DOI: https://doi.org/10.54393/pjhs.v2i02.28

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
Volume 2, Issue 2 (July-Dec 2021)

Original Article

Evaluation of Hypothyroidism and Hyperthyroidism in Children Below Five Year of Age Residing in Lahore

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Keywords: Children, Hypothyroidism, Hyperthyroidism, Thyroid

How to Cite:
Attique, B. ., Elahi, S., & Kausar, H. (2022). Evaluation of Hypothyroidism and Hyperthyroidism in Children Below Five Year of Age Residing in Lahore. *Pakistan Journal of Health Sciences*, *2*(02). https://doi.org/10.54393/pjhs.v2i02.28

Article History
Received: 10th July 2021
Accepted: 8th August 2021
Published: 31st December 2021

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ABSTRACT

Hypothyroidism and hyperthyroidism occur due to insufficient production and over production of thyroid hormones. Identification of thyroid diseases at neonatal and developing years enable physicians to treat thyroid dysfunction at the appropriate time and correspondingly aid to find hyperthyroidism in children below 3.5 year of age which is rare in children below five years of age. **Objectives:** To determine hyperthyroidism and hypothyroidism in children below 5 years of age by a biochemical screening of FT_3, FT_4, and TSH in the blood sample. Determine the prevalence of thyroid dysfunction in children. **Methods:** 5ml blood samples were collected from hypothyroid and hyperthyroid children. Blood samples were centrifuged. Levels of FT_4 and FT_3 in the serum was determined by radioimmunoassay (RIA) and level of TSH was determined by immuno-radiometric Assay (IRMA). Samples were analyzed, by computerized gamma counter. Thyroid hormone level distribution was analyzed by using Chi-Square and T-Test. **Results:** Sixty five children were selected for the study, 34 male and 31 female children. Among 13 abnormal children, 4 (30.8%) were hyperthyroid because of their TSH level < 0.3 mIU/L and remaining 9 (69.2%) children were hypothyroid there TSH > 5.0 mIU/L. Goiter was found in three children which is a rare entity in children below 5 years of age. The goiter was found in children who had hypothyroidism. **Conclusion:** There was no significant age difference between hypothyroid and hyperthyroid children. The prevalence of hyperthyroidism and hypothyroidism was more in female as compared to male but the difference was not significant. There was no significant difference in the normal concentration of serum of thyroid hormone between male and female children.

INTRODUCTION

The thyroid gland is butterfly wrought and located below the larynx and has a weight of about 15g to 25g in adults and approximately 3g in newborn but the weight increases with age. The metabolic active hormones released by the thyroid gland are thyroxine (T_4) which is secreted in the amount of 93% and triiodothyronine (T_3) 7% in amount. Triiodothyronine is present in the circulation in small quantity for a short period of time and four times potent than T_4. A major hormone produced by the thyroid gland is T_4 and it is less potent than T_3 and having longer half-life but biologically less active as compared to T_3 [1]. Thyroid disorders are primary, secondary and tertiary: primary diseases of the thyroid gland, secondary dysfunction of the pituitary gland and tertiary hypothalamic diseases. Thyroid diseases occur due to imbalance supply of iodine to the thyroid gland or interference of goitrogens to uptake the iodine and disrupt the functioning of the thyroid gland. Thyroid hormone mainly affect the growth of the children those who are hypothyroid and hyperthyroid [2]. The growth rate of hypothyroid children is very slow and in hyperthyroid children, the excessive growth rate of the skeletal bones results in the taller child at their early age due to fast growth the adult growth period of these children is preferably shortened because

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the bones are mature and close to epiphyses at an early age. The thyroid gland is also involved in the development and growth of the brain before the birth of the fetal and after the birth few postnatal years of life. The secretion in sufficient quantity of thyroid hormones is necessary for growth and maturation of brain before and afterward of birth if these hormones are not secreted in sufficient quantity the growth and maturation of the brain is very slow and smaller in size as compared to normal size of the brain. In some cases, the thyroid gland is totally absent in children they are mentally deficient in whole life [3].

Hyperthyroidism is the overstimulation of the thyroid gland leads to overproduction of thyroid hormones. Symptoms which are the sign of hyperthyroidism increased sweating, extreme weight loss, heat intolerance, muscle weakness, diarrhea, high state of excitability, nervousness, physic disorders, trembling of hands and insomnia. Toxic Goiter, Thyrotoxicosis, Grave's disease, thyroid Adenoma, and exophthalmos are the causes of hyperthyroidism [4]. Hyperthyroidism suppresses the anterior pituitary gland which in turn reduces the formation of TSH. TSH level is normally less (essentially zero) in patients suffering from Grave's disease. An autoimmune Graves's disease is caused by antibodies thyroid stimulating immunoglobulins (TSIs) produce against the TSH receptor. TSIs antibodies bound at the same place at TSH receptor where TSH bound with its receptor and the binding of TSIs results in continuous activation of the CAMPs system which results in excessive production of T3 and T4 hormones. The mean age for the beginning of symptoms of hyperthyroidism in children was found to be between 3.5-16 years [5]. Hyperthyroidism is rare in children below than 5 years old or in infants, Grave's disease leads to hyperthyroidism and exophthalmos.

