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RESEARCH ARTICLE
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FREQUENCY OF CONGENITAL HYPOTHYROIDISM IN NEONATES PRESENTING IN NEONATAL PERIOD

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ABSTRACT

Background: A disorder known as congenital hypothyroidism (CH) occurs when the thyroid gland is unable to produce enough thyroid hormones at birth. Thyroxine (T4) and triiodothyronine (T3) are the two main thyroid hormones, and they are essential for controlling growth, development, and metabolism throughout the body**.**

Aims: The main objective of the Guthrie test to detect congenital hypothyroidism in newborns as soon as feasible and immediate intervention and therapy are made possible by early detection, and this is essential to avert the negative consequences of untreated CH, including intellectual impairment and growth abnormalities.

Study design: It was a cross sectional study conducted in the Pediatrics Department Sheikh zayed Hospital Rahm yar khan. The duratin of this study was 18 months, from Jully 2022 to December 2023.

Methds: There were a total of 2640 participants in this study. 2640 healthy infants, both genders, with birth weights >2.5 kg after 78 hours of life till 28th day of life.

Results: The study population was consists of N=2640 newborns. Mothers' age range was 20-37 years with a mean age of 28.5±5.0 years. A total of mothers 63% were 27-33 years of age. 51% were male, and 49% were female. Both genders were born at gestational ages of 37 to 42 weeks, with 3.5 kg being the average birth weight for 59% of them. Just 0.07% of the mothers of these babies had a history of hypothyroidism overall, and 0.45% of them had taken drugs to treat their hypothyroidism while pregnant. The Guthrie method was 100% effective in screening all newborn babies in hypothyroidism. Of the 2640 neonates, 2637 (99.98%) had normal TSH levels, and 3 (0.11%) had higher TSH levels. Congenital hypothyriodism (CH) was therefore present in 0.11% of

cases. TSH levels were 6.2 ± 4 mIU/l on average. When the data was examined for any correlations between CH and the aforementioned characteristics, it was discovered that CH was statistically significantly correlated with both the mother's drug use and hypothyroidism during pregnancy, $p<0.005$.

Conclusion: The Guthrie method has made a substantial contribution to the global success of newborn screening programs by making it easier to identify and treat metabolic abnormalities such as congenital hypothyroidism early on. Further enhancements to the effectiveness of this crucial public health intervention will come from ongoing work to optimize screening techniques, increase awareness of the significance of early identification, and expand access to newborn screening.

Keywords: Congenital hypothyroidism, Newborn, Thyroide stimulating hormone and Gestational period.

INTRODUCTION

A neonate with congenital hypothyroidism (CH) has either no thyroid function at all or an underactive thyroid gland at birth. Hormones generated by the thyroid gland are essential for metabolism, growth, and development. In CH, the thyroid gland produces insufficient thyroid hormone which if not addressed, can result in a variety of developmental problems[1]. Congenital hypothyroidism can cause a variety of symptoms, if treatment is not received, symptoms may include jaundice, poor feeding, constipation, lethargy, low muscle tone, swollen cheeks, large tongue, hoarse cry, delayed growth and development, and intellectual impairment[2]. Fortunately, newborn screening programs frequently detect congenital hypothyroidism. A tiny blood sample is drawn from babies soon after birth in several nations in order to screen for a number of illnesses, including CH. Thyroid hormone replacement treatment is an effective way to manage CH if it is identified early. Infants with congenital hypothyroidism can grow and develop normally with timely treatment, reducing the chance of problems like intellectual impairment[3].Congenital hypothyroidism (CH) is caused by thyroid gland failure, which results in insufficient thyroid hormone production, mainly in the form of triiodothyronine (T3) and thyroxine (T4). Thyroid dysgenesis, or improper development of the thyroid gland, thyroid dyshormonogenesis, or problems of the mother's thyroid that impact the function of the fetal thyroid, are some of the causes of this thyroid hormone deficit[4]. Thyroid hormones are essential for controlling the body's growth, development, and metabolism. They affect the rate of metabolism, tissue growth, and cellular differentiation. Thyroid hormones are therefore essential for brain development, and their deficiency in CH can have a wide range of impacts on many organ systems, especially during fetal development and the early stages of infancy[5]. For the brain to grow normally, thyroid hormones are necessary, especially in the early years of life. Cognitive impairments, developmental delays, and intellectual disability can result from low thyroid hormone levels[6].

