Spectrum of pediatric endocrine disorders as seen in Kenyatta National Hospital, a 14-year retrospective study from 2008 to 2021.

(Phoebe Wamalwa[1], Lucy Mungai[2], Paul Laigong[3], Anjum Omar[4], Prisca Amolo[5])

PRINCIPLE INVESTIGATOR:
DR. PHOEBE NASIMIYU WAMALWA
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DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH

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DECLARATION

This study is my original work and has not been presented for a degree in any other University.

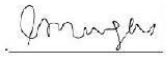
Dr. Phoebe Nasimiyu Wamalwa

Signature: _____ **Date:** *18th April 2023*

SUPERVISORS' APPROVAL

This project work has been submitted for examination with our approval as the University Supervisors:

Dr. Lucy N. Wainaina Mungai, MBChB, M.Med, Msc, Paed & Adol Endo(Barcelona)
Senior Lecturer, Department of Paediatrics and Child healFaculty of Health Sciences,
University of Nairobi.

Signature:  **Date:** *18th April 2023*

Dr. Paul Laingog, MBChB, M.Med, Paediatric Endocrinologist

Lecturer, Department of Paediatrics and Child health, Faculty of Health Sciences,

University of Nairobi.

Signature:  **Date:** *18th April 2023*

Dr. Anjumanara Omar, MBChB, M.Med, Fellowship Paed Endo

Lecturer, Department of Paediatrics and Child health, Faculty of Health Sciences,

University of Nairobi.

Signature: .....  ... **Date:** *18th April 2023*

Dr. Prisca Amolo, MBChB, M.Med, FESPE
Paediatrician and Paediatrics Endocrinologist, Kenyatta National Hospital.

Signature: ..... **Date:** *18th April 2023*

CERTIFICATE OF AUTHENTICITY

This Project is the original work of Dr. Phoebe Nasimiyu Wamalwa under the guidance of Dr. Lucy N.W.Mungai, Dr. Wanyoike Gichuhi, and Dr. Paul Laingong, Dr. Anjumanara and Dr. Prisca Amolo. It was not been presented in any other university for award of a degree or diploma. All referenced works have been cited.

Signature:  **Date:** *18th April 2023*

Professor Grace W. Irimu, MBChB (UoN), M.MED (Paed) (UoN), PHD (OU)

Chairperson, department of Paediatrics and Child health, Faculty of Health Sciences,

University of Nairobi.

DEDICATION

I would like to dedicate this work firstly, to the Almighty God who through His Grace enabled me to sail through this fellowship program successfully, and secondly to my family headed by my husband, who created a conducive environment for me throughout this process. I wish to thank my supervisors and the entire department of pediatrics and Child health at the University of Nairobi for guidance and encouragement as well as my sponsors, ELMA Foundation.

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ABBREVIATIONS

1. **ACTH** Adrenocorticotropic Hormone
2. **CAH** Congenital Adrenal Hyperplasia.
3. **CRH** Corticotropin Releasing Hormone
4. **DM** Diabetes Mellitus
5. **DSD** Disorders of Sexual Differentiation
6. **ESPE** European Society of Pediatric Endocrinology
7. **ESPE/LWPES** European Society for Pediatric Endocrinology /Lawson Wilkins Pediatric Endocrine Society
8. **FSH** Follicle Stimulating Hormone
9. **GH** Growth Hormone
10. **GHRH** Growth Hormone Releasing Hormone
11. **HbA1c** Glycated Hemoglobin
12. **HIV** Human Immunodeficiency Virus
13. **ICD** International Classification of Diseases
14. **ICPED** International Classification of Pediatric Endocrine Diagnoses
15. **IGF** Insulin-like Growth Factor
16. **ISPAD** International Society for Pediatric and Adolescent Diabetes
17. **KNH** Kenyatta National Hospital
18. **KNH-UON ERC** Kenyatta National Hospital-University of Nairobi Ethics Review Committee
19. **LH** Luteinizing Hormone
20. **MPHD** Multiple Pituitary Hormone Deficiency
21. **MSH** Melanocyte Stimulating Hormone
22. **PETCA** Pediatric Endocrinology Training Center for Africa
23. **PETCWA** Pediatric Endocrinology Training Center for West Africa
24. **PT** Premature Thelarche
25. **PA** Premature Adrenarche
26. **SDS** Standard Deviation Score
27. **SPSS** Statistical Package for Social Sciences
28. **T3** Triiodothyronine
29. **T4** Tetraiodothyronine or Thyroxine