Exophthalmos is also caused by hyperthyroidism ($1/3^{rd}$ hyperthyroid patient), the patient developed some degree of protuberance of the eyeball, when protuberance is severe stretches the optic nerve and damage vision. It's also an autoimmune disease because immunoglobulin found in patient blood which reacts with eye muscles, and high concentration TSIs found in patient blood [6]. Hypothyroidism is the less production of thyroid hormones due to an insufficient supply of iodine to the thyroid gland. It is more common in children, symptoms which are the sign of Hypothyroidism initial symptom prolonged jaundice, other symptoms include gain in weight, intolerant to cold, constipation, skin dryness and hair, respiratory disorder, abnormal development of thyroid gland (goiter) decreased blood volume, depressed hair growth mental retardation [7]. Myxedema in caused due to total lack of thyroid hormones function result in facial swelling and bagginess under the eye. Extreme hypothyroidism caused Cretinism in fetal life, newborn and childhood due to failure of the thyroid gland to produce thyroid hormone (congenital Cretinism lack of thyroid gland from birth and endemic Cretinism insufficient amount of iodine in the diet) which in turn sluggish body growth and mental retardation. A neonate born without a thyroid gland found out after a few days of birth sluggish physical movement and growth because inside the mother utero it was supplied with mother hormones [8]. Endemic colloid goiter which is caused due insufficient supply of iodine to the body as a result large concentration of TSH is secreted and large amount of thyroglobulin (Tg) protein formed inside the follicle cell and no iodine is present in the body for the attachment so triiodothyronine (T_3) and thyroxine (T_4) are not produced and Tg remains inside the colloid and gland grow 10 to 20 times larger in size [9]. Idiopathic nontoxic colloid goiter this is caused due to thyroiditis inflammation of the thyroid it is usually painless when the thyroid gland increases in size results in coughing and difficulty in swallowing food [10]. Toxic goiter is the result of abnormal enlargement two to three times' normal size of thyroid gland with excessive hyperplasia which is increased rate of cell production, initial stage is the development of cancer and follicular cell lining in folding into the follicle cells, surface area is increased and a large number of cells increase in great amount [11]. Thyroid nodules are an overgrowth of thyroid cell develop into a lump. Hot nodules (noncancerous) and cold nodules 9 to 10 benign (noncancerous) but some are cancerous. Thyroid nodules found in adults rarely found in children [12]. This study was planned to identify the thyroid diseases among children (0-5 age group) attending the Centre of Nuclear Medicine (CENUM), Mayo Hospital, Lahore.

METHODS

The research was conducted in Lahore. The testing and sample collection was completed at the Centre of Nuclear Medicine (CENUM) Mayo Hospital, Lahore. Newly diagnosed referred male and female children of age group (0-5) attending Centre of Nuclear Medicine (CENUM) Mayo Hospital, Lahore selected for blood sample collection and thyroid testing during the months of October 2018 to February 2019. The children taking any thyroid medication in the past are excluded from the study. The children below one year of age and had any systemic diseases like hepatitis and cardiac disease were also excluded. The blood serum biochemical analysis of TSH, FT_4, FT_3, and clinical assessment undertook only selected children. History of patients was taken and recorded by the perdition carefully. Thyroid gland physical examination allowed the assessment of functional condition, size, position, consistency, and interconnection with other structures. Demographic

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data of the patients was noted for a personal record including age, sex, current treatment and medication of thyroid diseases if any. Symptoms and sign of the diseases was recorded by the examination of skin, tremor eye and pulse rate.

