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Iodine Deficiency Disorders In Pregnant Women and Neonates

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Abstract:

Aim **-** Iodine Deficiency Disorders in Pregnant Women and Neonates at CCMMC Hospital Durg.

Material and Methods **-** Investigation was carried out in 23 pregnant women suffering from congenital hypothyroidism and compared with 30 normal control group composed of healthy pregnant women and followed-up to one month of delivery of the neonates. Cord blood samples was collected after birth of new born in specimen tube, and 5 ml blood will be collected in a dry, clean, plane tube from maternal and fetal. After clotting of blood, it is centrifuged at 3000 rpm. for 10 minutes. Serum will separated for the analysis of thyroid profile such as TSH, T4, T3, using ELISA and reagents kits will purchased from accu-bind. A spot morning urine sample from each mother was collected and assayed in duplicates for the determination of urinary iodide concentration (UIC) using ammonium persulphate digestion method

Results **-** ***Significance of study***- The emphasis on Iodine supplementation during pregnancy is not a routine practice in Durg district. In such situation an adequate dietary intake of Iodine throughout the gestation period has to be investigated. Therefore the present study has been planned to assess the maternal iodine status and thyroid function at the first second & third trimester and its influence on neonatal thyroid function and lastly screening of congenital hypothyroidism in neonates of Chhattisgarh, with a view to strongly recommend the implementation of neonatal screening programmer for iodine so that the optimal mental development of children can be achieved.

Keywords **-** ***IDD, CH, T3, T4, TSH, TRH, TBG, BW and UIC***

Introduction

The thyroid gland, which is situated in the neck, produces two important hormones: thyroxine (T4) and triiodothyronine (T3). The predominant thyroid hormone secreted by the thyroid gland is T4; only a small amount of T3 is produced by the thyroid gland. In the peripheral tissues, T3 is active form of hormone. All the circulating T4 needs to be converted into T3 for its action in peripheral tissues. Deficiency of thyroid hormones is called hypothyroidism & this can affect the function of virtually every system in the body. Production of thyroid hormone by the thyroid gland is controlled by thyroid-stimulating hormone (TSH) produced from the pituitary gland which in turn is controlled by TSH releasing hormone (TRH) produced by the hypothalamus. A small amount of T3 and a large amount of T4 are directly secreted by the thyroid gland into the bloodstream: in the blood T4 is more protein bound than T3.Thyroxine-binding globulin (TBG) is the major protein binding to thyroid hormones and albumin is a minor binder. In the peripheral tissues, T4 is DE iodinated to form T3 by enzyme called deiodinates.[1] Hypothyroidism can be classified into primary, Secondary and tertiary forms. Primary hypothyroidism is due to abnormalities intrinsic to the thyroid gland, while secondary hypothyroidism is due to pituitary disease which impairs TSH production and Tertiary hypothyroidism is mainly due to hypothalamic i.e. Thyroid releasing hormone deficiencies (TRH). TSH is the major hormone stimulating thyroid hormone production and whenever the thyroid gland fails, the production of thyroid hormone becomes suboptimal. Due to positive feedback from low thyroid hormone level, the TSH concentration increases and this characterizes primary hypothyroidism. Sometimes the increase in TSH concentration can stimulate the thyroid gland to keep thyroxine in the normal range, a condition called subclinical hypothyroidism. But when the thyroid gland fails completely and the high TSH is unable to keep thyroid hormone level in the normal range. Overt primary hypothyroidism occurs. In certain situation i.e. in pituitary damage, the secretion of TSH becomes low and this TSH hypos creation leads to secondary failure of the thyroid gland. This is called secondary hypothyroidism. TSH deficiency can be due to pituitary disease or hypothalamic disease due to a low TRH production.[2] In the classic form of the disease described by Hashimoto, the

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thyroid gland is enlarged due to lymphocyte infiltration, and the gland become rubbery. Hypothyroidism is due to auto immune damage to the thyrocytes. In a small proportion of the subject, antibodies that block the TSH receptor also lead to hypothyroidism. In many cases of chronic autoimmune thyroiditis the gland is not enlarged and it is termed as atrophic thyroiditis and is due to extensive fibrosis of the gland.

