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Original Research Article

Etiological Evaluation of Hypothyroidism in Clinical Practice

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Abstract:

Background: Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone. It is often the primary process in which the thyroid gland produces insufficient amounts of thyroid hormone. It can also be secondary due to other causes.

Objective: To study the etiological of hypothyroidism in children and to determine the clinical presentation in hypothyroidism and its associated co morbidities.

Methods: 100 cases were included in the study who met the inclusion criteria after taking informed consent from parents. Pre designed proforma was used to record the relevant patient details with special reference to clinical presentation and were subjected to further diagnostic work up as relevant to each case.

Results: Out of 100 cases, congenital hypothyroidism contributed to 66 % of cases among study group while acquired hypothyroidism was noted in 34 %. Dyshormonogenesis was more common than dysgenesis under congenital hypothyroidism and Hashimotos thyroiditis was more prevalent among adolesecent female under acquired hypothyroidism.

Conclusions: Hypothyroidism still represents a major public health problem and is an important cause of preventable mental retardation. Early diagnosis and treatment still remains the cornerstone of management. Therefore early recognition and treatment with thyroxine will help to improve the quality of life in these patients.

Keywords: Hypothyroidism, Mental Retardation, Thyroxine.

Introduction

Thyroid diseases are among the commonest endocrine disorders worldwide. India too, is no exception. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. Early diagnosis and treatment remains the cornerstone of management [1].

Among the varieties of hypothyroidism, congenital hypothyroidism (CH), one of the most common endocrinological pediatric diseases. The majority of cases are caused by agenesis, hypoplasia, dyshormonogenesis, or ectopia and thus will require lifelong replacement therapy, but there is also a transient form of the disorder. Some patients with transient CH recover during follow up without any replacement therapy whereas some need to receive thyroxine replacement therapy until the condition resolves [2].

In acquired hypothyroidism Hashimto thyroiditis is the most common form of thyroiditis in childhood and the most frequent cause of pediatric thyroid disease in iodine-replete areas of the world [3]. Diagnostic approaches, such as thyroid profile test, ultrasonography and scintigraphy helps to determine the subtype of hypothyroidism and are useful and help to decide the treatment. [4]

Materials and Methods

The present study is a prospective observational study conducted at Indira Gandhi Institute of Child Health, Bangalore for a period of 18 months from January 2015 to June 2016 after taking informed consent from study group.

Inclusion Criteria: All children, from birth to 18 years of age with clinical suspicion of Hypothyroidism and abnormal thyroid function test attending Outpatient and Inpatient department at Indira Gandhi Institute of Child Health over a period of 18 months.

Exclusion Criteria: Children who are previously diagnosed and on treatment will be excluded from the study.

Method of Collection of Data: 100 cases were included in the study who met the inclusion criteria after taking informed consent from parents. Pre designed proforma was used to record the relevant patient details with special reference to clinical presentation. Each patient was examined for clinical features like coarse facies, feeding difficulties, ,macroglossia, prolonged physiological jaundice, constipation, open posterior fontanelle or anterior fontanelle, dry, thick skin, hoarse voice, growth retardation, delayed dentition, protuberant abdomen, umbilical hernia, short stature, obesity, lethargy, delayed puberty and irregular menstrual cycles, poor scholastic performance and mental retardation.

The study group was then subjected to thyroid function test which included:

- Thyroid Stimulating Hormone (TSH) assay.
- Total T4/ Total Thyroxine levels.
- Free T4 / Free Thyroxine levels.

If the TSH assay was high for that age and Total T4 low, suggestive of hypothyroidism the case was included in the study. Further diagnostic work up as relevant to each case was done, that included:

- Ultrasound neck.
- Antibody assay - anti TPO Ab / antithyroid microsomal Ab.
- Technetium Thyroid Scan.
- Radioactive Iodine Uptake (RAI-U).

Thyroid Imaging Tests

A. Thyroid Ultrasound: Simple, non-invasive test, to evaluate the size, enlargement, position of thyroid gland. Ultrasound can tell whether a nodule is a fluid-filled cyst, or a mass of solid tissue.

B. Thyroid radio nuclide uptake and scan:

Iodine 131, I^{131} or sodium pertechnectate 99 Tc^{99} is used for this purpose. Absence of radio nuclide uptake can also be seen with thyroid dysgenesis.

