THE PREVALENCE AND SPECTRUM OF THYROID DISEASES AMONG CHILDREN AND YOUTH SEEN AT THE ENDOCRINE CLINIC, KENYATTA NATIONAL HOSPITAL FROM 2008 TO 2021

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DECLARATION

I declare that this dissertation is my work and has not been published or presented for a degree in any other institution.

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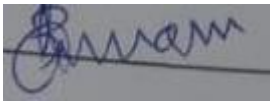
Signature:  **Date:** 10/09/2023

LIST OF ABBREVIATIONS

AMOS	Analysis of a Moment Structures
CH	Congenital hypothyroidism
ERC	Ethical Review Committee
IQ	Intelligence Quotient
KNH	Kenyatta National Hospital
PISD	Standard deviation
T3	Triiodothyronine
T4	Thyroxine
TBG	Thyroxine-binding globulin
TSH	Thyroid-stimulating hormone
UoN	University of Nairobi
WHO	World Health Organization
	Principal Investigator
SPSS	Statistical Package for Social Sciences

DEFINITION OF TERMS

Spectrum: the range/types of thyroid diseases found among study participants- euthyroid, hypothyroid or hyperthyroid

Reference ranges for thyroid functions test (ng/dl): TSH :0.4-5.7, T4: 5.3-15.7, T3 0.8-2.5.

Euthyroidism: is a state of normal production and secretion of T3 and T4 from a thyroid gland with normal serum hormone levels. (1)

Hyperthyroidism: is the production and secretion of an excessive amount of thyroid hormone (TriiodothyronineT3 and/ or Thyroxine T4) from the thyroid gland with high serum hormone levels. (1)

Hypothyroidism: is the reduced production and secretion of T3 and/ or T4 from the thyroid gland with low serum hormone levels. (2)

Management approaches: the type of treatment offered to those diagnosed with thyroid diseases, i.e., medical or surgical

Clinical outcomes: the result among the patients diagnosed with thyroid disease. Will be determined by the last recorded status of the patient in the file.

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ABSTRACT

Background: Thyroid diseases are responsible for common endocrinopathies in childhood. Early diagnosis is essential in the integration of an appropriate treatment approach and control of irreversible damage to the nervous system. However, the prevalence of thyroid diseases in the local setting has not been investigated. Thyroid diseases constitute common endocrine disorders that untreated can lead to preventable mental retardation, slowed growth and adverse outcomes that could result in death. Low level of awareness and limited knowledge of the identification of the condition results in late diagnosis, which increases the risk of adverse outcomes. Currently, the true burden of thyroid diseases among children is not well known in Kenya as there is a paucity of evidence on the magnitude of thyroid disease in children in our setting.

The purpose of the study: The main objective of this study was to determine the prevalence of thyroid diseases in children and youth at Kenyatta National Hospital from 2008 to 2021.

Methodology: This was a retrospective cross-sectional study carried out within 13 years. All paediatric and adolescent patients seen at Kenyatta National Hospital Endocrinology clinic between January 2008 to December 2021 were included in the study. Data collection was carried out using a data abstraction form from the patient's file. Data collected was coded and analyzed using Statistical Package for Social Sciences (SPSS version 28) was used in data analysis. Descriptive statistics were used to describe the proportions and clinical characteristics of the sample population. Prevalence was calculated as a proportion of the entire sample population and represented as a percentage. Chi-square or Fischer's exact test was used to investigate factors associated with different types of thyroid diseases. Logistic regression was used to determine factors associated with hypothyroidism and goitre.

Results: The findings established that out of 2238 patients attending the endocrinology clinic, 147 had thyroid disease representing a 6.56%, (95%CI: 5.6 – 7.7%) prevalence. Among those with thyroid disease, 82(55.8%) of the patients had hypothyroidism, 43(29.3%) had goitre, 14(9.5%) had hyperthyroidism while 8(5.4%) had suspected thyroid tumour. Among patients with thyroid disease,79(53.7%) of patients were female, the median age was 18 (4.5 – 28) months with almost half of the patients (44.9%) who were aged ≤2 years. In investigating clinical characteristics, the majority of the patients with thyroid disease presented with vomiting (84.4%), coughing (83.7%), palpitations (78.9%), weight loss (58.5%) excessive sweat (53.7%) and poor sleep (51.0%). The findings revealed that age, weight, symptom duration, vomiting, coughing and weight loss were significantly associated with types of thyroid disease.

Conclusion: The prevalence of thyroid disease shows an increasing trend of thyroid disease. The commonly identified clinical characteristics include vomiting, poor sleep, weight loss and excessive sweat. Thus, there need for early screening of thyroid disease in children to improve child developmental status. Further, increase health education on thyroid diseases in the general public to help parents understand the common symptoms of thyroid disease such as weight loss, coughing, excessive sweat and palpitations.

1. CHAPTER ONE: INTRODUCTION

The thyroid is a small gland that is in the middle of the lower neck and has a butterfly shape as shown in Figure 1.1(3) The thyroid gland performs various physiological functions that include metabolism, growth, differentiation and proliferation of cells, and homeostasis. The thyroid gland secretes the thyroxine (T4) and the triiodothyronine (T3) hormones, which are involved in the regulation of the highlighted physiological functions.(4) The thyroid hormones function by binding to the thyroid hormone receptors and through their involvement in the transcription of specific genes.(2),(5) The thyroid hormones bind to the thyroid hormone receptor elements that are in the promoters of the target genes. Thyroid hormones play a major role in defining child development process especially through regulating nervous system myelination, organ function, growth as well as skeletal development(6,7).

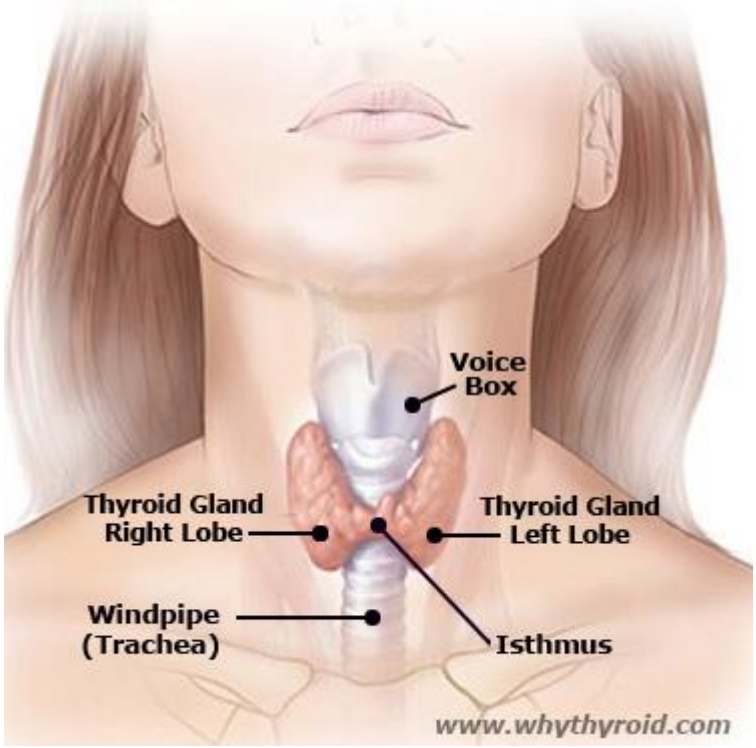


Figure 1.1: Image of the thyroid gland (3)

The levels of thyroid hormones in the plasma are tightly regulated by the thyroid-stimulating hormone secreted by the pituitary gland and the thyrotropin-releasing hormone secreted by the hypothalamus.(8) The thyrotropin-releasing hormone neurons located in the paraventricular nucleus of the hypothalamus can detect the levels of thyroid hormones in

serum.(9) Thyroid hormones bind the beta thyroid hormone receptors in the paraventricular nucleus of the hypothalamus resulting in increased or suppressed expression of thyroid-releasing hormone genes to respond to the levels of circulating thyroid hormones (Figure 2).

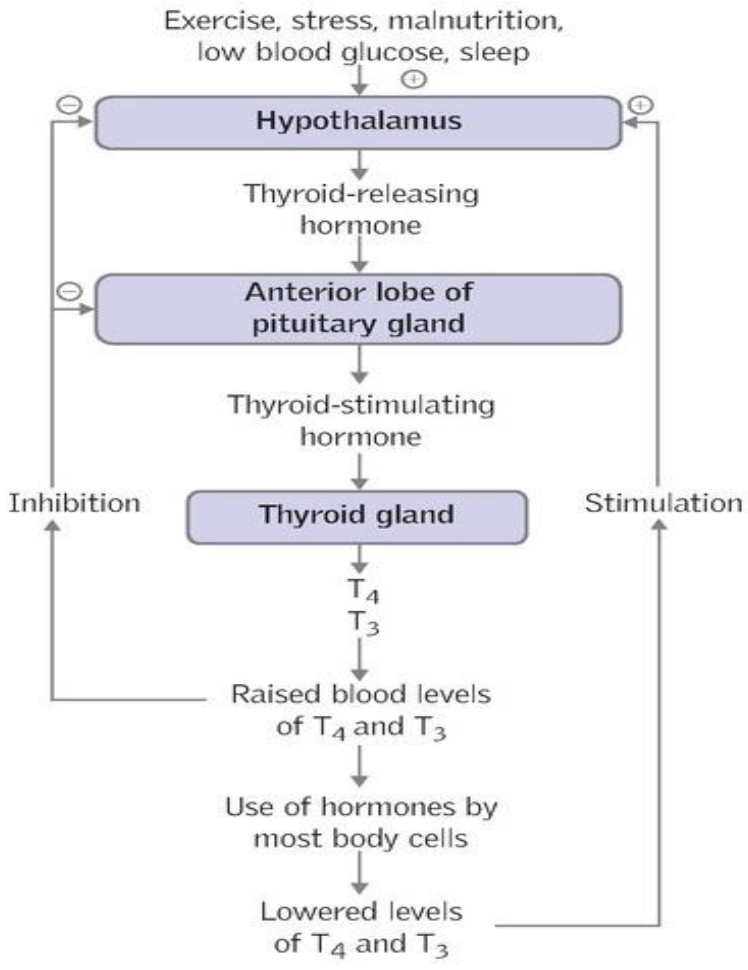


Figure 1.2: Regulation of the thyroid hormones (10)