Iodine is an essential element for the production of thyroid hormones, tri iodothyronine (T3), and thyroxin (T4). Women need more iodine during pregnancy to maintain normal metabolism as well as to meet the requirements of T4 and iodide transfer to the fetus. Iodine deficiency and hypothyroidism during pregnancy have long been known to be associated with neurological deficits and mental retardation; however, there is also evidence for an increased risk of adverse effects on obstetrical outcomes such as preeclampsia or placental abruption, and negative effects on the offspring such as preterm birth, fetal death, or low birth weight (BW). The urinary iodine concentration (UIC) is considered as a good indicator of previous days dietary iodine intake, as over 90% of iodine absorbed is eventually excreted in urine.[3] Congenital hypothyroidism (CH) is one of the major health problems and the common preventable cause of mental retardation in children. It has an incidence of 1 in 1700 births in India[4] and 1:3000-4000 live births in worldwide.[5] If CH is diagnosed promptly and treated early, irreversible mental retardation can be prevented. Because signs and symptoms of CH are often scarce at birth, newborns are screened at birth for early diagnosis of CH. Neonatal screening programs for detection of CH in neonatal period are widespread in the developed countries for the last three decades[6] and are fast gaining momentum in the developing world as well. In most screening programs blood samples are collected within 5-6 days of age, but with large number of babies being discharged early, cord blood samples are being used as well[7] In our country, it is very difficult to follow up all babies once discharged. Also, an effective social system whereby babies could be reached at home is practically non-existent. Thus cord blood remains a very practical alternative for screening purposes, and thus is the practice in some Asian countries. Mixed cord blood samples for TSH values have compared well with filter paper samples taken in the first few days of life. Use of cord blood TSH as a screening tool is an attractive preposition because of its simplicity and accessibility.[8] The Indian Academy of Pediatrics recommends the use of cord blood samples for screening for congenital Hypothyroidism. Very few reports of cord blood values of only TSH exist in Indian literature and thus this study is being carried out.[9] The term neonatal screening or newborn screening is used to describe various types of tests that are done during the first few days of a newborn life. Neonatal hyothyroidism is one of the most common preventable causes of mental retardation in children. The complications of NH such as intellectual impairment and neurodevelopment delay present later in life when it is too late to be treated or reversed. Timely is very important to effect adequate neurocogenitive development during the critical first 3 years of life. The earlier the treatment is started, the higher the IQ levels are achieved later in life. If iodine deficiency and neonatal thyroid failure continue for about 3 months, this leads to irreversible brain damage. It is estimated that about 10% or more of newborns in severe goiter endemic areas are at risk of NH and resultant compromised physical and mental development.[10] During pregnancy, recommended dietary allowance of iodine is increased by 50% due to (i) physiological increase in maternal and fetal hormone Production and (ii) increase in renal iodine losses. Consequently, if pregnant mother is iodine deficient, there is decrease synthesis of thyroxine by fetal thyroid that leads to compromised mental and physical development of the fetus.[11] According to WHO, the median UIC level of<150 µg /I amongst pregnant mothers indicates ID in the community. Pregnant women with normal thyroid stimulating hormone (TSH) levels often have low free T4 levels, even in areas in which iodine intake is sufficient within the general population. This condition is termed as hyothyroxinemia. Hyothyroxinemia can negatively affect neonatal behaviourand infant cognitive functioning.[12] There is limited data on the prevalence of ID among the PMs in India. It has been shown that in some countries iodine intake was sufficient among school age children, but not with pregnant women.[11] Such findings justified the need for continuous monitoring of iodine nutrition status in these two vulnerable populations. Further, no data are available on maternal iodine status and neonatal thyroid function in Durg district, Chhattisgarh. Therefore present study has planned to assess the maternal iodine status and thyroid function at the trimester and its influence on neonatal thyroid function.

Material and Methods

The study was conducted in the Dept. of Biochemistry and in collaboration with Obstetrics and Gynecology Dept. at **Chandulal Chandrakar Memorial Medical College and Hospital, Kachandur Durg**, Chhattisgarh. Investigation was carried out in 23 pregnant women suffering from congenital hypothyroidism and compared with 30 normal control group composed of healthy pregnant women and followed-up to one month of delivery of the neonates.