Additionally, bone formation and skeletal development are influenced by thyroid hormones. Skeletal deformities, small height, and growth retardation can all be caused by insufficient amounts. Thyroid hormones influence how the body produces and uses energy, which were controls metabolism. Reduced metabolic rate, cold sensitivity, weight gain, and other metabolic disorders can result from low thyroid hormone levels[7]. Heart health and cardiovascular function are impacted by thyroid hormones. Heart problems such as bradycardia, cardiomegaly and pericardial effusion can result from congenital hypothyroidism. To avoid these negative effects, newborn screening programs are essential for the early discovery and treatment of CH. Prompt initiation of thyroid hormone replacement treatment is necessary to restore normal thyroid hormone levels and lessen the negative effects of CH on development, growth, and general health[8].

Dr. Robert Guthrie's groundbreaking work in the early 1960s marked the beginning of neonatal metabolic screening. He gave an example of how biochemical factors may be measured by placing blood from a newborn's heel onto dried blood spots, which are specific filter paper cards. This test involves drawing blood from a newborn's heel onto a particular filter paper card. It is also referred to as the heel prick test or newborn screening test[9]. Congenital hypothyroidism can be detected

using the Guthrie test, sometimes referred to as newborn screening or the Guthrie bacterial inhibition assay. Nonetheless, it can obliquely aid in the detection of congenital hypothyroidism and is a common component of standard newborn screening programs in many nations. A baby with congenital hypothyroidism is born with either missing thyroid tissue or an underactive thyroid gland. If not identified and treated in a timely manner, it may result in major health issues [10]. Thyroid-stimulating hormone (TSH) levels in a newborn's blood sample are measured as the main screening technique for congenital hypothyroidism. This is due to the fact that in many screening programs, thyroxine (T4) or thyroxine plus TSH levels are measured, which is an indirect method of analyzing thyroid function in newborns. Further diagnostic testing may be necessary if elevated TSH levels or low T4 levels found during newborn screening suggest the possibility of congenital hypothyroidism [11].

Furthermore, there is disagreement on the impact of L-T4 dosage, treatment initiation time, and diagnostic severity on long-term results. While most treated individuals get normal cognitive outcomes, it is unclear how L-T4 therapy affects neurologic development. Certain studies indicate that treated patients continue to have deficits when compared to healthy, euthyroid controls[12].

Reducing the burden of preventable intellectual impairments and developmental disorders and resolving this discrepancy require improved access to newborn screening programs in low-income nations. This could entail putting into practice affordable screening methods, raising awareness among communities and healthcare providers, and resolving issues with infrastructure and resources. Additionally, measures to promote healthy neurodevelopment in vulnerable populations and improve newborn screening can be strengthened by addressing iodine deficiency through supplementation or fortification activities.

The main objective of the Guthrie test to detecting congenital hypothyroidism in newborns as soon as feasible and immediate intervention and therapy are made possible by early detection, and this is essential to avert the negative consequences of untreated CH, including intellectual impairment and growth abnormalities.

METHODS

The study was cross-sectional study. This study was conducted in the Pediatrics Department Sheikh zayed Hospital Rahm yar khan. The duratin f this study was 18 months, from Jully 2022 to December 2023. A total number of participant was (N=2640) in this study. After consent from parents, 2640 healthy newborns of both the genders with birth weight >2.5 kg after 78 hours of life till 28th day of life. Inclusion criteria: information was recorded on age, sex, weight, gestational age, mother age, history of thyroid disease in the mother, usage of antithyroid medications by the mother throughout pregnancy, and address. Exclusion criteria: Sick infants and preterm babies born between 37 and 42 weeks of pregnancy were not included. Heel stick on an authorized filter paper card provides a dried blood spot (DBS) for newborn babies (NBS) suitable techniques for testing. Filter paper specimens are sent to the NBS laboratory for testing once they have dried. For the purpose of screening for Congenital hypothyroidism, 72 hours of age to 28th day of life the ideal time for collecting the NBS specimen. This time frame corresponds to the typical rise in TSH concentration (60–80 mIU/L) that occurs in term newborn children a few hours after delivery and subsides over the course of the following five days. Specimens obtained within the first 72 hours of life have the potential to cause false-positive TSH results elevations while employing any method of screening tests. In the CH screening program, the TSH test strategy is used as the primary test, to confirm the diagnosis; use Guthrie method. All the information was recorded on specially designed proforma. Data of all the cases was entered into SPSS.26 and analyzed data f participants.

