of 160 newborns. The highest frequency is 3.0-6.9 mU/L while lowest was 11.0-14.9 mu/l,

Figure 2 revealed a bar chart distribution with a peak of 160-189.9 nmol/L the chart showing positively skewed distribution the minimum of the curve falls between 70-99.9 nmol/L

The ranked type non-parametric value was used. Reference values were placed in ascending order and ranked to determine the lower reference limit using the formulary r=0.025 (n+1) for lower limit and r=97.5 (n + 1) for upper limit.

Table 1

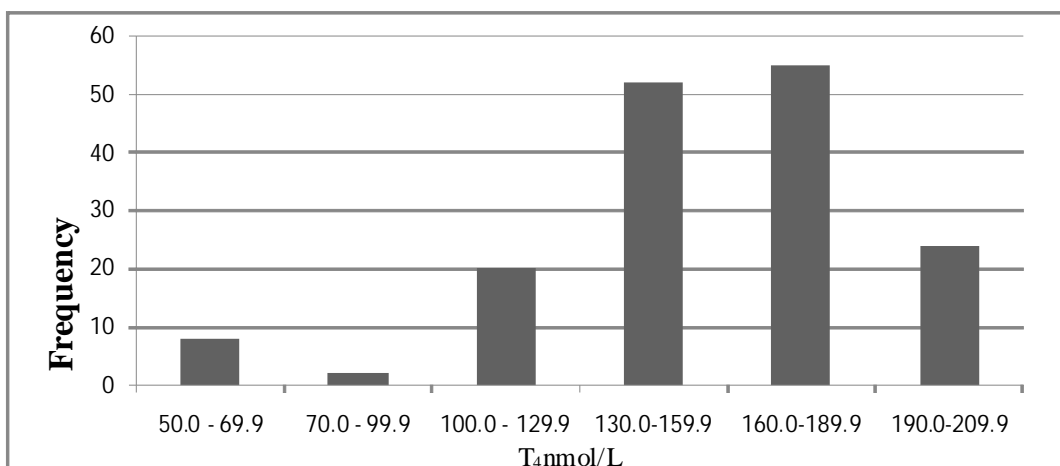| TSH Mu/L Reference Interval |
| --- |
| Lower reference limit 0.22 (0.21 – 0.23) mU/L |
| Upper reference limit 29.2 (21.8 – 29.2) mU/l |
| Reference Interval = 0.21 – 29.2 mU/L |
| TSH Mean = 3.31 mU/L ± 2.56 |

Table 2

T4 nmol/L Reference Interval
Lower reference limit 63.0 (55.0 – 66.0)
Upper reference limit 201.2 (201.1 – 202.9)
Reference interval = 63.0 – 202.9
T_4 Mean = 143.5 ± 136 nmol/L

The study had a total of 160 cord samples analysed. This comprised of 82 females and 78 males.
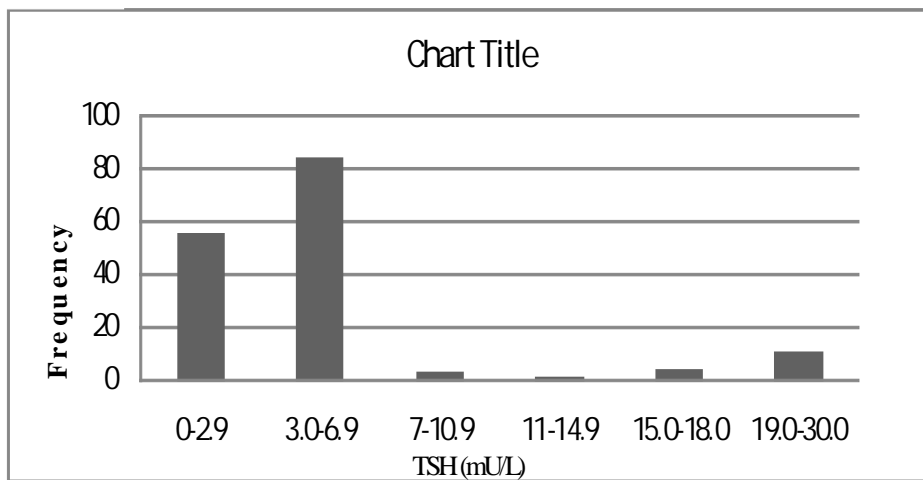
Figure 1 A bar chart showing the distribution of thyroid stimulating hormone (TSH).

Figure 2: A bar chart showing the distribution of thyroxine (T_4).

Discussion

This study was set out to establish the reference intervals of serum T_4 and serum TSH of Nigeria newborn at term. The study revealed serum T_4 reference of 63 – 201nmol/L, and serum TSH reference interval of 0.22-29.2mU/L. Previous work done in this same area (Jos) revealed a TSH level of 15.0 – 30.4mU/L[11]. The reason for discrepancy then was attributed to iodine deficiency. But now there is improvement in this region due to iodization of salt in diet and increase awareness of the deficiency.

The reference values obtained in this work differs greatly with that done in Bahrain[14]. In that study the cord blood samples were used to determine the reference interval of TSH FT_4 and TSH intervals and TSH. Interval was found to be 2.5 – 37.3mU/L. This reference range difference could be due to geographical factors, diet, and use of different assay method[14].

In Saki South west Nigeria Mean neonatal plasma TSH is Saki was above the adult reference interval and significantly higher than the level seen in Ibadan (9.82 ± 1.64 vs 4.18 ± 1.17 mU/L, P <0.05). The incidence of neonatal chemical hypothyroidism (NCH) in Saki was 14.7 per 1000 babies/ No case of NCH was seen in Ibadan. These results suggest environmental iodine deficiency and relative chemical hypothyroidism of mothers and neonates in Saki when compared to mothers and neonates from non-iodine.

This was significantly higher than that obtained in Jos.

Normal cord TSH values show a wide range 1 – 38.9mU/L[9] and this is closer to this work of 0.22 – 29.2.

Use of cord blood TSH as a screening tool is an attractive preposition because of its simplicity and accessibility: Fuse[21] et al had shown that mixed cord blood is a good sampling technique for screening congenital hypothyroidism.

In India[6] a TSH cutoff 20mU/L was established.

However our TSH values were lower than discovered by khadilker[17] et al who in a study of 203 neonate found a mean cord TSH value of 12.3 ± 4.9mU/L.

This result demonstrated a comparable trend as with the normative data for cord blood TSH values reported by various workers across the globe[18-20]. It was concluded that we may safely use the widely accepted cutoff cord blood TSH value of 20mU/L for the purpose of screening for CH. The used of cord blood TSH as a screening tool is an attractive preposition because of its simple sampling technique for screening. Walfish[21] concluded that cord blood TSH had a better specificity and sensitivity as compared to filter paper.

Conclusion

In the background of iodine deficiency region and high intake of goitregenous substances, it was found paramount to revisit the study of thyroid disorders in newborns and to re-establish a base line.

This study revealed the present thyroid status at birth and gives us a guide towards screening for congenital hypothyroidism which will ultimately justify establishing a neonatal screening program in collaboration with the pediatrician in Jos.

Congenital hypothyroidism is one of the preventable inborn error of metabolism among many others, which may be responsible for high neonatal death in this country.

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