Blood and Urine Sample Collection

Cord blood samples was collected after birth of new born in specimen tube, and 5 ml blood will be collected in a dry, clean, plane tube from maternal and fetal. After clotting of blood, it is centrifuged at 3000 rpm for 10 minutes. Serum will separated for the analysis of thyroid profile such as

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TSH, T4, T3, using ELISA and reagents kits will purchased from accu-bind [13,14]. A spot morning urine sample from each mother was collected and assayed in duplicates for the determination of urinary iodide concentration (UIC) using ammonium persulphate digestion method [15].

Control Group:
Control group comprises of total 50 normal healthy 25-40 years adult, age & sex matched pregnant women for study group will be selected.

Data Analysis
Data were expressed as mean ±SD. Mean values were assessed for significance by unpaired student –t test. A statistical analysis was performed using the Statically Package for the Social Science program (SPSS, 21.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.05$ were considered statistically significant.

Follow Up
Overall 23 patients were followed up at time of normal checkup in hospital and after delivery from hospital. The follow up system consisted of measurement of T3, T4, TSH and Urinary Iodine. The follow up program included clinical examination, hematological analysis, Thyroid profile and urinary iodine at each checkup. The follow up end date was 13th March 2017.

Observations and Results

Table no 1:- Shows Age wise distribution of Control group and congenital hyperthyroidism Patients

Age Group	Control Group (n=30)	Pregnant Women (n=23)	Lactating Women (n=23)
25-27 yrs.	10	09	09
28-30 yrs.	08	07	07
31-33 yrs.	05	04	04
34-36 yrs.	05	03	03
Above 36	02	0	0

Table no 2:- Shows Activity of T3, T4 and TSH in Control group and pregnant women (suffer from CH).

Parameters	T3 (Unit) Mean ± SD	T4 (Unit) Mean ± SD	TSH (Unit) Mean ± SD	Urinary Iodine Mean ±SD
Control Group(n=30)	102.03 ± 28.03	9.14 ± 1.12	1.95± 0.65	200.9 ± 44.35
Subjects (n=23)	32.38± 11.47	8.21 ± 1.72	63.88± 25.28	101.96 ± 31.38
'P' Value	< 0.001	< 0.49	< 0.001	< 0.001

Table no 2 shows the activity of T3, T4, TSH and UI in normal control group and CH pregnant women. Level of T3 and urinary Iodine was highly significantly decreased in patient group, TSH but T4 activity was insignificant (in normal range), because of physiologic changes associated with pregnancy require an increased availability of thyroid hormones to meet the needs of mother and fetus during pregnancy. Pregnancy has an effect on other thyroid functions with significant changes in iodine metabolism, serum thyroid binding proteins, and the development of maternal goiter, especially in areas with various levels of iodine deficiency.

Table no 3:- Shows Activity of T3, T4 and TSH in Control group and lactating women (suffer from CH).

Parameters	T3 (Unit) Mean ± SD	T4 (Unit) Mean ± SD	TSH(Unit) Mean ± SD	Urinary Iodine Mean ± SD
Control Group (n=30)	97.53 ± 21.28	10.5 ± 1.98	2.43± 1.25	192.9 ± 37.35
Subjects (n=23)	28.38± 9.47	9.39 ± 2.72	59.81± 23.28	98.26 ± 27.38
'P' Value	< 0.001	< 0.52	< 0.001	< 0.001

Table no 3 shows The level of T3 and UIC was highly significantly decreased in patient group but TSH was significantly increased found in CH lactating women but T4 activity was insignificant.

Table no 4:- Shows Activity of T3, T4 and TSH in Neonates.

Parameters	T3 (Unit) Mean ± SD	T4 (Unit) Mean ± SD	TSH (Unit) Mean ± SD	Urinary Iodine Mean ± SD
Control Group (n=23)	99.87 ± 20.40	8.88 ± 1.43	4.88 ± 1.41	186.13 ± 36.92
Subjects (n=23)	17.09 ± 3.86	10.69 ± 2.62	16.21 ± 6.39	473.87± 139.70
'P' Value	< 0.001	< 0.32	< 0.001	< 0.001

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Table no 4 shows the level of thyroid function and urinary iodine in neonates. It shows the activity of TSH and Urinary Iodine were significantly increased, and T4 level remains normal in range but T3 activity was highly significantly decreased found compare to normal group becouse the fetus is totally dependent on maternal thyroxine supply during the first trimester of gestation and up to mild gestation for normal neurologic development and nervous system maturation. Because the progression of pregnancy and fetal, neonatal and child health are dependent on adequate thyroid hormone supplementation throughout pregnancy, trimester-specific reference intervals for thyroid functions can be crucial for both maternal and fetal health.