Laboratory Diagnosis

For laboratory diagnosis, a 5ml blood sample was collected from each patient had hypothyroidism and hyperthyroidism Blood samples were kept at room temperature for one hour and then the sample was centrifuged (2000 x g) at low speed for 5 minutes at 18 to 25 ºC for the separation of serum. Serum of samples were stored at -20-25 ºC before analysis. Level of FT_4, FT_3, and TSH were analyzed in the serum sample. Estimation of FT_4 and FT_3 levels were determined by radioimmunoassay (RIA) and level of TSH was determined by immuno-radiometric Assay (IRMA) by using commercial kits of Immunotech *Inc.* (Beckman, Czech Republic). With commercially prepared sera IRMA and RIA batches are run at high, medium and low concentration. Analysis of samples, measurement of radioactivity, and the formation of the standard curve was completed by using computerized ((Cap-RIA 16, CAPINTEC; *Inc.* USA) gamma counter. Duplicate of all the assay was prepared. Imprecision profile of all the RIA and IRMA assay was less than 10% CV. Standardized value of CENUM lab for FT_4, FT_3, and TSH will be considered as normal: 11.5 – 23.0 pmol/L for FT_4, 2.8 – 5.8 pmol/L for FT_3, 0.3 - 5.0 mIU/L for TSH respectively

Criteria for the disease will be: For Hyperthyroidism: TSH was < 0.3 mIU/L and FT_4 > 22 pmol/L, For Hypothyroidism: TSH was > 5.0 mIU/L and FT_4 < 11. 0 pmol/L, TSH > 10.0 mIU/L regardless of FT_4 concentration was also counted as hypothyroid.

Statistical Analysis

Thyroid hormone level distribution was analyzed using Microsoft Excel. To determine the significant difference between the two arbitrary groups Chi-Square Test was applied. To determine the significant difference between the two mean values T-Test was applied. The result of the test was considered significant if the p-value is < 0.05.

R E S U L T S

During the study period, 74 patients attended CENUM for thyroid function test (TFT). 9 children were below 1 year of age were excluded from the study. 65 of them between ages 1 to 5 years fulfill the selection criteria and selected for study. The mean age (± SD) of the children was 2.5 ± 1.2 years with age range between 1 to 5 years. Among them, 34 were male children and 31 were female children. Family history of thyroid dysfunction was found in 1 female patient out of 65 patients. Goiter was found in 3 (4.7%) patients. Out of 34 male, 1 male patient had goiter and out of 31 females only 2 female patients had goiter. As the p-value comes out 0.09 which is > 0.05 so there was no significant difference between male and female ages enrolled during the study period.

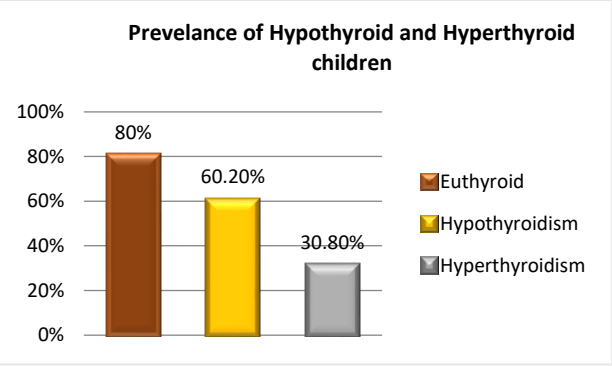

Figure 1: Prevalence of thyroid dysfunction in the total population.

Through TFT analysis the results showed that 52 (80%) children were euthyroid based on the criteria of normal TSH (0.3 – 5.0 mIU/L) level range and 13 (20%) children had thyroid dysfunction (hypothyroidism and hyperthyroidism) because there TSH serum level is not lie in the normal range. Among 13 abnormal children, 4 (30.8%) were hyperthyroid because of their TSH level < 0.3 and remaining 9 (69.2%) children were hypothyroid there TSH > 5.0. The incidence of hypothyroidism was double as compared to hyperthyroidism. **Table 1** showed the incidence of thyroid dysfunction (hyperthyroidism and hypothyroidism) in female and male children. The statistical analysis showed that there was a no significant difference in the incidence of hypothyroidism and hyperthyroidism between male and female children because the p-values are 0.2 and 0.6 > 0.05.

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Group of patients (No.)	Hypothyroid N (%)	Hyperthyroid N (%)	Total N (%)
Male (n = 34)	04 (11.8%)	01 (2.9%)	05 (14.7%)
Female (n=31)	05 (16.1%)	03 (9.7%)	08 (25.8%)
p-value	0.610	0.259	0.263

Table 1: Prevalence of hypothyroidism and hyperthyroidism in male and female children

Out of 52 euthyroid children, 29 male children and 23 female children lie in the normal range of on the basis of FT_4 and TSH analysis. Only 7 male and 2 female children FT_3 level was tested during the study period and the results lie in the normal range on the basis of FT_3 analysis. **Table 2** showed a comparison of the mean of FT_4, FT3, and TSH in euthyroid children. The statistical analysis showed that there is no significant difference between male and female serum level of FT_4, FT_3, and TSH because the p-values are > 0.05.