The presence of abnormal levels of thyroid-stimulating hormone, thyroxine, and the T3 hormones in serum is associated with clinical thyroid diseases. However, subclinical thyroid disease occurs when there are abnormal levels of serum thyroid-stimulating hormones and normal levels of thyroid hormones.(2) Thyroid disease is a group of conditions that include benign and malignant disorders impacting the structure and function of the thyroid gland.(11) Common thyroid diseases include hypo and hyperthyroidism and thyroid tumours.(11),(12),(13) Understanding the clinical characteristics of thyroid diseases is important in the early diagnosis and management among children and adolescents ensuring the children develop normally.(13),(14)

Low levels of thyroid hormones due to the inability of the thyroid gland to produce inadequate amounts are associated with primary hypothyroidism.(2) The inability of the thyroid gland to produce adequate amounts could be linked to iodine deficiency since iodine is required in the production of these hormones.(15),(16) Secondary hypothyroidism occurs when there is a decline in the stimulation of the thyroid gland by a thyroid-stimulating hormone, which is associated with hypopituitarism or hypothalamic disease. Some of the causes of hypothyroidism include thyroid inflammation, Hashimoto's thyroiditis, postpartum thyroid infection, iodine deficiency, and non-functioning thyroid. Hypothyroidism is associated with delayed developmental milestones which include delayed time to crawl, walk, and talk.(2)

The presence of thyroid hormones in excessive levels in serum results in a condition known as hyperthyroidism.(17) The overproduction of thyroid hormones is linked to the presence of antibodies against thyroid-stimulating receptors that stimulate the thyroid gland leading to excessive production of the hormones.(17) In the presence of low levels of iodine, the overproduction of thyroid hormone could be linked to toxic goitre and toxic adenoma.(18),(19) The causes of hyperthyroidism include Graves disease, the overreaction of modules within the thyroid gland, thyroid inflammation, and excessive iodine.(17) Brown noted that Graves' disease is responsible for 95 % of cases of hyperthyroidism.

Despite their relatively low incidence and prevalence, thyroid diseases are responsible for debilitating long-term effects.(12),(14),(20),(21) In sub-Sahara Africa where there are sub-optimal diagnostic facilities, the documentation of clinical characteristics associated with hyperthyroidism and hypothyroidism is scarce.(20) Without early diagnosis and treatment, thyroid diseases such as hypothyroidism and hyperthyroidism can result in irreversible and permanent nervous system damage, which impact negatively the health and quality of life of the affected individuals.(15),(22) In developing countries such as Kenya with a population that is already overwhelmed by enormous healthcare challenges, the impact of thyroid diseases among children and adolescents could be calamitous.(23)

A retrospective study conducted in a rural hospital in Kenya where data was gathered for three years found a thyroid malignancy rate of 11.7%. Overall, 220 patients had undergone thyroidectomies out of the 222 patients who were studied.(24)

Another study conducted at Kenyatta National Hospital found a thyroid disease prevalence of 96.14% among patients visiting the thyroid clinic at KNH. The data for this study was collected retrospectively over 6 years and involved 1554 patients out of which 60 did not have thyroid disorders.(25) The prevalence shown above is quite high mainly because the

population under study were patients visiting the thyroid clinic. It is estimated from the patients' registers that 1560 patients are seen in the thyroid clinic every year at KNH.

Due to improvements in medical capabilities and better methods of sharing health information, many people are seeking care in hospitals. A search of the literature indicates that not many studies have been conducted at KNH on this topic, especially on children. We have therefore decided to conduct this study to provide information updates on the magnitude of thyroid diseases at KNH and the current management approaches.

2. CHAPTER TWO: LITERATURE REVIEW

2.1. Overview of thyroid disease in children and adolescents

Thyroid disease is majorly malignant or benign disorders that have an influence on the structure and the functionality of the thyroid gland (7). They are the second common endocrine conditions in children.(26). The common thyroid diseases include hypothyroidism and hyperthyroidism.(27) Primary hypothyroidism is characterized by thyroid hormone production in the thyroid gland that is inadequate to meet the needs of the organism.(28) A heterogeneous group of developmental abnormalities accounts for a high percentage of all cases of congenital hypothyroidism due to thyroid dysgenesis.(28) Defects in one of the steps of thyroid hormone synthesis, referred to as dyshormonogenesis, are found in patients with congenital hypothyroidism.(29) Patients with thyroid hormone resistance due to a defective nuclear thyroid hormone receptor present with elevated circulating levels of T4 and T3 with normal or increased serum TSH concentration.(28).

The overproduction of thyroid hormone is connected with the condition known as hyperthyroidism. The condition known as thyrotoxicosis can develop when there is an increase in the synthesis of thyroid hormones, which can lead to a hypermetabolic state (30) Graves' disease, which is connected with other disorders such as autoimmune problems including rheumatoid arthritis and lupus, is one of the most common reasons why children develop hyperthyroidism. It is also one of the most common causes of hyperthyroidism in adults (5),(31),(32)(33).Persisting congenital hyperthyroidism and familial hyperthyroidism of non-autoimmune origin due to gain-of-function mutations in the TSH receptor gene have been identified. The mode of inheritance is autosomal dominant.(34)

The onset of hyperthyroidism in these familial cases occurs at various times from infancy to adulthood, but neonatal hyperthyroidism has not been described.(33) In contrast, severe non-familial congenital hyperthyroidism due to gain-of-function mutations has been described in neonates. These mutations are different from those identified in the familial cases and are identical to those found in thyroid adenomas.(34) Other rare causes of hyperthyroidism in childhood are TSH-producing pituitary adenomas, pituitary resistance to thyroid hormones and ingestion of exogenous thyroid hormone or iodine.(35) The plasma concentrations of total thyroxine are increased in familial elevation of the thyroxine-binding protein (TBG), but

T4 concentrations are normal, as is thyroid function. Oestrogens may also increase TBG concentrations.(36)

The incidence of congenital hypothyroidism varies with the geographic area. It ranges from as high as 1:3,300 neonates in Europe to as low as 1:5,700 neonates in Japan but averages 1:4500 neonates in most other areas.(37) The prevalence rates in the neonatal period for the various thyroid disorders that can lead to neonatal hypothyroidism have been reported as being 1:4,000 for thyroid dysgenesis, 1:30,000 for thyroid dyshormonogenesis, 1:40,000 for transient hypothyroidism and 1:100,000 for central hypothyroidism (hypothalamic-pituitary disorders.(24) The vast majority of cases of congenital hypothyroidism seem to be sporadic, with the exception of inborn defects of thyroid hormone production or dyshormonogenesis, both of which are inherited in an autosomal recessive manner.(38) It appears that females are more likely than boys to be born with a thyroid condition called congenital hypothyroidism. It is assumed to be less common in black people, despite the fact that Hispanics have a higher incidence of the condition than whites do. There was a familial clustering of thyroid developmental abnormalities, as shown by new data from population-based studies on families of children with congenital hypothyroidism due to thyroid dysgenesis. This suggests that genetic factors could be involved in the aetiology of congenital hypothyroidism (38)

A study conducted in Nigeria revealed that, overall, hypothyroidism was the most common thyroid disorder, accounting for 91.7% of all thyroid disorders seen among children in two teaching hospitals in South-West Nigeria.(39) Congenital hypothyroidism (58.3%) was the most common type of hypothyroidism, followed by acquired hypothyroidism (20.8%). Down syndrome patients accounted for 57.1% of all children with congenital hypothyroidism. One (7.1%) of them had thyroid aplasia, while another one (7.1%) had panhypopituitarism. Children with acquired hypothyroidism predominantly presented within 5–10 years of age.(39)

Other studies involving participants from Africa indicate that the incidence of thyroid disorders ranges between 0.1% to 0.13%.(20),(21) In a study that examined the pattern of thyroid diseases in 546 children and adolescents for 10 years, Oyenusi,(21) reported an incidence rate of 0.13%. In a retrospective study that involved the assessment of 8,350 case notes of children and adolescents admitted to a Nigerian Hospital, a thyroid disease incidence rate of 0.12% was reported.(20) The authors further noted that 66.7% of positive cases had hyperthyroidism while 22.2% had hyperthyroidism.[27] Another author also noted that the majority of thyroid disease patients (46.7 %) had hypothyroidism.(21)

Another retrospective study conducted in Nigeria revealed that the age range at presentation of children reported was 5 days to 13 years with a male-to-female ratio of 1.7:1.(40) Out of the 18 children, three (16.7%) had euthyroidism, five (27.2%) had hyperthyroidism, which included one incidence of neonatal thyrotoxicosis, ten (55.6%) had hypothyroidism, five (27.2%) had euthyroidism, and eight (44.4%) had goitre. There were two occurrences of transitory hypothyroidism along with nine cases of conccgenital hypothyroidism among the children who were diagnosed with hypothyroidism. The average age of a kid when they were given the diagnosis of congenital hypothyroidism was 9.81 months. Only two (22.2%) of those born with congenital hypothyroidism displayed symptoms before the age of 3 weeks, and the average amount of time that children with goitre experienced neck swelling before they were diagnosed was 19.6 months. There was one case of thyroid carcinoma among children (5.6%). Common issues that arise in management include incorrect initial referrals and a failure to follow up on 22.2% of instances (40). A study in Ghana revealed that nontoxic goiter