30. **THPO** Thrombopoietin
31. **TIDM** Type 1 Diabetes Mellitus
32. **TRH** Thyrotropin Releasing Hormone
33. **TSH** Thyroid Stimulating Hormone

DEFINITION OF TERMS

1. **Adolescence:** Age between 10 to 19 years by WHO but recently re-classified as between 10 and 24 years
2. **Contrasexual:** Possessing secondary sexual characteristics appropriate to the opposite sex.
3. **Diabetes inspidus:** A condition characterized by inability to concentrate urine, excess thirst, and urination as a result of deficient antidiuretic hormone or resistance at the receptor level.
4. **Diabetes mellitus:** A disease in which the body's ability to produce or respond to the hormone insulin is impaired, resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in blood. The diagnosis is made when random blood glucose level is above 11.1 mmol/l in the presence of obvious symptoms of diabetes like excess thirst, frequent urination, and weight loss, or when fasting blood sugar is above 7.0 mmol/l or when HbA1c is above 6.5%.
5. **Dyshormonogenesis:** A defect in synthesis of hormones due to an enzyme failure.
6. **Goitre:** Abnormal swelling at the anterior aspect of the neck because of thyroid gland dysfunction.
7. **Hypercalcemia:** High blood calcium levels.
8. **Hypergonadotropic hypogonadism:** Over-secretion of excess hormones from the pituitary gland and hypothalamus due to failure of ovaries or testes to produce sex hormones**.**
9. **Hypernatremia:** High blood sodium level
10. **Hyperthyroidism:** Secretion of excess thyroid hormones
11. **Hypocalcemia:** Low blood calcium levels
12. **Hypogonadotropic hypogonadism:** Under secretion of sex hormones from the ovaries or testes due to failure of the pituitary gland or the hypothalamus.
13. **Hyponatremia:** Low blood sodium level
14. **Hypothalamo-pituitary:** Affecting both the hypothalamus and pituitary glands
15. **Hypothyroidism:** Inability of the thyroid gland to secrete sufficient thyroid hormones
16. **Iatrogenic:** Relating to illness caused by medical treatment
17. **Neoplasia:** Abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the surrounding normal tissues and persists in the same excessive manner after cessation of the stimuli that provoked the change.

18. **Obesity:** Abnormal or excess fat accumulation that presents a risk to health. It is considered when a body mass index is above the 95th centile for age and sex.
19. **Polygenic:** More than one gene
20. **Puberty:** The time in one's life when sexual maturity takes place. Age at onset is usually 9 years for boys and 8 years for girls.
21. **Type 1 diabetes mellitus:** A chronic hyperglycemic condition caused by a lack of insulin production by the pancreas.
22. **Type 2 diabetes mellitus:** A chronic hyperglycemic condition caused by resistance of tissues to insulin action.
23. **Loss to follow up:** Lack of attendance at clinical visits for at least 6 months from last clinic appointment.

ABSTRACT

Background

Pediatric endocrinology is an expanding subspecialty in both developed and developing countries and therefore well-equipped hospitals with relevant resources is mandatory to match the rising needs. There is no data on the characterization of endocrine cases seen in children and adolescents in Kenya at the moment.

Broad objective:

To determine the spectrum of pediatric endocrine disorders in Kenyatta National Hospital among children and adolescents aged 25 years and below.

Study design:

This was a 14-year hospital-based retrospective, descriptive study.

Study setting:

This study was carried out in the pediatric endocrinology unit and records department at Kenyatta National Hospital, Nairobi, Kenya. The hospital is a tertiary referral and teaching institution that serves as a major patient referral facility receiving patients from all the 47 counties in Kenya. Patients seen in this clinic come as self-referral, internal referral from clinics within the hospital, or from level 4 and 5 county hospitals in the country. The clinic is run every Tuesday by pediatric endocrinologists and has an attendance of approximately thirty clients per day. It also serves as a teaching clinic for medical students, pediatric resident doctors and pediatric endocrinology fellows.