However it should be confirmed by an ultrasonography because absence of uptake can also see with TSH beta gene mutations, TSH receptor inactivating mutations, iodide trapping defects and with maternal thyrotropin receptor blocking antibodies (TRB- Ab) where thyroid gland is actually present. Increased uptake of radioactive isotope is seen with dyshormonogenesis which are beyond the iodide trapping. Further testing by perchlorate discharge test can help to identify defective oxidation and organification.

Technetium Thyroid Scan: Technetium-99m is used as a radioactive tracer can be detected in the body by medical equipment (gamma cameras) and its half-life for gamma emission is 6.0058 hours (meaning 93.7% of it decays to ^{99}Tc in 24 hours). Its biological half-life of 1 day allows for scanning procedures which collect data rapidly but keep total patient radiation exposure low. The same characteristics make the isotope suitable only for diagnostic but never therapeutic use. The scanner picks up where and how much the radioactive substance was taken up by the thyroid. This helps determine the structure, location, size, and activity of the gland.

^{99}Tc Thyroid scan and uptake are studied after iv administration of 3 microCurieTc. Normal % thyroid uptake is 0.4 -2.5 %.

Radioactive Iodine Uptake (RAI-U)

I^{131} has greater sensitivity in detecting thyroid lesion as it is organified. Imaging with I^{131} allows to know quantitative uptake measurement, iodine transport defects and abnormalities in thyroid oxidation. The lowest possible dose should be alteast 50 microCurie. If organification defect is suspected Perchlorate discharge test can be performed.

Perchlorate discharge test:

10 mg/kg given intravenously 2 hours after I^{123} scan. Radioactive iodine uptake measurement is checked before and one hour after the test.

Interpretation: release of radioactive uptake <10 % - normal, 10-20 % borderline, >20 % abnormal. This test detects organification defects.

Antibody assay: Thyroid Peroxidase Antibodies / Antithyroid microsomal antibodies.

Results

Out of 100 cases studied, 39 % were male and 61 % were female. Male to Female ratio was 0.6 Out of 100 cases, majority of cases were diagnosed between 6 to 12 years of age. Congenital hypothyroidism (66 %) was more common than acquired hypothyroidism (34%).

Table 1: Etiology of Congenital Hypothyroidism In The Study Group.

Etiology	Number Of Cases	Percentage (%)
Thyroid Agenesis	22	33.3
Thyroid Hypoplasia	1	1.5
Ectopia	14	21.2
Thyroid Dyshormonogenesis	28	42.4
Isolated Tsh Deficicency	1	1.5
Total	66	1oo

Among congenital hypothyroidism, Dyshormonogenesis (42 %) was more common followed by thyroid agenesis (33%) and ectopia (21 %).

Table 2: Etiology of Hypothyroidism Based On Age

Age (Years)	Agenesis	Dyshormonogenesis	Ectopic- Lingual	Ectopic Sublingual	Total =66	Percentage %
< 1	6	2	0	0	8	12.1
1-5	8	6	5	1	20	30.3
6-12	10	16	4	3	33	50
13- 18	0	4	1	0	5	7.6

Maximum number of cases were diagnosed between 6- 12 years of age with Dyshormonogenesis (50%) being more common ,followed by thyroid agenesis seen maximum between 1- 5 years of age.
Thyroid lingual ectopia (64 %) was more common than sub-hyoid type (36 %).

Table 3: Etiology of Acquired Hypothyroidism.

Acquired Hypothyroidism	Number Of Cases	Percentage
Autoimmune –Hashimoto Thyroiditis	31	91.2
Post-Operative Radiation	3	8.8
Total	34	100

Hashimotos thyroiditis (91%) was more common among acquired hypothyroidism.

Table 4: Frequency Of Auto Immune -Hashimotos Thyroiditis Based On Age

Auto Immune -Hashimotos	Frequency	Percentage %
1-5 Year	1	3.2
6-12 Years	9	29.0
13- 18 Years	21	67.8
Total	31	100

Out of 100 cases, 67 % were sporadic in nature while 33 % had consanguity.

