Neonatal Screening for Congenital Hypothyroidism in Tertiary Care Centers

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ABSTRACT:

Introduction: Neonatal screening for **c**ongenital hypothyroidism (CH) is one of the prime achievements in Preventive Medicine. Most of neonates born with CH have no detectable physical signs, symptoms and showed normal appearance. Neonatal hypothyroidism is virtually overlooked and late diagnosis leads to most severe outcome of CH, mental and growth retardation.

Aim: To find out the prevalence of congenital hypothyroidism in new born babies delivered at tertiary care centers and provide early diagnostic, preventive and therapeutic services.

Material and Methods: The study was conducted in post natal ward of tertiary care centers at Greater Noida (multicentric hospital based study) of Gautam Buddha Nagar districts to find out the prevalence of congenital hypothyroidism. A total of 314 newborn babies were included in present study which was conducted during Feb 2014 to Dec 2016. Cord blood / venous blood samples were taken of congenital hypothyroidism (CH) suspected neonates. Thyroid stimulation hormone (TSH) and T4 (free) were used to screen the neonates. Neonates with abnormal hormonal levels TSH ≥ 25µIU/ml, T4(free)≤ 1.0 ng/dl in cord blood and TSH ≥10µIU/ml, T4(free) ≤0.58 ng/dl in venous blood or any doubtful results rechecked with repeat sample. On the initial screening samples were considered to have positive screening test for CH & were classified as transient hypothyroid (TSH level 25-50µIU/ml) & permanent hypothyroid (TSH level > 50µIU/ml). The data was analyzed using standard statistical techniques.

Results: The Prevalence of CH in tertiary care centers at Greater noida district Gautam Buddha Nagar was 7/314 live births. CH neonates detected in venous blood samples 3 Male and 3 Female whereas 1 Male CH neonate detected in Cord blood sample.

CONCLUSION: The Prevalence of CH in study area 7/314 live births but all neonates were transient (TSH level 25-50µIU/ml) hypothyroid which is greater than global incidence of 1:3000 to 1:4000. It is highlighted that incidence of CH is high in Indian population as compared to western counterparts. Study importance of the neonatal screening programs.

Keywords- Neonatal screening, congenital hypothyroidism (CH), Iodine deficiency, Mental retardation.

INTRODUCTION: Congenital hypothyroidism (CH) is the most common preventable cause of mental retardation (Michael O Ogundele, et al 2010). It is one of the most common disorders leads to mental impairment and growth retardation in neonates. In most of the developed countries, the neonates screen to rule out the CH for early diagnosis and early treatment. CH is usually episodically and occurs in one in 3000-4000 babies (Simsek E et al 2003, Buyukgebiz A, 2003). Overall neonates with CH is caused by an abnormal progress of the thyroid gland that is a occasional disorder and account for 85% of the cases and remaining 15% of the cases are caused by dyshormogenesis. The clinical features of CH are so subtle, at the time of birth many infants do not shows any sign and symptoms of CH, the delay diagnosis leads to the most severe outcome of CH, mental and growth retardation may occur with lack of thyroxine the degree of retardation depend upon the severity of the thyroxine deficiency. When there is only a partial lack of thyroxine, little deterioration in the mental function may occur. When the production of thyroxine is totally absent and the baby does not get any treatment, mental retardation may be severe. However, this will not occur if the early treatment will be initiated, emphasizing the importance of newborn screening. Global incidence is 1:3000 to 1:4000 live births, the incidence being higher among Asian and Hispanic children. Indian incidence is 1:1757. Normal male: female ratio is 2:1(Mandy Brown Belfort et al 2012).The common etiologies are thyroid dysgenesis (aplasia, hypoplasia and ectopic) and dyshormonogenesis. Thyrotropin receptor blocking antibodies, maternal medications, iodine deficiency, genetic mutations are other causes (Stephen Lefranchi, 2011). Overall 95% newborns with CH do not shows any sign and symptoms at the time of birth but universal newborn screening allows for early diagnosis and treatment resulting optimal neurodevelopmental outcome. Some newborn babies may present with mild symptoms that often go to unrecognized problem like as excessive sleeping, low body temperature, reduced interest in feeding, Sluggishness in the both physical and mental activity, slowness of growth, poor muscle tone, low or hoarse cry, infrequent bowel movements. A small percentage of babies have clinical features of low hairline, thick scalp, and wide open anterior fontanelle, eyes far apart with depressed nasal bridge, macroglossia, apneic episodes, umbilical hernia, and prolonged jaundice (UK Newborn Screening Programme Centre Policies and Standard, 2005.). The new born screening program may not start in many developing countries, In India it is still in its early stages due to poor infrastructure and economic suppression. In some of countries like UK, T4 is measured to rule out the CH and followed by TSH when T4 is low. Some projects measure TSH as the primary screen (Korada M et al, 2008). In present study we have include both analytes T4 (free) and TSH for screening purpose. CH may be permanent (TSH> 50 uIU/ml) or transient (TSH >25 to 50 uIU/ml). Causes for transient hypothyroidism are antithyroid drugs, iodine excess, iodine deficiency, TSH receptor blocking agents and transient hypothyroxinaemia of prematurity. The Global incidence of maternal hypothyroidism in pregnancy is overt (0.3 to 0.5 %) or subclinical hypothyroidism (2 to 3%).The chronic autoimmune thyroiditis is the most common cause of maternal hypothyroidism in iodine sufficient areas. In view of these facts we have not included these type of patients who's are having maternal history of thyroid or on anti thyroid treatment because due to permanent administration of drugs may also effect the fetus, other causes are previously treated graves, thyroid cancer, drug and external radiation induced hypothyroidism and pituitary dysfunctions, associated adverse fetal and neonatal outcome include preterm birth, intrauterine growth restriction (IUGR), congenital anomalies, fetal distress in labour and fetal leads parental deaths. However these complications are avoided with adequate treatment of hypothyroidism ideally early pregnancy. The