Material/participants and methods:

This study comprised children and adolescents with endocrine conditions aged 25 years and below seen in the outpatient pediatric endocrinology clinic at Kenyatta National Hospital between January 2008 and December 2021. A search was conducted in the hospital records department using the ICD coding system to yield patient registration numbers. A systematic review of patient files was carried out. Data was obtained from patients' files by the principal investigator using a structured data collection instrument to seek the following information: Patients' demographic data, referral source,

presenting complaints, diagnosis, time between symptom onset and presentation to hospital and duration in months from last clinical review to determine loss to follow up.

Data management:

Data collected via the questionnaire was checked for completeness and free of error prior to entering into the Microsoft Excel 2017 spreadsheet. Thereafter the data was exported to the Statistical Package for Social Science (SPSS) version 23.0 for analysis. Demographic characteristics of the patients were summarized as frequencies and percentages for categorical data and as means with standard deviations or median with interquartile range for continuous data. The pattern of endocrine disorders as well as their respective presenting complaints and demographic characteristics were analyzed and presented as frequencies and percentages. The time interval between onset of symptoms and actual visit at the hospital was calculated as the difference between the time of onset of symptoms and the time of actual visit at the hospital and categorized into time intervals where the results were presented as frequencies and percentages, as well as a mean with standard deviation. The percentage of patients who were lost to follow up was the proportion of patients who were marked as lost to follow up over the total sample size and presented as a percentage.

Expected main outcome measure/Study utility:

This study endeavored to determine the pattern and frequency of endocrine disorders in children and adolescents seen at the Pediatric Endocrinology Unit in Kenyatta National Hospital; characterize their presenting complaints; illustrate their demographic characteristics; determine the time interval between onset of symptoms and actual visit and lastly determine the percentage of patients who were lost to follow up.

Information from this study will be used to guide policymakers on allocation of resources towards management of pediatric endocrine conditions. In addition, an understanding of the pattern of referrals will guide on areas of focus for continuous medical education for primary healthcare providers and pediatricians to make timely decisions regarding their management. It will also serve as a basis for further research on specific endocrine conditions.

RESULTS:

A total of 2238 cases patients were seen at KNH in the period of January 2008 to December 2021. Calcium and phosphate disorders were the leading at 35.2% followed by glucose and lipid metabolism disorders, growth disorders, testes and male reproductive tract conditions and thyroid disorders at 17.02%, 14.3%, 11.2% and 7.55% respectively. There was a sharp declining trend among cases of rickets and failure to thrive with a clear increasing trend in type 1 diabetes and hypothyroidism over the years. Diabetic ketoacidosis was the most common clinical presentation at diagnosis of type 1 diagnosis followed by weight loss at 90.2% and 35.7% respectively. Among disorders of the testes, 50% and 43% of patients presented with unilateral and bilateral undescended testes correspondingly whereas 88.4% of patients with disorders of the penis presented with hypospadias. Congestive cardiac failure was the mostly occurring initial presentation amongst cases of hypothyroidism followed by poor growth at 56.3% and 33% sequentially. Patients with rickets commonly presented with pneumonia and delayed milestones at frequencies of 36.3% and 34.1 correspondingly. Majority of the patients with hypothyroidism, numerical chromosomal disorders, type 1 diabetes and testes and male reproductive tract disorders were admitted initially before clinic follow up. Nairobi county constituted the bulk of total referrals followed by Kiambu, Murang'a and Kajiado counties at 68%, 7.4%, 3.9% and 2.8% respectively. There was a male preponderance in cases of rickets (57.8%), failure to thrive (60.5%), hypothyroidism (58.4%) and numerical chromosomal abnormalities (53.8%). A female preponderance was noted in hyperthyroidism (60%) and type 1 diabetes (51.6%) while 84.8% of DSD cases presented with ambiguous genitalia. Majority of calcium and phosphate metabolism disorders (95.5%), growth disorders (87.4%), testes and male reproductive tract disorders (36.5%), DSD (68.6%) and hypothyroidism (66.9%) were diagnosed within the 1-to-23-month age bracket whereas 36.4% of type 1 diabetes got diagnosed within 10 to 18 years within which the 10-to-14-year age group comprised 20.1%. 30% of type 1 diabetes cases got diagnosed within 19 to 25 years of age. The median age at diagnosis varied with diagnosis as follows: short stature, 2.5 years; tall stature, 2.3 years; delayed puberty, 14.5 years; non-pathological sexual variants, 5.5 years; precocious puberty, 4 years; DSD 5 months; hypothyroidism 8 months; disorders of penis 1 year; maldescended testes 3 years; hypoglycemia 1 month; type 1 diabetes 9 years; rickets 9 months; dysmorphic features 5 months; and numerical chromosomal abnormalities, 6 months. There was a delay in duration between symptom onset and presentation to hospital in majority of cases including cases of failure to thrive (mean 121 days, median 26 days), type 1