Table 5: Prevalence of Consanguity in Study Population

Consanguity	Number Of Cases
Non consanguineous	67
2 nd degree	19
3 rd degree	14
Total	100

Table 6: Clinical Presentation of Hypothyroidism

Clinical Presentation	Frequency
Developmental delay	44
Short stature	42
Thyroid swelling	53
Obesity	58
Coarse facies	14
Constipation	16
Delayed puberty	18
irregular menstrual periods	22

Obesity was more common followed by goitre and developmental delay. Under congenital anomaly, Cardio vascular anomaly (60%) was more common in the study population, among which PDA was common.

Discussion

Thyroid diseases are among the commonest endocrine disorders worldwide. India too, is no exception. Hypothyroidism still represents a major public health problem and is an important cause of preventable mental retardation. The prevalence of hypothyroidism in India is 11%, compared with only 2% in the UK and 4·6% in the USA. Compared with coastal cities (eg, Mumbai, Goa, and Chennai), cities located inland (eg, Kolkata, Delhi, Ahmedabad, Bangalore, and Hyderabad) have a higher prevalence. The reason behind the higher mean thyroid - stimulating hormone concentration and range in India compared with western countries is possibly linked to long-standing iodine deficiency in the country. Although an easy-to-detect and inexpensive-to-treat disease,

patients with hypothyroidism in India often remain undetected and untreated.

Hypothyroidism in pregnant women if untreated or inadequately treated can compromise fetal neurocognitive development. A nationwide screening programme for congenital hypothyroidism should be very high to diagnose at the early age since early treatment will prevent irreversible mental retardation. Indeed, there is an inverse relationship between intelligence quotient (IQ) and the age at diagnosis the clinical manifestations are often subtle or not present at birth because it is due to trans-placental passage of some maternal thyroid hormone. Therefore detailed history, clinical examination and thorough laboratory investigations will help us to detect the cases at the earliest.

In the present study, percentage of congenital hypothyroidism was more than acquired hypothyroisim when compared to that of Anju seth et al study .The reason for the high prevalence of congenital hypothyroidism than acquired would be due to the latter study group observed cases only beyond 5 years of age.

Table 7: Comparison of Congenital Hypothyroidism with Different Studies

Studies	Anju seth et.al [5] (2011)	Tamam et al [6] (2009)	Susana et al [7] (2011)	Present study
Dyshormonogenesis	22 %	43 %	14 %	42 %
Agenesis	52 %	22 %	35 %	33 %
Ectopia	30	32 %	50 %	21%

In the present study, dyshormonogenesis was more common than other types of congenital hypothyroidism which is similar to Tamam et al study. The difference between the present study and to that of other study groups would be due to different selection of age group for the study and variation in epidemiology and genetic factors contributing to the disease.

Table 8: Comparison of Acquired Hypothyroidism – Hashimotos Thyroiditis with Similar Studies

Studies	Venkateswarlu et al [8] (2015)	Anju seth et al [5] (2011)	Present study
Hashimotos thyroiditis	63 %	56 %	91 %
Mean age at presentation	8-16 years	12-14 years	13-18 years

Hashimotos thyroiditis is the most common cause of acquired hypothyroidism in the present study. This is similar to the other studies mentioned above. Adolescent females contributed to the majority of cases in the present study, similar to the other studies. Obesity is the most common clinical presentation followed by thyroid swelling and short stature in the present study. Anju Seth et al study reported short stature as the commonest clinical presentation. Congenital hypothyroidism appears to be associated with an increased risk of congenital malformations. Of these, the majority were cardiac anomalies since the development of thyroid gland takes place during the embryogenesis of cardiac formation. In the study group, cardiac PDA was common than all.

Conclusion

Thyroid hormones are unique because of their important role in fetal and early neonatal brain development. It also regulates the growth and development during the first two decades of life. Early detection of hypothyroidism can reduce its preventable cause of mental retardartion. Indeed, there is an inverse relationship between intelligence quotient and the age at diagnosis. In our present study, majority of cases were diagnosed between 6 -12 years of age and congenital hypothyroidism was the most common type of hypothyroidism; in which dyshormonogenesis was more prevalent than dysgenesis. Hashimotos thyroiditis was common among adolescent female, under acquired hypothyroidism. Therefore early detection and replacement of thyroid hormones must be carried out at the earliest to significantly improve the quality of life in these children.

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