Thyroid hormone (normal range; unit)	Euthyroid Children	Mean of serum	p-value
FT_4 (11.5 – 23.0 pmol/L)	M = 29 F = 23	M = 17.2 $\pm$ 3.5 F = 16.8 $\pm$ 2	0.62
FT_3 (2.8 – 5.8 pmol/L)	M = 07 F = 02	M = 4.9 $\pm$ 0.9 F = 4.6 $\pm$ 0.6	0.73
TSH (0.3 – 5.0 mIU/L)	M = 29 F = 23	M = 2.0 $\pm$ 1.2 F = 1.8 $\pm$ 0.9	0.53

Table 2: Comparison of mean FT_4, FT_3, and TSH level in euthyroid children

D I S C U S S I O N

Disorders disturbing the thyroid gland characterize the most common endocrinopathies hyperthyroidism and hypothyroidism in childhood. By clinical presentation and etiology find out the thyroid disorders in children considerably differ from adults [13]. The aim of the study was to find the frequency, causes and symptoms of thyroid dysfunction in early childhood and treat them at the appropriate time. According to anthropometric measures, family history was found in one child and goiter was found in three children. Analysis of thyroid hormones level was detected by thyroid function test (TFT) in 65 children (34 male and 31 female) of 1 to 5 year of age, 13 (20%) children were detected with thyroid dysfunction with age range was 1 to 4 year. In Hyderabad India the incidence of thyroid dysfunction was checked in 63 children (42 female and 31 male), 33 (52.3%) was detected with thyroid dysfunction, the age group in between 1 to 3 years and 9-12 year (14). Tertiary care hospital in western India checked the prevalence of thyroid dysfunction was tested in 498 children. 65 (13%) children were detected with thyroid dysfunction in two age groups: 0-1 year and 9-12 year [15].

Most (80%) of the children in this study had normal function of thyroid (euthyroid). Hyperthyroidism and hypothyroidism were detected in 20% of children. The prevalence of hypothyroidism (60.2%) was double compared to hyperthyroidism (30.8%). In Hyderabad India 63 children were suspected with thyroid disorders, 58.3 % children with normal thyroid function the prevalence of hypothyroidism (30.6%) were more as compared to hyperthyroidism in (11.1%) [14]. In India, 800 children were referred for thyroid problem 19% were euthyroid 76% were hypothyroid with five-time more incidence as compared to 2% hyperthyroid children [16]. Accordance with Singh et.al in India the study was reported in which 65 abnormal children out of 498, 98.3% had hypothyroidism is highest recorded as compared to previous studies [15]. The observation accordance to Shah et.al in India reported 56.25 % were euthyroid, 37% had hypothyroidism and 6.25 % had hyperthyroidism [17]. The incidence of hyperthyroidism is less as compared to hypothyroidism. According to ocular demonstration, the grave disease is very in infants and children as compared to adults [18]. Hyperthyroidism is rare in children below than 5 years old or in infants [19].

In this study female children had an elevated ratio of TSH and FT_4 serum level as compared to male children. The more female are affected by thyroid dysfunction and exhibited increased five times more incidence of hypothyroidism and hyperthyroidism in comparison to male children however the difference was insignificant. The p-value shows there was no significant difference in the incidence of hyperthyroidism and hypothyroidism in between male and female children. Accordance to Singh et.al in India the gradual rise of thyroid dysfunction in female with age and female to male ratio was 1.2:1 [14]. In the observation of Yelluri, the female's children are high predominant over male children, female to male ratio was 1:2 with incidence of 66.7% [15]. Desai et.al observed female to male ratio 2.9:1 [20]. The observation accordance to Shah et.al in India reported female to male ratio was 3:1 [17].

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There was no significant difference serum level of TSH, FT_3, and FT_4 in between male and female euthyroid of children ($p > 0.05$). Accordance with Corcoran et.al concentration of serum FT_3 and FT_4 was not changed from 3 weeks to 10 years of age and found no sex difference in this regard [21]. In children, it is imperative to correct thyroid dysfunction to achieve optimal growth and development. Early diagnosis and treatment are essential to prevent irreversible and permanent nervous system damage and developmental delay, especially in infants as they are extremely vulnerable to thyroid dysfunction. Appropriate medical care of children with thyroid disorders requires refined knowledge of the ontogeny of the thyroid system and an appreciation of distinct characteristics of thyroid function in childhood [13].

CONCLUSIONS

Goiter was found in three children which is a rare entity in children below 5 years of age. The goiter was found in children who had hypothyroidism. Hypothyroidism starts to develop at the age of 3 years. A total of 13 abnormal children in which 4 (30.8%) were hyperthyroid and 9 (69.2%) were hypothyroid. There was no significant age difference between hypothyroid and hyperthyroid children. The prevalence of hyperthyroidism and hypothyroidism was more in female as compared to male but the difference was not significant. There was no significant difference in the normal concentration of serum of thyroid hormone between male and female children.

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