In another study conducted in Ghana, Nontoxic multinodular goitre represented the commonest thyroid disorder seen over the study period, representing over a quarter of all thyroid admissions. The difference in age of admission between the various thyroid disorders was highly significant.(12)

In another study, the authors noted that the occurrence of Graves' disease increases gradually with an increase in age among children.(14) About 80 % of childhood Graves diagnosis has occurred among children aged 11 and above. Evidence also suggests that thyroid diseases are common among female children and adolescents.(10),(41) It was also reported that among the positive cases the ratio of female to male was 5:1.(20) The incidence of thyroid diseases was also shown to be high among females.(21) Other researchers have also indicated a slight female preponderance in thyroid disease cases.(10),(41) A study involving Chinese patients below 3 years of age also showed a high occurrence of Hashimoto's thyroiditis among females (12 females, 7 male(42)

2.2. Clinical characteristics associated with thyroid diseases

The aetiology and clinical presentation of thyroid disorders in children and adolescents substantially differ from that in adults.(43) Thus, paediatric medical care requires an appreciation of specific characteristics of thyroid disorders in childhood and adolescence,

which could facilitate early diagnosis and treatment. Thyroid disease can present with overt symptoms, insidiously, or with isolated thyromegaly.(5) In children, thyroid disease can refer to either the presence of overt clinical symptoms or isolated biochemical abnormalities that have little to no impact on the child's physiological functioning. In the clinical setting, hypothyroidism is seen far more frequently than hyperthyroidism. The average age of patients who presented with paediatric thyroid diseases was found to be 4.9 years old, with a range of ages spanning from 3 months to 14 years in the study that was carried out in Nigeria and investigating paediatric thyroid disorders. At the time of presentation, 54% of patients were younger than five years old, 29% of patients were aged between 5 and 10 years old, and 16% of patients were older than 10 years old.(39) The median age at presentation was found to be 1.6 years.(21) The age at presentation plays a major role in influencing the treatment pattern and outcomes. Early diagnosis limits adverse outcomes.

The clinical manifestation of hyperthyroidism may be rather unspecific and minimal in the initial phase of Graves' disease because the disease usually develops over several months.(5),(32) Children suffering from hyperthyroidism how likely to show signs of restlessness and fidgeting. Children will also show enlarged thyroid, muscle weakness especially the proximal, and shaking of hand upon arm extension.(1) Hyperthyroidism among children is also characterized by alteration in growth with children showing accelerated growth but puberty is delayed. hyperthyroidism is also associated with the advanced maturity of a child's skeletal system. Children and adolescents suffering from Graves' disease are likely to depict behavioural disorders associated with anxiety and attention deficits or hyperactivity.(1) Laboratory evaluation of Graves' disease show increased thyroxine and T4 levels. Thyrotropin is also suppressed to levels below 0.1mIU/L. The levels of thyroid-stimulating immunoglobulin and thyrotropin receptor antibodies were elevated. The examination of the thyroid gland shows unusually dense, solid, and heterogeneous tissue with increased vascularization.(1)

Congenital hypothyroidism among newborns is not associated with any clinical symptoms.(1) Although the foetus may produce low levels of thyroid hormones, they benefit from the maternal thyroid hormone transferred through the placenta and therefore they can maintain normal bodily functions hence they remain asymptomatic.(1) However, if they're not screened and provided with the required treatment newly-born children with congenital hypothyroidism are likely to suffer prolonged jaundice, lethargy, poor feeding, constipation, and a hoarse cry.(10) The other major clinical characteristics associated with untreated congenital hypothyroidism include umbilical hernia, macroglossia, and mottled skin.

Children may also suffer from slow heart rates and low muscle tone with delayed reflexes.(40)

The major clinical characteristics of acquired hypothyroidism such as Hashimoto thyroiditis include lack of regular menstrual cycle, indigestion, tiredness, and cold intolerance.(44) Acquired hypothyroidism is also associated with delayed or advanced puberty.(45) Physical examination of children and adolescents with acquired hypothyroidism should show the presence of goitre. The patients may also have slowed heart rate, slow reflexes, and swelling of facial skin and soft tissues and the extremities.(1) Hypothyroidism is associated with the accumulation of glycosaminoglycans in the tissues around the scheme resulting in oedema. (46) Children with hypothyroidism show challenges with linear growth and often end up with compromised adult height. (1)

2.3. Management of thyroid diseases in children and adolescents

Congenital hypothyroidism can be treated through thyroid hormone replacement, which should be prioritized within the first two weeks after birth. (37) Hormone replacement therapy is important in ensuring that the thyroid hormone is normalized early enough to prevent irreversible damage to the newborns such as the negative effects on IQ. (1) To ensure prevent negative neurocognitive outcomes, it is important to rapidly normalize the thyroid hormones and maintain euthyroidism when the child is below the age of 3 years. (1) It is therefore important for children with congenital hypothyroidism to undergo regular laboratory checks as a means of ensuring adequate treatment and prevention of sub-physiologic thyroid hormone levels.(12),(47),(48),(49) Drug treatments that can be used in the management of congenital hypothyroidism among children include levothyroxine. It is recommended that calcium ions or supplementation should be provided based on the physician's recommendation since it interferes with drug absorption.(1) The management of acquired hypothyroidism should focus on maintaining chemical and biochemical euthyroidism. Effective management also helps to maintain the linear growth of children and adolescents. Levothyroxine is also used in the treatment of acquired hypothyroidism.(1)

The first treatment used in the management of Graves' disease among children is antithyroid drug therapy which involves the use of methimazole. For cases where paediatric patients show significant signs and symptoms of hyperthyroidism, cardio-selective beta-blockers are used temporarily after which the thyroid hormone levels are normalized using methimazole. The treatment of paediatric patients with methimazole is associated with the risk of bone

marrow suppression and liver toxicity.(1) Therefore, children with signs such as fever and sore throat should be assessed for possible neutropenia through the determination of a complete blood count. Liver function tests should also be carried out to rule out liver toxicity or take the necessary steps in case of a positive test.(1)

Children who experience liver toxicity and bone marrow suppression due to the use of methimazole or those who do not achieve biochemical remission after the sixth year following the initiation of the treatment are considered for definitive therapy.(50),(51) Definitive therapy is associated with reduced risk, predictable course of the disease, and reduced laboratory surveillance.(1) Paediatric patients can also receive elective definitive therapy to address persistent symptoms after the normalization of thyroid hormone levels.(1) The definitive therapy search is radioiodine ablation aims at achieving permanent hypothyroidism.(1)

A retrospective study conducted in a tertiary hospital in Mogadishu, Somalia between 2017 and 2019 sampled 976 patients with thyroid disorders. Among the thyroid disorders discovered, euthyroid sick syndrome accounted for 58.8% followed by hypothyroidism at 15.4%.(52)

Most of the studies reviewed on thyroid diseases were conducted on adult patients. There are limited studies on this topic in Kenya. None of the studies reviewed in Kenya were conducted specifically on paediatric patients. Based on this finding from the literature, the current study will play a big role in identifying the prevalence and spectrum of thyroid diseases among paediatric and young adults attending the endocrinology clinic at KNH.

2.4. Critique of the cited studies

The study by Oluwayemi et al., conducted in Nigeria on Paediatric Thyroid Disorders looked at the distribution of thyroid disorders among the study participants.(39) This was a retrospective observational study. The data collection process was carried out according to the design. The author has not described the percentage of patients with thyroid disorders as a prevalence given that this was not a follow-up study; patients presented and were diagnosed with thyroid disorders without follow-up. The author also goes ahead to describe the figures of thyroid disorders as an incidence. As highlighted earlier, this was not a cohort study hence incidence was wrongly used. The analysis of data is well presented from demographics to management approaches of the study participants. This study sample all the patients that were

seen in the endocrinology clinic; this allows external validity. It was also a multicentre study carried out in two hospitals which increased the sample size for generalizability, sharing of findings and networking. The retrospective nature of the study where data was collected from records may not have allowed the investigators to seek clarification in case of missing data.

A retrospective study conducted in Somalia by Hassan et al., and published in PubMed in 2021 looked at the Spectrum and Prevalence of Thyroid Diseases among Thyroid Patients in a tertiary hospital in Mogadishu, Somalia.(52) This study has only sampled patients with thyroid disease and not all patients seen with endocrine diseases. This approach does not allow the author to estimate the overall burden (prevalence) of thyroid disease in the study population. The data used in this study was gathered in accordance with the study design. The author has used secondary data from the database. This author, therefore, did not have control over the way the data was collected and entered into the database, and it could have been difficult to flag any entry errors. Data entry errors if any may have biased the results of the study. We find that the author analysed and presented results in accordance with the study topic except that the prevalence of thyroid disease in the study population was not brought out. Overall, the study was well done and presented.

The main weakness of this study was the use of convenience sampling which may not allow generalization of the results to the population in addition to being a single-centre study. The descriptive nature of the study did not allow the author to look into factors that may be associated with thyroid diseases to necessitate targeted public health responses.

2.5. Justification of the study

Thyroid diseases such as hyperthyroidism and hypothyroidism constitute common endocrine disorders that, if untreated, cause preventable mental retardation and slowed growth among children. Thyroid diseases are also associated with adverse outcomes that could result in death.(53) The cause of morbidity and mortality in these patients is mainly due to delay in diagnosis. (55) Our study aims to pick the types or spectrum of thyroid disorders and their clinical characteristics at diagnosis in our set-up. This is essential in giving continuous medical education to healthcare professionals at all levels of health institutions to raise their suspicion index, thus enabling early diagnosis and treatment of thyroid patients early.