diabetes (mean 80 days, median 18 days), DSD (mean 724 days, median 90 days), hypothyroidism (mean 79, median 30 days) and maldescended testes (mean 629 days, median 280 days). Considerable number of cases, 29.9%, got lost to follow up. In particular selected cases that were lost to follow up were as follows: short stature (29.6%), rickets (23.9%), hypothyroidism (50%), numerical chromosomal abnormalities (45%), type 1 diabetes (31.25%), penile disorders (19.5%) and DSD (77.6%).

We therefore recommend special training to primary care physicians and nurses on early identification of endocrine disorders, to have elaborate population education program on early symptom recognition in type 1 diabetes allocation of more resources towards increasing cases of T1DM. Further studies are required to help understand factors associated with delay in diagnosis and loss to follow up in pediatric patients with endocrine disorders. Lastly, KNH should consider active patient tracking system to reduce loss to follow up cases.

1. LITERATURE REVIEW

1.1 Introduction

Pediatric Endocrinology is a subspecialty that deals with diseases of the endocrine system. The endocrine system involves hormones and glands such as the pituitary, thyroid, gonads, pancreas, and the adrenals. There has been notable inequality in pediatric endocrinology and diabetes care between developed and developing countries in terms of scientific investigation and treatment [1]. There is an increasing focus on training more subspecialists in the developing countries to improve on quality of care to the pediatric population and consequently avert premature mortality and improve their quality of life. Training of pediatric endocrinologists in developing counties was among the five areas raised at the 7th Joint ESPE/LWPES Congress in Lyon, France in September, 2005, as part of a statement of minimal acceptable care [1]. This led to development of the Pediatric Endocrinology Training Center for Africa (PETCA) with the aim of improving quality and access to health care through training of pediatricians from Africa in pediatric endocrinology in 2007 and subsequently Pediatric Endocrinology Training Centre for West Africa (PETCWA). PETCA has so far trained 62 pediatric endocrinologists including 9 from Kenya[2]. A study on various endocrine disorders in children will hopefully attract more general practice pediatricians to join the sub specialty hence reducing the patient: subspecialist ratio. Most pediatric endocrine disorders can be treated or managed if early diagnosis is made. In the recent years, more emphasis has been placed on reduction of neonatal deaths, management ofinfectious diseases like HIV and malaria than endocrine disorders. Description of various endocrine disorders including thyroid disorders in children and adolescents will therefore enable the policy makers to channel resources appropriately and motivate medical practitioners to look out for these disorders in the general population and refer accordingly. Kenyatta National Hospital is the oldest hospital in Kenya. It is a public, tertiary, referral hospital for the Ministry of Health. It is also the teaching hospital of the University of Nairobi, College of Health Sciences. It is the largest hospital in the country and has a bed capacity of 1,800 [3]. However, due to congestion, the patient numbers can rise as high as 3,000 [4]. Pediatric endocrinology clinic in KNH first became functional in 2008 and sincethen there is no data to characterize the spectrum of disease conditions seen.

1.2 Epidemiology

The prevalence rates of endocrine disorders amongst children and adolescents are not known and largely poorly appreciated in most low income countries[5]. This stems from inadequacy of screening facilities and few trained health professionals. As a result, a considerable number of children die before receiving accurate diagnosis or getting appropriate management even after diagnosis due to poor socio-economic status hampering affordability of follow-up[2]. Nevertheless, diabetes mellitus forms a major disease entity among these conditions, and is the most studied in both developing and developed countries[1, 3].