Discussion

Hypothyroidism in India is caused by a deficiency of Iodine in salt. India has a high prevalence of hypothyroidism which affects one in 10 people. This compares with a prevalence of less than 2% in the United Kingdom and less than 5 in the United States. Inland cities Kolkata, Delhi, Ahmadabad, Bangalore and Hyderabad had a higher prevalence of Hypothyroidism at around 12% than the coastal cities the Mumbai, Goa & Chennai, with 6% most of the study.[4] Physiologic changes associated with pregnancy require an increased availability of thyroid hormones to meet the needs of mother and fetus during pregnancy. Pregnancy has an effect on other thyroid functions with significant changes in iodine metabolism, serum thyroid binding proteins, and the development of maternal goiter, especially in areas with various levels of iodine deficiency. The fetus is totally dependent on maternal thyroxine supply during the first trimester of gestation and up to mild gestation for normal neurologic development and nervous system maturation. Because the progression of pregnancy and fetal, neonatal and child health are dependent on adequate thyroid hormone supplementation throughout pregnancy, trimester-specific reference intervals for thyroid functions can be crucial for both maternal and fetal health. Manglik[16] and colleagues in their study of using cord blood TSH to screen children with congenital hypothyroidism, concluded that a cut off value of TSH >20mIU/L is adequate for neonatal thyroid screening in Indian settings. Stefen[17] and colleagues in their study on newborn screening strategies for congenital hypothyroidism suggested that screening programs utilizing primary TSH test strategy need to develop age-related TSH cutoffs to maintain an acceptable recall rate. TSH screening test strategies have the potential to detect infants with CH characterized by “delayed TSH rise,” but only if they collect a routine or discretionary second specimen, which is routinely recommended in low-birth-weight and acutely ill infants. In most situations, T4 (total) levels are sufficient for diagnosis of hypothyroidism and monitoring treatment, but free T4 can be obtained as a more robust marker of the bioavailable T4, when readily accessible. When availability or cost is a constraint, estimation of free T4 should be definitely done in the following situations.[18,19] In premature newborns, T4 (total) values may be low because of abnormal protein binding or low levels of thyroxin binding globulin (TBG) due to immaturity of liver function, proteinuria or under nutrition. Therefore, free T4 values provide a better estimate of true thyroid function in premature or sick newborns. ree T4 should be asked for in case of finding a low T4 with normal TSH. If free T4 is normal, it can be a case of congenital partial (prevalence 1:4000-12000 newborns) or complete (prevalence 1:15000 newborns) TBG deficiency. TBG levels should be evaluated to confirm this but this test is not available routinely. If free T4 is also low along with low T4 with normal TSH, central hypothyroidism should be suspected. During monitoring for adequacy of treatment, we usually monitor with T4 (total) level. This assumes a normal TBG level. This can be confirmed by measuring free T4 or TBG levels once at the time of the first post treatment T4 measurement. Dashe et al[20] estimated a normal reference range for TSH during gestation in singleton and twin pregnancies. TSH decreased significantly during the first trimester, and the decrease was greater in twins (both $P< 0.001$). For singleton first-trimester pregnancies, the approximate upper limit of normal TSH was 4.0 multiples of the median, and for twins, 3.5 multiples of the median. Thereafter, the approximate upper limit was 2.5 multiples of the median for singleton and twin pregnancies. According to these studies, monograms that adjust for fetal number and gestational age may greatly improve disease detection.

Significance of study:

The emphasis on Iodine supplementation during pregnancy is not a routine practice in Durg district. In such situation an adequate dietary intake of Iodine throughout the gestation period has to be investigated. Therefore the present study has been planned to assess the maternal iodine status and thyroid function at the first second & third trimester and its influence on neonatal thyroid function and lastly screening of congenital hypothyroidism in neonates of Chhattisgarh, with a view to strongly recommend the implementation of neonatal screening programme for iodine so that the optimal mental development of children can be achieved.

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