RESULTS

The study population consisted of N=2640 newborns. Mothers' age range was 20-37 years with a mean age of 28.5±5.0 years. A total of mothers 63% were 27-33 years of age, while 27% mother age were 20-26 years. Among the total population of N=2640 newborns, 51% were male, and 49% were female. The gestational age of both gender were born ≥37-42 weeks. The weight of

newborn babbies 59% had a birth weight of 3.5 kg. Out of total, only 0.07% mothers of these newborn had a history of hypothyroidism while 0.45% mother of these newborn had a history of drug intake for hypothyroidism during pregnancy. All new born babbies 100% were screen using efficiently using Guthrie method to detect hypothyroidism [Table 1].

Among 2640 newborns, 2637 (99.98%) (had normal level of TSH while 3 (0.11%) newborns had elevated TSH level. Hence frequency of congenital hypothyriodism (CH) was 0.11%. Mean TSH level was 6.2 ± 4 mIU/l. When data was analyzed for association of CH with above variables, it was found that CH had statistically significant association with mother's hypothyroidism and mother's drug intake during pregnancy,$p<0.005$ see in Table 2.

Table 1. Demographic variables of participants

Variables	**n=** 2640 **(%)**
Mothers age	
20-26 years	700(27%)
27-33 years	1650 (63%)
>34 years	290 (11%)
Mean±SD	28.5±5.0
Gender	
Male	1350 (51%)
Female	1290 (49%)
Gestational age (Weeks)	
>37-42 Weeks	2640(100%)
>42 Weeks	0%
Mean±SD	38.1±2
Birth weight (kg)	
3	900(34%)
3.5	1550 (59%)
>4	190 (7%)
Mean±SD	3.1±0.2
Screening method	
Guthrie method	2640 (100%)
Maternal history of hypothyroidism	
Yes	2 (0.07%)
No	2638 (99.9%)
Anti-thyroid medication take during pregnancy	
Yes	12 (0.45%)
No	2628(99.5%)

Table 2. Detection of Congenital hypothyriodism by Guthrie method

Parameters	**Hypothyriodism based on TSH level**		**P=value**
	Normal (n=2637)	**Congenital hypothyriodism (n=3)**	
Mothers age			
20-26 years	517 (19.5%)	1(0.03%)	0.112

27-33 years	2000(75.5%)	2(0.07%)	
>34 years	120(4.5%)	0%	
Gender			
Male	1550 (58.7%)	2(0.07%)	0.534
Female	1087 (41.1%)	1(0.03%)	
Gestational age (Weeks)			
>37-42 Weeks	2637 (99.9%)	3(0.11%)	0.612
>42 Weeks	0%	0%	
Birth weight (kg)			
3	1200 (45.5%)	1(0.03%)	0.542
3.5	1410(53.4%)	2(0.07%)	
>4	30 (1.1%)	0%	
Screening method			
Guthrie method	2637 (99.95%)	3(0.11%)	
Maternal history of hypothyroidism			
Yes	2 (0.07%)	2(0.07%)	<0.005
No	2638 (99.92%)	1(0.03%)	
Anti-thyroid medication take during pregnancy			
Yes	12 (0.45%)	1(0.03%)	<0.005
No	2628 (0.009%)	2 (0.07%)	

DISCUSSION

Most cases of congenital hypothyroidism are indeed caused by dysfunction of the thyroid gland itself. This dysfunction can occur due to various reasons, including: the term "thyroid dysgenesis" describes the thyroid gland's aberrant development or disappearance. Thyroid aplasia, hypoplasia, and ectopic thyroid tissue are among its possible manifestations[13].

Defects in the synthesis of thyroid hormones are the hallmark of a hereditary condition called thyroid dyshormonogenesis. Mutations was impacting the enzymes responsible for the production, transportation, or use of thyroid hormones may be the cause. Congenital hypothyroidism in the neonate can result from maternal thyroid abnormalities, such as autoimmune thyroid disease or maternal hypothyroidism, which impact the generation of thyroid hormone in the fetus[14]. Congenital hypothyroidism can result from inadequate maternal iodine intake during pregnancy, which can affect the fetal thyroid hormone production. Genetic mutations impacting thyroid hormone receptors or other thyroid-related genes can result in congenital hypothyroidism[15].

The present study population consisted of 2640 newborns. Mothers' age range was 20-37 years with a mean age of 28.5±5.0 years. The results of this study were indicate in which most f the mothers were age above 26 years. A newborn with a male to female ratio of 1.2:1 means that there is one female infant for every 1.2 male newborns. This ratio indicates that there are somewhat more male infants than female newborns. A ratio of 1:1 denotes a similar percentage of male to female births. Normally, there are 1.05–1.07 female births for every male birth at birth. It's important to remember, though, that slight fluctuations in the sex ratio can happen naturally and can fluctuate between people and geographical areas[16].