Nasir et al[9] looked at the spectrum of endocrine disorders at the Pediatric Endocrine Clinic in King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia in a 10-year retrospective study and found out that nutritional rickets was the most common presentation followed by ambiguous genitalia arising from congenital adrenal hyperplasia in 46 XX genetic females. They noted that familial short stature was a frequent reason for referral and the most common cause for obesity was nutritional. It is worth noting that over the 10-year period, 16 cases of congenital hypothyroidism were diagnosed before the program for screening was put in place while 134 cases were identified after the screening program hence emphasizing the need for neonatal thyroid screening programs to prevent neurological sequel. There was notable increasing trend in type 1 diabetes. From this study, they concluded that there is need for trained pediatricians to take care of the pediatric population.

Jaja et al [10] in a tertiary hospital, Port Harcourt Teaching hospital in Southern Nigeria looked at the pediatric endocrine conditions over a period of 5 years and noted that the commonest endocrine disorders were pubertal disorders followed by diabetes mellitus, thyroid disorders and calcium phosphate metabolism and bone disorders. There was a marked female preponderance amongst the children and adolescents who were referred to the department. They described the main challenges being high cost of investigations necessitating referral of samples to private laboratories. This is despite the fact that most of the patients seen were in middle social class (social class 3). The result of unaffordable cost of tests was loss to follow up and discontinuity of care.

Ayotunde O. Ale et al[11] as well studied on the Spectrum of Endocrine Disorders as seen in a Tertiary Health Facility in Sagamu, Southwest Nigeria over a 3-year period between January 2016 and December 2018 amongst adult patients. Two thousand seven hundred and sixty-five patients were seen during the period with a mean age of 16-88 years.

They found out, just like Nasir et al that there was female preponderance. The internal referral system was the main means of referral. Type 2 diabetes mellitus was the most common presentation followed by thyroid disorders, metabolic syndrome and hypothalamic–pituitary disorders. This study reflected the worldwide trend in pediatric endocrine disorders.

Osei et al[12] also looked at the Spectrum of Endocrine Disorders in Central Ghana in a retrospective review that was conducted over a five-year period between January 2011 and December 2015 at the outpatient endocrine clinic in Komfo Anokye Teaching Hospital. This study just like the one by Ayounde et al involved adult patients aged 18 years and above. They found that of the three thousand and seventy studied patients, type 2 DM and thyroid disorders were the majority and highlighted the need for more trained pediatric endocrinologists to handle the increasing number of pediatric endocrine cases in the population.

Belloto et al[13] looked at the Pattern and Features of Pediatric Endocrinology Referrals in a tertiary center in Italy. In this 6-year retrospective study, reasons for referrals, assignment in the priority ranks in terms of urgency, patient characteristics in terms of age, sex, pathological findings, need for additional tests and the final diagnosis were explored. The most frequent reason for referral among the 2165 studied patients were growth, puberty, adrenal and thyroid disorders. Sex differences were detected in several referrals: There was a female preponderance in thyroiditis, precocious puberty and precocious adrenarche. Male preponderance was found in disorders of growth and delayed puberty. This was explained by likely difficulty in detecting precocious puberty in boys and the biased trend towards diagnosing healthy boys who may not appear tall enough in the given population. More than 50% of precocity cases were sent after the age that defines precocious puberty while about 22% of females and 35% of males were sent prior to the time that defines delayed puberty. The median age at diagnosis of growth problems was 11 years, a fairly old age that may negatively impact treatment outcomes. Approximately thirty three percent of cases were lost to follow up. This study however did not look at the socio-economic characteristics of the referred patients.