affected fetus may experience neurodevelopment impairments, particularly if both fetus and the mother are hypothyroid during gestational period (UK guidelines final version July of 2006).

MATERIAL AND METHODS: The observational multicentric hospital based study was conducted over a period of 2 years from Feb 2014 to 2016 at Greater noida of District Gautam Buddha Nagar. The aim of present study is to detect all cases of congenital hypothyroidism as early as possible, with an acceptable cost-benefit ratio and to avoid false positive results. A total of 314 pregnant women aged 20 to 45 years and their neonates were included in the screening study. All of the mothers were no past history of thyroid disease and no history of continuous long life taken drugs. All newborn mothers were healthy and none experienced complications during the pregnancy/delivery. The cord blood / venous blood samples were collected by a trained staff nurse. 3ml Blood sample collected in a plain vaccutainor, kept for clotting and centrifuged at 4500 RPM for 15 minutes. Serum T4 (free) and TSH analyzed to screen the baby for congenital hypothyroidism. The new methods have increased sensitivity and specificity in the detection of CH. However, despite the development of more accurate test programs, approximately 5% of CH cases may still be missed in any screening program. The reasons could be failure of sample collection, unsatisfactory samples, misinterpretations of samples and unsatisfactory recalls, the condition being subclinical or as is true for programs which measure only TSH, failure to detect infants with central CH (La Franchi SH et al, 1985, Fisher DA, 1983, Evans C et al 2011, Najafi M et al 2011).

All babies delivered at tertiary care centers (hospitals) in the stipulated time period were included. The exclusion criteria were

[1] Baby's mother case of thyroid Disorder/treatment taking for thyroid disorders

[2] Baby's family not permanent resident of study area.

On first day of baby, detailed head to toe examination and systemic examination was done by the pediatrician and entered in case profiles. The newborn baby screen for CH and analysed for T4 (free) and TSH assay. The TSH concentration > 25 µIU/ml in the cord blood, TSH concentration > 10 µIU/ml in the venous blood and T4 (free) is below the reference range on initial screening sample were considered to have positive screening result. Any abnormal or doubtful values was rechecked or repeated within 3 days. Patients were followed up till discharge and further follow up was conducted in those cases with congenital hypothyroidism.

RESULTS: Of 314 neonates screened, 167 (53.18%) were male and 147 (46.81%) female with a male to female ratio of 1.13;1 of all neonates attending tertiary care centers at Greater noida.