The central tendency or average gestational age of the infants in the sample is represented by the mean gestational age of 38 weeks. In this particular case, it implies that the majority of babies were delivered between 37 and 39 weeks of pregnancy. Overall, this data sheds light on the normal distribution of gestational ages of the sample's infants, most of whom were born at or near full term (38 weeks), with a tiny percentage born just before or after that period[17]. Of the babies in this study, 59% had birth weights of 3.5 kg, while 7% had weights greater than 4 kg. The birth weight was 3.1±0.1 kg on average. According to these findings, most neonates are appropriately sized for their age. In terms of neonatal health, low birth weight—defined as less than 2500 grams or 5.5 pounds—is concerning since it raises the baby's risk of developing many problems, such as infections, developmental delays, and even death[18].

The proper growth of the fetus throughout gestation is dependent on the thyroid activities of both the mother and the fetus. Although thyroid activities in mothers and fetuses are autonomously regulated, which means they function somewhat independently of one another, they are not totally independent[19]. The thyroid systems of the mother and the fetus interact dynamically, and changes in the mother's thyroid function can impact the fetal thyroid status and vice versa. Thyroid hormones are produced by the mother's thyroid gland to nourish the growing fetus and keep the mother's metabolic rate stable. Thyroid hormones from the mother cross the placenta and influence the levels of thyroid hormones in the fetus[20].

By the tenth week of pregnancy, the fetal thyroid gland starts to form, and by the twelfth week, it starts to function. Thyroid hormones in utero are necessary for the growth and development of the fetus, particularly the development of the brain[21].

According to our studies, the prevalence of maternal hypothyroidism is modest (0.07%), and 0.45% of pregnant women take medication for hypothyroidism. More specifically, these findings point to a relationship between the chance of having babies with congenital hypothyroidism (CH) and maternal hypothyroidism. Congenital hypothyroidism (CH) is the term for an underactive thyroid gland that is present from birth and, if ignored, can cause a number of developmental problems. Maternal hypothyroidism can affect fetal thyroid hormone levels and play a role in the development of CH in infants, especially if it is not appropriately treated during pregnancy[22].

It is important to monitor a mother's thyroid function throughout pregnancy because babies with CH are more likely to be born to hypothyroid moms. In order to reduce the possibility of unfavorable results for the mother and the unborn child, it also emphasizes the necessity of proper care and treatment of maternal thyroid diseases.

These results add to the increasing amount of data demonstrating the link between fetal/neonatal outcomes and the thyroid health of the mother. In order to achieve the best possible pregnancy and neonatal health, they stress the significance of early detection, intervention, and management of maternal thyroid problems as part of standard prenatal care[23].

The Guthrie method, sometimes referred to as newborn screening, measures the thyroid-stimulating hormone (TSH) levels of neonates in order to identify congenital hypothyroidism (CH). The Guthrie test can occasionally identify congenital hypothyroidism indirectly even though it doesn't measure TSH levels directly. In a lab setting, the blood spots on the Guthrie cards are examined. Since elevated TSH levels in infant blood samples reflect that the thyroid gland is not making enough thyroid hormones in response to the pituitary signal, they may be indicative of congenital hypothyroidism. When increased TSH levels are found by the Guthrie screening test, further testing is typically carried out to confirm the diagnosis of congenital hypothyroidism. Further blood tests to gauge thyroid hormone (T4 and T3) and thyroid antibody levels, as well as imaging examinations to evaluate the anatomy and physiology of the thyroid gland, may be necessary for this. A newborn's elevated serum TSH level suggests that the growing brain is not receiving enough thyroid hormone[24]. In the current study, 99.8% of the babies had normal TSH levels, whereas 0.11% had high TSH levels. As a result, 99.8% of CH cases occurred. According to our findings, 3 kids out of 2640 in had TSH levels greater than 20 mIU/L after 72 hours, and 2 newborns had CH when the test was repeated on the seventh day [25].

In the current investigation, we discovered a statistically significant correlation between mother's drug use during pregnancy and her hypothyroidism. A statistically significant correlation between CH and the mother's hypothyroidism was discovered. The authors also discovered that newborns with hypothyroid moms who did not take the antithyroid medication during pregnancy had a higher incidence of CH.

CONCLUSION

The Guthrie method has made a substantial contribution to the global success of newborn screening programs by making it easier to identify and treat metabolic abnormalities such as congenital hypothyroidism early on. Further enhancements to the effectiveness of this crucial public health intervention will come from ongoing work to optimize screening techniques, increase awareness of the significance of early identification, and expand access to newborn screening.

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