The study is essential to identify clinical characteristics of children/adolescents with thyroid disorders which helped create guidelines to identify the symptoms and required investigations where possible and also when to refer. Due to the challenge of reduced resources and lack of neonatal screening for congenital hypothyroidism, patients are diagnosed late when motor development has already been affected.(11),(54) Our study aims to present the data from this study to the policymakers so that the need for neonatal screening is seen and hopefully implemented

Currently, the true burden of thyroid diseases among children is not well known in Kenya due to the paucity of evidence on the magnitude and spectrum of thyroid diseases in our setting. The few studies on thyroid diseases in Kenya are mainly on adults and are not directly related to the topic under study. This study addressed the gap by providing recent data.

2.6. Research Question

3. **Research Question:**

   What is the magnitude of, and clinical characteristics associated with thyroid diseases in children and youth seen in the endocrinology clinic at KNH from 2008 to 2021?

3.1. Study Objectives

3.1.1. Primary Objective

To determine the prevalence of thyroid diseases among children and youth seen in the endocrinology clinic at KNH from 2008 to 2021

3.1.2. Secondary Objectives

1. To determine the spectrum of thyroid disease at diagnosis among children and youth seen in KNH between 2008 and 2021.
2. To identify the clinical characteristics of children/adolescents with thyroid disorders at diagnosis in children and youth seen in KNH between 2008 and 2021.

3. CHAPTER 3. RESEARCH METHODOLOGY

3.1. Study design

This was a retrospective prevalence and descriptive study. The retrospective nature of the study allowed the researcher to use the available data obtained from case files.(55) It was a quantitative measurement of the number of patients, a description of the spectrum range of thyroid disease in children and clinical characteristics of the patients as included in the files.

3.2. Study Setting

The research was carried out at Kenyatta National Hospital Pediatric endocrinology clinic. Kenyatta National Hospital is the main national referral hospital, located in Nairobi, Kenya. The hospital serves 7500 inpatients daily and about 550,000 outpatients annually. The Hospital has a well-equipped endocrinological clinic with thyroid disease specialists. It was started in 2008. The Hospital's endocrinological unit serves patients from around the country. The endocrinological clinic serves about 30 patients weekly.

3.3. Study population

The proposed study targeted a population of pediatric and young adult thyroid disease patients. The study involved patients aged 25 years and below seen at Kenyatta National Hospital endocrinology clinic between 2008 and 2021.

3.4. Inclusion and Exclusion criteria

3.4.1. Inclusion criteria

i. Patients presenting at the endocrinology clinic between 2008 and 2021.
ii. Diagnosed with thyroid disease
iii. Aged 25 years and below
iv. With complete records indicating age, gender, and thyroid disease diagnosis outcome

3.4.2. Exclusion criteria

i. Patients with other endocrinopathies e.g., diabetes
ii. Patients seen in the clinic but aged above 25 years
iii. Patients who were found not to have thyroid disease e.g., those with thyroid infections

3.5. Sample size calculation

This study included a whole population survey involving all the patients with endocrine disorders seen at KNH from 2008-2021.

3.6. Sampling technique

All files of patients who sought care at the endocrinology clinic between 2008 and 2021 were reviewed. Once the files were retrieved, files that met the inclusion criteria, and data were extracted and put in the data extraction form.

3.7 Case definition

Table 3.1: Reference ranges for Triiodothyronine, Thyroxine, Thyroid stimulating hormone

Age	T3 (ng/dL)	T4 (ng/dL)	TSH (mU/L)
1-5 years	2.73-4.95	0.8-1.8	0.7-6.6
6-10 years	2.73-4.69	1.0-2.1	0.8-6.0
11-18 years	2.67-4.62	0.8-1.9	0.6-5.8
>18 years	2.10-4.40	0.9-2.5	0.4-4.2

- **Hypothyroidism:** A patient being followed in the endocrine clinic with high TSH and low thyroid hormone.
- **Hyperthyroidism:** A patient being followed in the endocrine clinic with low TSH and high thyroid hormone.
- **Goitre:** A patient who has thyroid swelling with normal TSH and thyroxine hormone diagnosed clinically or through ultrasound.

Those with thyroid swelling and low thyroid hormone were classified as hypothyroidism; those with swelling and high thyroid hormone were classified as hyperthyroidism.

- **Thyroid tumour:** Patients being followed in the endocrine clinic with thyroid adenomas diagnosed clinically or through ultrasound.

3.7. Study variables

Independent variables: Age, gender, family history

Dependent variables:

✓ Thyroid disorders (Yes, No),

✓ The spectrum of disease: Presence of hyperthyroidism or presence of hypothyroidism or euthyroid goitre

✓ Management approach (surgical, medical, irradiation)

✓ Clinical outcomes as per the last notes written in the file;

a. Dead

b. Alive

i. Weight z-score at diagnosis and the last visit, height z- score at diagnosis and the last visit

ii. Development milestones at diagnosis, and at the last visit as indicated in the file
iii. The pubertal stage at diagnosis and the last visit
iv. Normal or abnormal thyroid test as indicated in the file

c. lost to follow-up, not seen at the clinic >6 months before the study

3.9. Research tool

A data abstraction tool was used to find relevant information from the patient files. The data abstraction tool was developed based on the identified research objectives. The information sought was already available in patient files considering that was retrospective data captured from January 2011 to December 2020. The data abstraction tool was specific and only include information that is relevant to this study.

3.10 Research assistant recruitment

The researcher recruited two research assistants to help in the data collection process. The research assistants were nursing officers with diploma certificate qualifications in any medical field. The research assistants were required to know how to extract data from patient files with ease, which helped maintain the accuracy and reliability of the data extracted. The research assistants were trained on how to retrieve specific data based on the data abstraction tool that was utilized. The training duration was 2 days.

3.11 Data collection

The data collection process began after approval from the KNH-UoN Ethics review committee and KNH administration. The principal investigator together with the help of recruited research assistants captured the outpatient numbers from the patients' register in the endocrinology clinic from the year 2008 to 2021. The outpatient numbers were then presented to the records person in the records department who was assigned the task of retrieving patient records (files) for this study using the outpatient numbers. The principal investigator and research assistants were given the retrieved files. The retrieved files were then scrutinized and those that met the inclusion criteria were used for data collection. The files that did meet the inclusion criteria were returned for filing. Data abstraction was then conducted on the files that meet the inclusion criteria by filling in the data abstraction tool. Once this information was extracted, the files were returned for filing.

3.12 Quality assurance

To get demographic and clinical data, a trained research assistant worked under the direction and supervision of the primary investigator to fill out the data collecting form. This was done

in order to obtain the data. The minimum qualification for the research assistant that was recruited is a diploma in nursing, which indicates that they are competent. In addition, the research assistants participated in training for a total of two days to ensure that they have a solid understanding of the research tool in question as well as ethical research procedures. On the first day of the course, participants spent their time getting acquainted with the study instrument. Interaction with the responders and practice with the tool were the primary focuses of the second day of the training. The main investigator (PI) was in charge of directing the process of collecting the data and regularly supervising the research assistants to ensure that they collected accurate information. The Principal Investigator was responsible for recruiting a competent statistician who was responsible for evaluating, cleaning, and analyzing the data that was obtained.

3.13 Data analysis and management

3.13.1 Data management.

After compiling all of the data, the principal investigator went over and checked, as well as cleaned, all of the raw data in order to guarantee the accuracy and completeness of the questionnaires. The next step was the acceptance and entry of the data, although any data collecting tables that were found to be incomplete were excluded from the subsequent analysis. The raw data was kept in a secure location behind a lock and key. This prevented the loss of data and ensured that it was only accessible to the principal investigators, protecting the confidentiality of the information. The finished data abstraction forms were then entered using Epi-data version 3.1 software into a pre-designed data template. This template was then stored in a computer protected by a password and backed up on a flexible compact disc as well as an external hard drive.

3.13.2 Data analysis and Presentation

Data was coded and analyzed through SPSS ver. 23 and AMOS. Continuous variables e.g., age was presented using Mean (SD) while categorical variables e.g., gender, presence or absence of thyroid disease etc. were presented using frequencies (n) and percentages (%). Proportions were used to describe binary categorical variables. Chi-square or Fischer's exact test was used to investigate factors associated with different types of thyroid diseases. Logistic regression was used to determine factors associated with hypothyroidism and goitre. The level of significance was assessed at 95% confidence level. Quantitative data was presented in percentages and frequency tables.

3.14 Study validity and reliability

The study sampled all the patients who meet the inclusion criteria. This ensured that external validity is met as the patients sampled are the same as the study population. Internal validity was assured by defining all the dependent and independent variables adequately. Data reliability was ensured by having a reliable data collection tool. In addition, a predesigned data template was used to enter data to minimize errors during entry.

3.15 Ethical consideration

The study was submitted to the KNH/UoN Ethics and Review Committee for approval. A consent waiver was applied for as there was no direct contact between the investigator and the patients. The study commenced only after formal approval.

Anonymity and Confidentiality: The researcher maintained anonymity and confidentiality by using none identifiers such as codes that cannot link a participant with the information provided during the study. The data obtained was used solely for this study to improve the implementation of service integration policy and not to divulge personal information to the public. Recorded data was under the custody of the principal researcher until validation within one year after which the data will be destroyed.

3.16 Dissemination of findings

The study findings shall be presented to the UoN Department of Pediatrics and Child Health, as part of the requirements of the Master of Medicine Program Requirement, in both hard and soft copies. The findings will also be presented to Kenyatta National Hospital to help in improving the level of care. The study will also be published to help share knowledge on thyroid diseases in Kenya.

4. CHAPTER FOUR: RESULTS

The study investigated thyroid diseases at Kenyatta National Hospital from 2008 to 2021. A total of 147 children with thyroid disease were identified.