Distribution of serum TSH levels (uIU/ml)	n	%
0-4.9	149	47.45
5-9.9	131	41.72
10-14.9	25	7.96
15-19.9	05	1.59
20-24.9	02	0.64

>25	02	0.64A
Total	314	100

Table/fig- 1 Distribution of serum TSH levels among the screened neonates (n=314)

The distribution of serum TSH value among the screened neonates is shown in table 1 .The control mean T4(free) ,TSH level in venous blood (0.95 ± 0.17, 2.8 ± 2.41) and cord blood (0.90 ± 0.18, 7.2 ± 2.2) respectively, shown in table/fig2 .The mean level T4(free) ,TSH level among neonates patients in venous blood (1.10± 0.31, 5.54 ±3.16) and cord blood (1.14 ± 0.30, 10.14 ± 6.38) respectively, shown in table/fig3 . Overall 13 neonates (4.14%) were re-called. The prevalence of CH among all subjects studied was 9/314 or 7/314 live births. The maternal age range 20-45 years. All the cases were full term, no premature baby included in this study. The p value of T4 (free) and TSH was <0.05 which was statistically significant.

Parameter	**Venous blood neonates**	**Cord blood neonates**
	n=37, Mean±SD	**n=35, Mean±SD**
T4 (Free) ng/dl	**0.95 ± 0.17**	**0.90 ± 0.18**
TSH uIU/ml	**2.80 ± 2.41**	**7.2 ± 2.2**

Table/Fig2: T4 (free) and TSH levels among neonates control subjects.

Parameter	**Venous blood neonates**	**Cord blood neonates**	**p value**
	n=195, Mean±SD	**n=47, Mean±SD**	
T4 (Free) ng/dl	**1.10 ± 0.30**	**1.14 ± 0.30**	**<0.05**
TSH uIU/ml	**5.54± 3.16**	**10.14.± 6.38**	**<0.05**

Table/Fig3: T4 (free) and TSH levels among neonates patients.

DISCUSSION: Neonatal screening program have been initiated started worldwide to screen the neonates for CH which is 7 fold more common and the effect of early T4 replacement on neuropsychological outcome is even more dramatic congenital hypothyroidism has become the neonatal condition par excellence that meets all criteria for population based screening. Recent studies revealed out the increase in incidence of congenital hypothyroidism in US are being reviewed and debated on. Likewise there is a controversy and lack of agreement on the cut off values used to detect congenital hypothyroidism (Johnny Deladey et al Aug 2011). In this study a cut off value of TSH 25 uIU/ml (Cord blood) and TSH 10 uIU/ml (Venous blood) is taken. Despite India having a higher reported incidence (C S Pandav, et al 1992). Hypothyroxinemia (low T4 and normal TSH) this condition occurs most commonly in premature infants and is found in 50% of babies born less than 30 week of gestation often T4 free is less affected

than total T4. In a term neonate with a low T4 free but normal TSH level, true central hypothyroidism, which is quite rare, should be ruled out. Mutations in the gene coding for the beta subunit of TSH or the thyrotropin releasing hormone receptor could be the cause (Zegher F et al 1995, Spady DW et al 1988) Central hypothyroidism could coincide with other anterior pituitary hormone deficiencies, hypoglycemia. Hyperthyrotropinemia (normal T4 and Elevated TSH) Elevated TSH levels with Normal T4 levels could persist for years. Iodine excess, especially when the iodine containing antiseptics are used, may cause transient hypothyroxinemia in preterm babies (Klein RZ et al 2000, Hudaoglu OG et al 2009) Low T4 and elevated TSH primary CH is the most common cause of condition. However , transient cases, which may be caused by maternal antithyroid medication, exposure to tropical iodine, maternal iodine deficiency or excess, maternal TSH receptors blocking antibodies, medications (Dopamines, steroids) or prematurity (< 30 weeks) may also occur. All these cases should be treated as CH for the first 3 years of the life by taking in to an account the risk of mental retardation. The re-evaluation after 3 years is needed in such patients, (Yang RL et al 2005, Hopfner S, et al 2005). In the present study the actual incidence is higher therefore stresses on the need for routine newborn screening for all neonates, before discharge.

LIMITATIONS: Cord blood / Venous blood samples collected from the neonates only and restricted for tertiary care centers of the study area at Greater noida of Gautam Buddha Nagar district only.

CONCLUSION: The main purpose of the study was to screen the neonates for congenital hypothyroidism because the early diagnosis and treatment with adequate doses of L-T4 rescured affected children from mental retardation. It is reemphasized that incidence of CH is high in Indian population. CH continues to remain most common cause of mental retardation and hence must be identified early and treated. Adequate follow up strategies should come into place (important to distinguish transient and permanent CH), Newborn screening should be made compulsory in all centers for early detection and early treatment.

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