4.1. The prevalence of thyroid disease at Kenyatta National Hospital

The findings established that out of 2238 patients attending the endocrinology clinic, 147 had thyroid disease representing 6.56%, (95%CI: 5.6 – 7.7%) as shown in Figure 4.1.

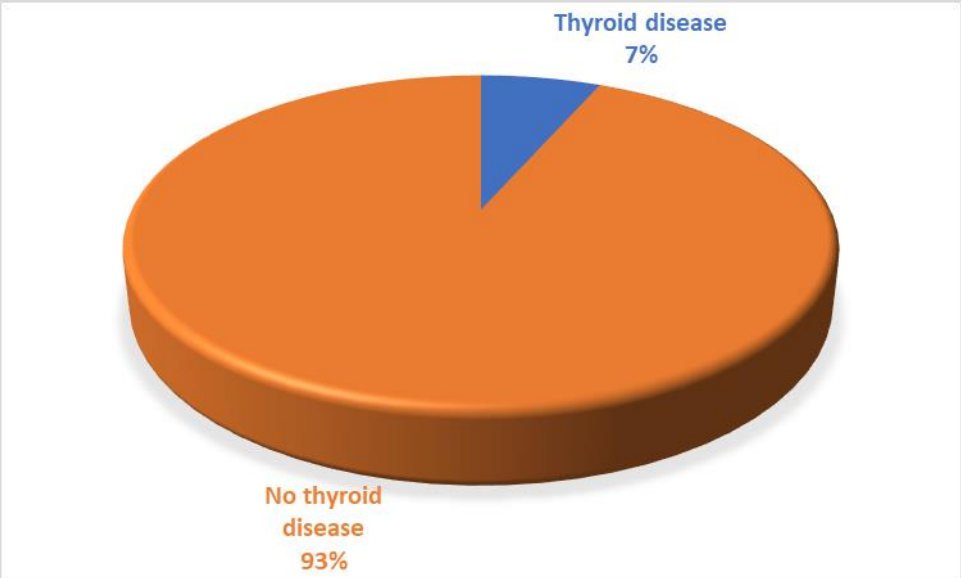


Figure 4.1: Prevalence of thyroid disease among patients at KNH

4.2. The spectrum of thyroid disease in children and young adults seen in KNH between 2008 and 2021

The results showed that 82(55.8%) of the patients had hypothyroidism, 43(29.3%) had goitre, 14(9.5%) had hyperthyroidism while 8(5.4%) had suspected thyroid tumor as showed in Figure 4.2.

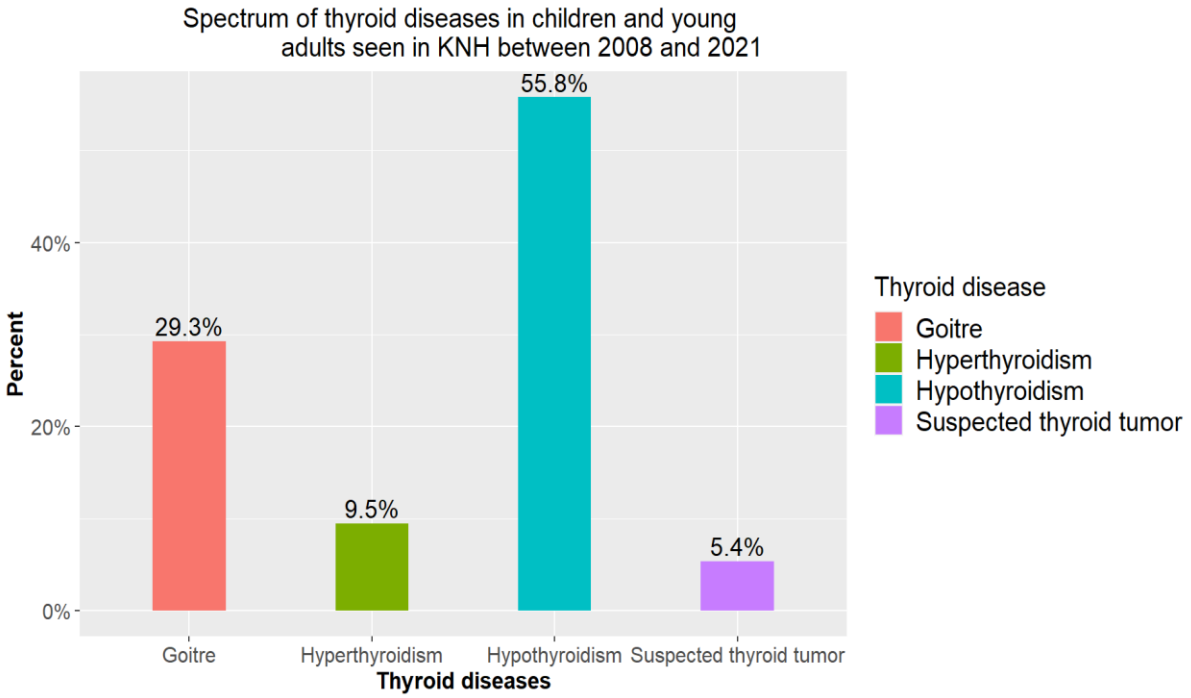


Figure 4.2: The spectrum of thyroid disease in children and young adults seen in KNH between 2008 and 2021

4.3. The clinical characteristics of children/adolescents with thyroid disorders in children and young adults seen in KNH between 2008 and 2021.

4.3.1. Demographic characteristics of children with thyroid disease at Kenyatta National Hospital

The findings established that 79 (53.7%) of patients were female. The median age was 18 (4.5 – 28) months with almost half of the patients who were aged ≤2 years. The findings also revealed that 92 (62.6%) had normal weight as shown in Table 4.1.

Table 4.1: Demographic characteristics of children with thyroid disease at Kenyatta National Hospital

Demographic characteristic	**Frequency n (%)**
Age	
<= 2 years	**66(44.9)**
2-3 years	58(39.5)
4 - 5 years	16(10.9)
> 5 years	7(4.8)
Gender	
Male	68(46.3)
Female	**79(53.7)**
Type of patient	
Admitted	9(6.1)
Outpatient	138(93.9)
Weight	
Underweight	98(66.7)
Normal	38(25.9)
Overweight/obese	11(7.5)
Referral status	
Referral	38(25.9)
Non-referral	109(74.1)
Symptom duration (Mean± SD) months	104.9±61.19

4.3.2. Disease-related characteristics among thyroid disease patients at KNH

The findings established that the median duration of symptoms was 27(IQR: 7 – 60) months. The presenting symptoms included palpitations 116(78.9%), excessive sweat 68(46.3%), poor sleep 68(46.3%), frequent stool 60(40.8%) and 33(22.4%) had delayed milestone as shown in Table 4.2.

Table 4.2: Disease-related characteristics among thyroid disease patients at KNH

	Hypothyroidism (N=82)	**Euthyroid goiter (N =43)**	**Hyperthyroidism (N =14)**	**Suspected thyroid tumour (N=8)**	**P-value**
	n (%)	**n (%)**	**n (%)**	**n (%)**	
Delayed milestone	**65(79.3)**	3(7.0)	3(21.4)	2(25.0)	<0.001
Down syndrome	**68(82.9)**	2(4.7)	3(21.4)	2(25.0)	0.332
Weight loss	11(13.4)	21(48.8)	**12(85.7)**	6(75)	<0.001
Excessive sweating	3(3.7)	25(58.1)	**10(71.4)**	2(25.0)	<0.001
Frequent stool	12(14.6)	22(51.2)	**9(64.3)**	2(25)	<0.001
Poor sleep	6(7.3)	25(58.1)	**11(78.6)**	4(50.0)	<0.001
Palpitations	10(12.2)	17(39.5)	**12(85.7)**	7(87.5)	<0.001

4.3.3. Management interventions used among thyroid disease patients at KNH

The results revealed that majority of the patients, 82(55.8%) used hormonal replacement, 14(9.5%) were treated using anti-thyroid drugs, 42(28.6%) used surgery, 5(3.4%) had propranolol while 8(5.5 as shown in Table 4.3.

Table 4.3: Management interventions used among thyroid disease patients at KNH

Management approaches	**Frequency (n)**	**Percent (%)**
Treatment approaches		
Anti-thyroid drugs	14	9.5
Surgery	42	28.6
Propranolol	5	3.4
Hormone replacement	82	55.8

4.4. Association between patient characteristics of children/adolescents with thyroid disorders in children and young adults seen in KNH between 2008 and 2021.

The results established that age (p =0.028), the weight of the child (p =0.002) and duration of symptoms (p =0.003) were found to be associated with thyroid disease as shown in Table 4.4.

Table 4.4: Clinical characteristics of children/adolescents with thyroid disorders in children and young adults seen in KNH between 2008 and 2021

	Hypothyroidism (N=82)	**Euthyroid goitre (N=43)**	**Hyperthyroidism (N=14)**	**Thyroid tumour (N=8)**	
	n (%)	**n (%)**	**n (%)**	**n (%)**	**P-value**
Age					
<= 2 years	44(53.7)	12(27.9)	9(64.3)	1(12.5)	
2-3 years	31(37.8)	18(41.9)	4(28.6)	1(12.5)	0.028
4 - 5 years	5(6.1)	10(23.3)	1(7.1)	1(12.5)	
> 5 years	2(2.4)	3(7.0)	0	5(62.5)	
Gender					
Male	44(53.7)	15(34.9)	6(46.2)	3(33.3)	0.195
Female	38(46.3)	28(65.1)	7(53.8)	6(66.7)	
Type of patient					
Admitted	8(9.8)		1(7.7)		0.149
Outpatient	74(90.2)	43(100)	12(92.3)	9(100)	
Weight					
Underweight	49(59.8)	36(83.7)	9(64.3)	4(50)	
Normal	25(30.5)	6(14.0)	4(28.6)	3(37.5)	0.002
Overweight/obese	8(9.8)	1(2.3)	1(7.1)	1(12.5)	
Referral status					
Referral	19(23.2)	12(27.9)	5(38.5)	2(22.2)	0.691
Non-referral	63(76.8)	31(72.1)	8(61.5)	7(77.8)	
Symptom duration (Mean±SD) months	49.15±11.2	235±50.11	62±13.11	53±32.19	0.008

4.4.1. Association between presenting signs and symptoms among patients with thyroid disease at KNH

The results from the analysis also revealed that vomiting (p =0.040), neck swelling (p = 0.001) and coughing (p =0.008) were significantly associated with thyroid disease as shown in Table 4.5.

Table 4.5: Presenting signs and symptoms among patients with thyroid disease at KNH

	Hypothyroidism (N=82)	**Euthyroid goiter (N =43)**	**Hyperthyroidism (N =14)**	**Suspected thyroid tumour (N=8)**	**P-value**
	n (%)	**n (%)**	**n (%)**	**Thyroid tumor n (%)**	
Delayed milestone	**65(79.3)**	3(7.0)	3(21.4)	2(25.0)	<0.001
Down syndrome	**68(82.9)**	2(4.7)	3(21.4)	2(25.0)	0.332
Weight loss	11(13.4)	21(48.8)	**12(85.7)**	6(75)	<0.001
Excessive sweating	3(3.7)	25(58.1)	**10(71.4)**	2(25.0)	<0.001
Frequent stool	12(14.6)	22(51.2)	**9(64.3)**	2(25)	<0.001
Poor sleep	6(7.3)	25(58.1)	**11(78.6)**	4(50.0)	<0.001
Palpitations	10(12.2)	17(39.5)	**12(85.7)**	7(87.5)	<0.001

5. CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

The present findings sought to determine the prevalence of thyroid diseases in children and adolescents. The findings from the present study established that the prevalence of thyroid diseases was 6.56%. These findings are comparable to other previous studies (Chabchoub et al., 2006; Ogbera & Kuku, 2011). A study conducted in Tunisia by Chabchoub et al., (2006) established that the prevalence of thyroid disease was 6.3%. Similarly, Ogbera and Kuku (2011) in a systematic review investigating the epidemiology of thyroid disease in Africa affirmed that the extent of autoimmune thyroid disorders remains relatively unknown due to a high level of underdiagnosis however the available literature shows that the prevalence ranges between 1.2 to 9.9%. These findings however were higher compared to findings from a study done in Ethiopia which revealed that the prevalence of thyroid disease among children and adolescents was 1.2% (58). This difference could be attributed to the difference in time settings where there was a high rate of underdiagnosis in previous years compared to the current context. Even though the rate of underdiagnosis is still high, there have fundamental steps made to help improve the diagnosis of thyroid disease in local hospitals. In another study conducted in Nigeria investigating the presence of thyroid disease in children and adolescents, the incidence of thyroid disease was 0.12% (Oyenusi et al., 2012). The prevalence of thyroid disorders in children appears to be increasing. This could be due to increased diagnosis of the disease resulting from available resources compared to previous years.

The findings from our present study also established that hypothyroidism (55.5%) was the common type of thyroid disease followed by goitre (29.3%), hyperthyroidism (9.5%) and suspected thyroid tumour (5.4%). These findings are comparable to a study conducted in Israel which revealed that hypothyroidism was the commonly presenting type of thyroid disease occurring in 82% of the patients (60). Similarly, comparable findings to this study were also identified in a five-year study conducted in Nigeria which established that 55.6% of the patients had hypothyroidism, 44% had goitre, 27.8% had hyperthyroidism and 15.7% had euthyroidism (40). Further, another study conducted in Western India revealed that out of 65 patients with thyroid disease, 61 of them had hypothyroidism while four of them had hyperthyroidism (61). These findings have illustrated that hypothyroidism is a commonly occurring thyroid disease. This is majorly due to increasing environmental iodine deficiency which has been the main cause of thyroid disorders. Iodine is an essential component of

thyroid hormones but is also thought to make the thyroid gland more antigenic. However, these findings contrast those from a study done in Nakuru, Kenya which revealed that euthyroidism was the most common type of thyroid disorder (55%), hyperthyroidism (40%), subclinical hypothyroidism (3%) with only 1% having hypothyroidism (62).

The findings from our present study established that there was a significant association between age and thyroid disease. The results further show that 61.5% of children with hyperthyroidism, 53.7% with hypothyroidism, 27.9% of children with goitre and 22.2% of children with suspected thyroid tumours were aged ≤ 2 years. Our present findings are consistent with another study conducted in Nigeria by Oluwayemi et al who found that 54% of patients, were aged less than five years at presentation while 29% were aged between 5 and 10 years while 16% were older than 10 years.(39). These findings indicate that the age at presentation plays a major role in influencing the treatment pattern and outcomes where adverse outcomes are controlled among patients diagnosed early.

These findings however contrast those from a study conducted in Israel by Admoni et al which found that the average age at diagnosis was 13 years (60). Thus, the majority of patients in our study were diagnosed with thyroid disease very early due to presenting symptoms. Our findings also revealed that more than half of the patients were female (53.7%) although gender was not found to have a significant association with thyroid disease in our present study. These findings are comparable to a study conducted in Italy which found that the prevalence of thyroid disease was high in women compared to male children and adolescents (1). The findings revealed that goitre patients had the longest duration of symptoms. The longer duration of symptoms could be attributed to the understanding that sometimes the symptoms of goitre may disappear on their own, or may become larger. These findings are comparable to a study conducted in Ethiopia among school-going children by Tigabu et al. who established that the duration of symptoms was associated with goitre where children who had a longer duration of symptoms were more likely to be diagnosed with goitre (63)

Presenting signs and symptoms were also investigated in the current study. The findings revealed that vomiting was associated with the presence of thyroid disease. The majority of the patients (84%) were vomiting. Among the different types of thyroid disease, all of the patients with suspected thyroid tumours were vomiting, 93% of those with goitre presented with vomiting while 78% of those with hypothyroidism presented with vomiting. These

findings are comparable with Shim et al. who established that Patients with thyroid disorders may present with a wide range of gastrointestinal diarrhoea, frequent defecation, constipation, dyspepsia, nausea, vomiting and abdominal pain (64). Similarly, a case report conducted in China by Chen et al. established that even though vomiting among patients with hyperthyroidism is rare, it cannot be conclusively ruled out as a clue for thyroid disease (65).

Our present study also established that coughing was associated with an increased likelihood of thyroid disease and commonly occurring among goitre patients (97.7%) and hyperthyroidism (84.6%). Coughing has been effectively considered a symptom of thyroid disease with an increased proportion among patients with hyperthyroidism (66). It has also been identified that there is a significantly increased prevalence of respiratory symptoms in patients with hypothyroidism. The present findings also revealed that even though in our present study there was no association between delayed milestone and thyroid disease, delayed milestone was higher among patients with hyperthyroidism. These findings are in line with Calcaterra et al. who revealed that hyperthyroidism in children is characterized by a change in growth pattern, with affected children exhibiting faster growth but a delay in the onset of puberty. The advanced maturation of a child's skeletal system is also linked to hyperthyroidism in children. Children and adolescents who are affected by Graves' disease are more prone to display behavioural issues such as anxiety and attention impairments or hyperactivity than those who do not have the condition (1). The results also revealed that 58.5% of the patients with thyroid disease had weight loss. Comparably, a study conducted in Nigeria also found that all of the patients with thyroid disease presented with weight loss (40).

5.2 Conclusion

The findings established that 6.56% of patients attending the endocrine clinic had thyroid disease. Among those who had thyroid disease, 55.5% had hypothyroidism, 29.3% had goitre, 9.5% had hyperthyroidism and 5.4% had suspected thyroid tumours.

In investigating clinical characteristics, the majority of the patients with thyroid disease presented with vomiting (84.4%), coughing (83.7%), palpitations (78.9%), weight loss (58.5%) excessive sweat (53.7%) and poor sleep (51.0%). The findings revealed that age, weight, symptom duration, vomiting, coughing and weight loss were significantly associated with types of thyroid disease.

5.3 Recommendations

- To encourage early screening of thyroid disease in children to improve child developmental status.
- Increase health education on thyroid diseases in the general public to help parents understand the common symptoms of thyroid disease such as weight loss, coughing, excessive sweat and palpitations.
- Clinicians should consider the possibility of thyrotoxicosis in patients with unexplained and repeated vomiting.
- Further prospective research should be undertaken to investigate the outcomes associated with hypothyroidism and goitre among children who were diagnosed early.

Study limitation

This was purely an observational study hence the principal investigator did not have control over the diagnosis of the patients.

In case of missing information from the records, it was difficult to get the information as there was no contact with patients for clarification.

Screening was not done to diagnose congenital hypothyroidism; we have instead assumed that those diagnosed and a younger age had congenital hypothyroidism.

REFERENCES

1. Calcaterra V, Nappi RE, Regalbuto C, De Silvestri A, Incardona A, Amariti R, et al. Gender Differences at the Onset of Autoimmune Thyroid Diseases in Children and Adolescents. Front Endocrinol (Lausanne). 2020;
2. Rafieian-Kopaei M. International journal of green pharmacy IJGP : official publication of TIFAC CORE in Green Pharmacy. Int J Green Pharm. 2018;12(03):473–82.
3. Thyroid Gland - Function, Hormones, T3, T4, TSH, Disorders - Why Thyroid.
4. Wu Y, Koenig RJ. Gene regulation by thyroid hormone. Trends in Endocrinology and Metabolism. 2000.
5. Williams GR. E-Mail Thyroid Hormone Actions in Cartilage and Bone Regulation of Thyroid Hormone Action. 2012;
6. Brams EO. Thyroid disease : a case-based and practical guide for primary care. 2005;154.
7. Khan L. Thyroid disease in children and adolescents. Pediatr Ann. 2021;
8. Astapova I. Role of co-regulators in metabolic and transcriptional actions of thyroid hormone. Journal of Molecular Endocrinology. 2016.
9. Arrangoiz R, Cordera F, Caba D, Muñoz M, Moreno E, León EL de, et al. Comprehensive Review of Thyroid Embryology, Anatomy, Histology, and Physiology for Surgeons. Int J Otolaryngol Head & Neck Surg. 2018 Jul;7(4):160–88.
10. Anatomy and W. Anatomy and Physiology in Health and Illness.
11. Ogbera AO, Kuku SF. Epidemiology of thyroid diseases in Africa. Indian J Endocrinol Metab. 2011;15(Suppl2):S82.
12. Pearce EN, Andersson M, Zimmermann MB. Global iodine nutrition: Where do we stand in 2013? Thyroid. 2013.
13. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nature Reviews Endocrinology. 2018.
14. Sarfo-Kantanka O, Sarfo FS, Ansah EO, Kyei I. Graves Disease in Central Ghana: Clinical Characteristics and Associated Factors. Clin Med Insights Endocrinol

Diabetes. 2018;

15. Bello F. Hypothyroidism in adults: A review and recent advances in management. J Diabetes Endocrinol. 2012;

16. Vanderpump MPJ, Tunbridge WMG. Epidemiology and prevention of clinical and subclinical hypothyroidism. Thyroid. 2002;12(10):839–47.

17. Brent GA. Clinical practice. Graves' disease. N Engl J Med. 2008 Jun;358(24):2594–605.

18. Daniels GH, Dayan CM. Thyroid Disorders. 2006;146.

19. Franklyn JA, Boelaert K. Thyrotoxicosis. Lancet (London, England). 2012;379(9821):1155–66.

20. Onyiriuka AN, Abiodun PO, Onyiriuka LC, Omoruyi HO. Diabetes Mellitus in Childhood and Adolescence: : Analysis of Clinical Data of Patients Seen in a Nigerian Teaching Hospital. African J Trop Med Biomed Res. 2020 Nov;1(3):50–7.

21. Oyenusi EE, Ajayi EO, Akeredolu FD, Oduwole AO. Pattern of Thyroid Disorders in Children and Adolescents Seen at the Lagos University Teaching Hospital, Nigeria, Over a 10-year Period. Niger Med J. 2017;58(3):101.

22. Li M, Maso LD, Vaccarella S. Global trends in thyroid cancer incidence and the impact of overdiagnosis. lancet Diabetes Endocrinol. 2020 Jun;8(6):468–70.

23. Kimathi L. Challenges of the devolved health sector in Kenya: Teething problems or systemic contradictions? Africa Dev. 2017;

24. Hill AG, Mwangi I, Wagana L. Thyroid disease in a rural Kenyan Hospital. East African Medical Journal. 2004.

25. An analysis of thyroid diseases seen at Kenyatta National Hospital.

26. Iddah MA, Macharia BN, Hu J-F, Skafar DF. Autoimmune Thyroid Disorders. Corp ISRN Endocrinol. 2013;2013.

27. Kang MJ, Chung HR, Oh YJ, Shim YS, Yang S, Hwang IT. Three-year follow-up of children with abnormal newborn screening results for congenital hypothyroidism. Pediatr Neonatol. 2017;

28. Yang J, Yi N, Zhang J, He W, He D, Wu W, et al. Generation and characterization of a hypothyroidism rat model with truncated thyroid stimulating hormone receptor. Sci Rep. 2018;

29. Hermanns P, Claßen C, Pohlenz J. A Novel Homozygous Mutation in the Solute Carrier Family 26 Member 7 Gene Causes Thyroid Dyshormonogenesis in a Girl with Congenital Hypothyroidism. Thyroid. 2020;

30. Hong HS, Lee JY, Jeong SH. Thyroid disease in children and adolescents. Ultrasonography. 2017.

31. Kaguelidou F, Carel JC, Léger J. Graves' disease in childhood: Advances in management with antithyroid drug therapy. Hormone Research. 2009.

32. Cappa M, Bizzarri C, Crea F. Autoimmune Thyroid Diseases in Children. J Thyroid Res. 2011;2011:13.

33. Shahbaz A, Aziz K, Umair M, Sachmechi I. Prolonged Duration of Hashitoxicosis in a Patient with Hashimoto's Thyroiditis: A Case Report and Review of Literature. Cureus. 2018 Jun;10(6).

34. Caron P, Broussaud S, Galano-Frutos JJ, Sancho J, Savagner F. New variant (Val597Ile) in transmembrane region of the TSH receptor with human chorionic gonadotropin hypersensitivity in familial gestational hyperthyroidism. Clin Endocrinol (Oxf). 2020;

35. Beck-Peccoz P, Giavoli C, Lania A. A 2019 update on TSH-secreting pituitary adenomas. Journal of Endocrinological Investigation. 2019.

36. Jin HY. Thyroxine binding globulin excess detected by neonatal screening. Ann Pediatr Endocrinol Metab. 2016;21(2):105.

37. Hanley P, Lord K, Bauer AJ. Thyroid disorders in children and adolescents: A review. JAMA Pediatrics. 2016.

38. Wassner AJ. Congenital Hypothyroidism. Clin Perinatol. 2018 Mar;45(1):1–18.

39. Oluwayemi IO, Adeniji EO, Ogundare EO, Ayeni TO, Fatunla OAT. Pediatric thyroid disorders in two teaching hospitals in South-West Nigeria. Niger J Med. 2020;29(3):428.

40. Jaja T, Yarhere I. Clinical characteristics of children and adolescents with thyroid disorders seen at the University of Port Harcourt Teaching Hospital: A five year review. Niger J Paediatr. 2014;

41. Yelluri S. Incidence and etiology of thyroid disorders in children. Int J Contemp Pediatr. 2016;

42. Tang S, Yang M, Zhang D, Tong Y, Xin Y. Clinical Characteristics and Follow-Up of 19 Children With Hashimoto's Thyroiditis Aged Below 3 Years: A Single-Center Retrospective Analysis. Front Endocrinol (Lausanne). 2021;12(September):1–8.

43. Plamper M, Schreiner F, Gohlke B, Kionke J, Korsch E, Kirkpatrick J, et al. Thyroid disease in children and adolescents with PTEN hamartoma tumor syndrome (PHTS). Eur J Pediatr. 2018;

44. De Vries L, Bulvik S, Phillip M. Chronic autoimmune thyroiditis in children and adolescents: At presentation and during long-term follow-up. Arch Dis Child. 2009;

45. Ammar M. Van Wyk and Grumbach Syndrome: An Unusual Presentation of Acquired Hypothyroidism. J Endocrinol Diabetes. 2017;4(3):1–3.

46. Khera S, Venkateshwar V, Kanitkar M, Devgan A. Varied presentations of hypothyroidism in children. Med Journal, Armed Forces India. 2011;67(2):174.

47. Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS, et al. Guidelines for the Treatment of Hypothyroidism: Prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement. Thyroid. 2014 Dec;24(12):1670.

48. Bongers-Schokking JJ, Resing WCM, De Rijke YB, De Ridder MAJ, De Muinck Keizer-Schrama SMPF. Cognitive Development in Congenital Hypothyroidism: Is Overtreatment a Greater Threat Than Undertreatment? 2013;

49. Van Vliet G, Deladoëy J. Diagnosis, treatment and outcome of congenital hypothyroidism. Endocr Dev. 2014;26:50–9.

50. Bahn RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, Klein I, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Thyroid. 2011 Jun;21(6):593–646.

51. Bauer AJ. Approach to the pediatric patient with Graves' disease: When is definitive therapy warranted? Journal of Clinical Endocrinology and Metabolism. 2011.

52. Hassan-Kadle MA, Adani AA, Eker HH, Keles E, Muse Osman M, Mahdi Ahmed H, et al. Spectrum and Prevalence of Thyroid Diseases at a Tertiary Referral Hospital in Mogadishu, Somalia: A Retrospective Study of 976 Cases. Int J Endocrinol. 2021;2021.

53. Subramonian D, Wu YJ, Amed S, Sanatani S. Hyperthyroidism With Atrial Fibrillation in Children: A Case Report and Review of the Literature.

54. Zimmermann MB. Iodine deficiency and excess in children: Worldwide status in 2013. In: Endocrine Practice. 2013.

55. Powell JT, Sweeting MJ. Retrospective Studies. Eur J Vasc Endovasc Surg. 2015 Nov;50(5):675.

56. Ogbera A, Kuku S. Epidemiology of thyroid diseases in Africa. Indian J Endocrinol Metab. 2011;

57. Chabchoub G, Mnif M, Maalej A, Charfi N, Ayadi H, Abid M. Epidemiologic study of autoimmune thyroid disease in south Tunisia. Ann Endocrinol (Paris). 2006;

58. Mengistu M. The pattern of thyroid diseases in adult Ethiopians and experience in management. Ethiop Med J. 1993;

59. Onyiriuka AN, Abiodun PO, Onyiriuka LC. Thyroid Disorders in Childhood and Adolescence: Analysis of Clinical Data and Management Challenges in Patients Seen in a Nigerian Teaching Hospital. Greener J Med Sci. 2012;

60. Admoni O, Rath S, Almagor T, Elias-Assad G, Tenenbaum-Rakover Y. Long-Term Follow-Up and Outcomes of Autoimmune Thyroiditis in Childhood. Front Endocrinol (Lausanne). 2020;

61. Singh A, Purani C, Mandal A, Mehariya KM, Das RR. Prevalence of thyroid disorders in children at a tertiary care hospital in Western India. J Clin Diagnostic Res. 2016;

62. David L. CHARACTERIZATION OF THYROID DISORDERS AMONG PATIENTS ATTENDING SURGICAL CLINIC AT NAKURU LEVEL 5 HOSPITAL - NAKURU COUNTY , KENYA. 2021;

63. Tigabu E, Bekele KB, Dachew BA. Prevalence of goiter and associated factors among schoolchildren in northeast Ethiopia. Epidemiol Health. 2017;

64. Shim S, Ryu HS, Oh HJ, Kim YS. Thyrotoxic Vomiting: A Case Report and Possible Mechanisms. J Neurogastroenterol Motil. 2010;

65. Chen LY, Zhou B, Chen ZW, Fang LZ. Recurrent severe vomiting due to hyperthyroidism. J Zhejiang Univ Sci B. 2010;

66. Birring SS, Morgan AJ, Prudon B, McKeever TM, Lewis SA, Falconer Smith JF, et al. Respiratory symptoms in patients with treated hypothyroidism and inflammatory bowel disease. Thorax. 2003;

APPENDIX I: DATA ABSTRACTION TOOL

Table 0.1:Data abstraction tool Code no……

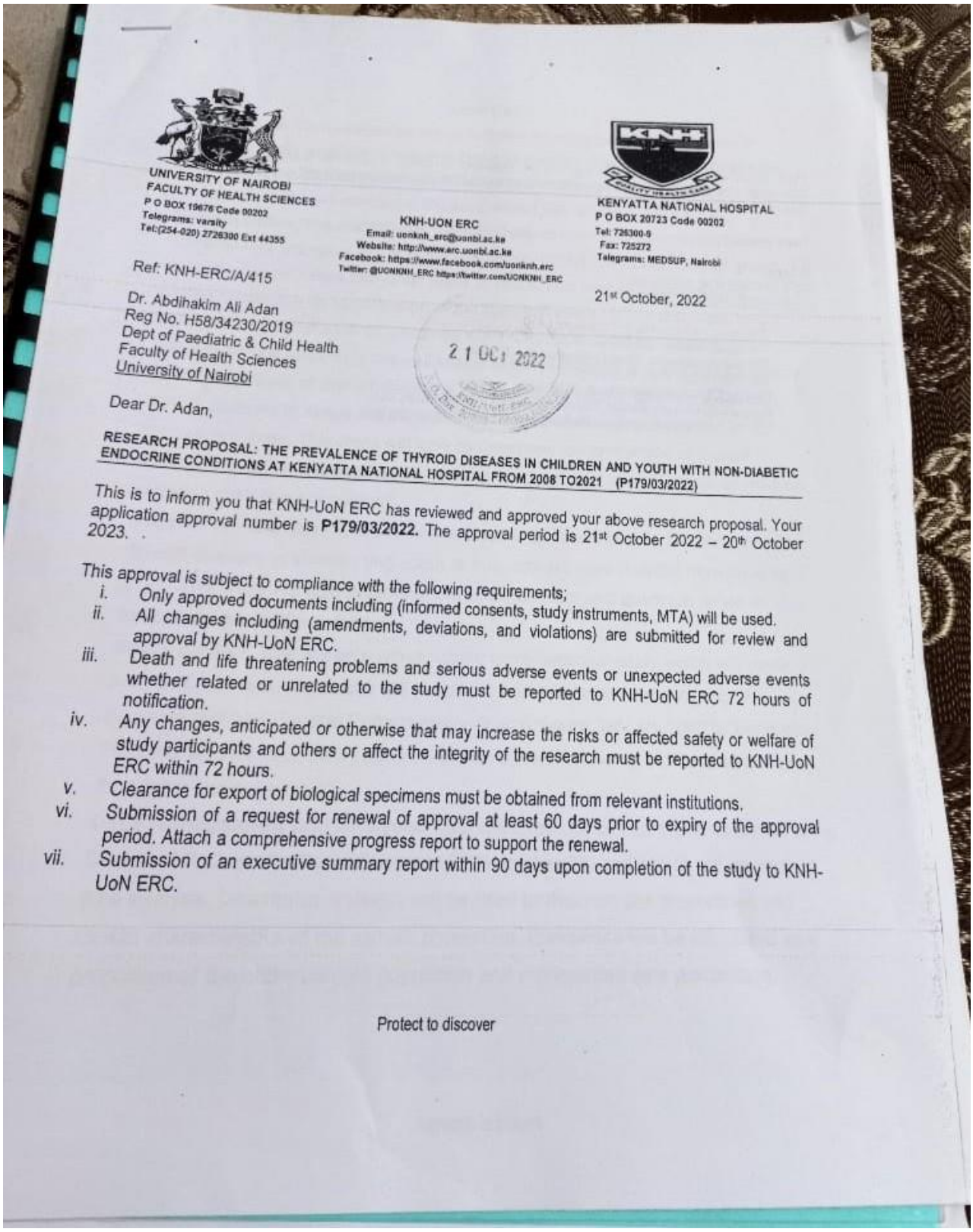
Date at first visit Date at last visit Age in years at diagnosis Age at last visit LAST SEEN	---------- …… ……. ---------- ---------- ---------- ---------- , 6 months or less More than 6 months	
		Tick as appropriate
Gender	Male	
	Female	
Weight in kg and z score AT diagnosis weight in kg and z score at the last visit	…… …. ----------	
Height in cm and z score at diagnosis	……	
Height in cm and z score at the last visit	----------	

The pubertal stage at diagnosis as indicated in the file a. Prepubertal(girls with no breast enlargement and boys with testicular volume 4mls and below) b. Pubertal (girl with enlarged breast and boy with testicular volume more than 4 MLS	---------- - ----------	
The pubertal stage at the last visit; a. Prepubertal(girls with no breast enlargement and boys with testicular volume 4mls and below) b. Pubertal (girl with enlarged breast and boy with testicular volume more than 4 MLS	---------- ------	
Family history of thyroid disease	Positive	
	Negative	
Presence of thyroid disease	Positive	
	Negative	
Referring county	……	
Thyroid disease diagnosis outcome	State the specific identified thyroid disease	
Clinical characteristics: Patients with hypothyroidism or hyperthyroidism at the last visit		
Weight Loss	Positive	

	Negative	
Excessive sweating	Positive	
	Negative	
Frequent Stools	Positive	
	Negative	
Poor Sleep	Positive	
	Negative	
Palpitations	Positive	
	Negative	
Family History	Positive	
	Negative	
Others	List other clinical symptoms	
Weight Loss	Positive	
	Negative	
Excessive sweating	Positive	
	Negative	
Frequent Stools	Positive	
	Negative	
Poor Sleep	Positive	
	Negative	
Palpitations	Positive	
	Negative	
Family History	Positive	
	Negative	
Level of developmental milestone	Normal	
	Delayed	
Others	List other clinical symptoms	
Management approaches	List the	Tick as appropriate

	management approaches:		
	Radiological		
	Medical		
	Surgical		
	Other:		
Clinical outcomes		Tick as appropriate	Indicate change that has occurred after treatment
Body weight in kg and z score	normal		
	low weight		
	High weight		
Body height/length	Normal		
	Short stature		
	Tall stature		
Milestone	normal		
	Delayed		
Thyroid function	normal		
	hypothyroidism		
	Hyperthyroidism		
Pubertal development	normal		
	delayed		
	precocious		
Lost to follow-up (has not been seen in the clinic for more than 6 months)	yes		
	No		

APPENDIX II: ETHICS REVIEW APPROVAL



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Ref: KNH-ERC/A/415

21st October, 2022

Dr. Abdihakim Ali Adan
Reg No. H58/34230/2019
Dept of Paediatric & Child Health
Faculty of Health Sciences
University of Nairobi

21 OCT 2022

Dear Dr. Adan,

RESEARCH PROPOSAL: THE PREVALENCE OF THYROID DISEASES IN CHILDREN AND YOUTH WITH NON-DIABETIC ENDOCRINE CONDITIONS AT KENYATTA NATIONAL HOSPITAL FROM 2008 TO2021 (P179/03/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P179/03/2022.** The approval period is 21st October 2022 – 20th October 2023. .

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Protect to discover

Prior to commencing your study, you will be expected to obtain a research li
Commission for Science, Technology and Innovation (NACOSTI) https://research-pc
also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

c.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Assistant Director, Health Information Dept., KNH
The Chairperson, KNH- UoN ERC
The Chair, Dept, of Paediatrics & Child Health, UoN
Supervisors: Dr. Lucy Mungai, Dept of Paediatrics & Child Health, UoN
Dr. Bashir Admani Dept of Paediatrics & Child Health, UoN

APPENDIX III: SIMILARITY REPORT

THE PREVALENCE AND SPECTRUM OF THYROID DISEASES AMONG CHILDREN AND YOUTH SEEN AT THE ENDOCRINE CLINIC, KENYATTA NATIONAL HOSPITAL FROM 2008 TO 2021

ORIGINALITY REPORT

14%	8%	9%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Markus Bettendorf. "Thyroid disorders in children from birth to adolescence", European Journal of Nuclear Medicine and Molecular Imaging, 2002 Publication	4%
2	www.ajol.info Internet Source	2%
3	ir.jkuat.ac.ke Internet Source	1%
4	link.springer.com Internet Source	1%
5	Scott A. Rivkees. "Thyroid disorders in children and adolescents", Elsevier BV, 2014 Publication	<1%
6	www.ncbi.nlm.nih.gov Internet Source	<1%
7	www.researchsquare.com Internet Source	<1%