A 28-year retrospective cohort study was done by Thomsett et al [14] in Queensland clinics between 1980 and 2007 to determine changes in referral patterns as well as proportion of diagnoses in major disease categories. This study looked at all children and adolescents with endocrine disorders as seen by a single consultant in 3 clinics. Nine thousand and sixty-two patients were seen during this period and male gender constituted 51%, female gender 48% while indeterminate sex was 1 %. It was

established that short stature accounted for most of the cases followed by type 1 diabetes mellitus and pubertal disorders. There was an increasing trend amongst cases of type 1 diabetes. Majority of pubertal disorders in this study had an organic cause leading to a conclusion that neonatal screening for congenital adrenal hyperplasia was long overdue and more resources needed to be channeled towards management of if increasing tall and short stature syndromes as well as type 1 diabetes mellitus. This study closely resembles the one done by Belloto et al except that obesity featured among the common diagnoses in the latter.

There is paucity of data on the characterization of the main clinical features at the time of presentation. Endocrine conditions can have widespread clinical symptoms at the onset and knowledge of these can be a warning sign to the caregivers or primary care physicians hence improving on timely referral or diagnosis. For instance, several conditions can present with neurological signs and symptoms hence ending up in neurology unit first [15]. These conditions include: pseudo tumor cerebri which may present with headache, vomiting, seizures, irritability and listlessness and may be a feature of adrenal insufficiency, diabetic ketoacidosis on treatment, hyperadrenalism, hyperthyroidism, and hypoparathyroidism [16]. Abnormal muscle strength, tone and gait could indicate thyroid, parathyroid, or adrenal disorders [17]. Movement disorders could point towards a thyroid disorder, parathyroid disorder, Addison disease, water and electrolyte metabolism disorder or a pituitary tumor [18]. Lastly, developmental delay may be one of the initial presentations in syndromes like Prader Willi syndrome, congenital hypothyroidism and CAH [19].

Jarrett et al conducted a 7-year study in Ibadan, Nigeria and looked at the burden of pediatric endocrine disorders [20]. They characterized data in terms of various endocrine conditions, age, sex and socioeconomic status as well as challenges encountered in managing them. Out of the 110 patients they studied, nutritional rickets and metabolic conditions were the commonest followed by DM, adrenal disorders, conditions of puberty, growth and thyroid. This agrees with some of the studies previously carried out in developing countries. However, they noted the main challenge to be lack of affordability of comprehensive care in terms of access to recommended tests, drugs and multidisciplinary team management owing to poor socioeconomic status in about 58% of the study population and hence approximately 60% were lost to follow up. These challenges likely cut across all developing countries and as result continued quality healthcare following timely diagnosis may remain a mirage.

1.3 Classification of Endocrine Disorders

Endocrine disorders are classified according to International Classification of Pediatric Endocrine Diagnoses [ICPED] Consortium as follows: short stature and tall stature, defined as height below 2 SDS or above 2 SDS of the mean respectively. These growth disorders may arise from primary, secondary, and idiopathic causes like chromosomal aberrations, nutrient deficiency and dyshormonogenesis. Puberty disorders include precocious puberty, contra sexual development of secondary characteristics, delayed puberty, and non-pathological developmental variations like constitutional growth delay. Causes of puberty disorders vary from central origins like tumors and genetic mutations to peripheral causes like gonadal, adrenal tumors and exposure to exogenous hormonal steroids. Diagnosis of precocious puberty is made if there is development of secondary sexual characteristics before the age of 8 years in females and 9 years in male[6].

Sex development and gender disorders include disorders of sex development and variations of gender development. Obesity may be polygenic, genetic, associated with central nervous system disorders or iatrogenic.

Thyroid disorders are classified as either hypothyroidism, hyperthyroidism, goiter, thyroid tumor or other unspecified thyroid conditions. Conditions of the pituitary gland, hypothalamus and central nervous system are classified according to function and etiology as either deficiencies of anterior pituitary hormones, overproduction of anterior pituitary hormones, vasopressin deficiency, hypothalamic dysfunction, congenital central nervous system malformations or acquired pituitary disorders. Disorders of the adrenal glands include primary or secondary adrenal insufficiency, excess of adrenal steroids and disorders of adrenal medulla. Testes and male reproductive tract conditions comprise of hypergonadotropic hypogonadism, maldescended testes, acquired testicular disorders without hypergonadotropic hypogonadism, tumors of testes, disorders of penis, scrotum, epididymis, efferent ducts, vas deferens and disorders of testicular blood vessels. Endocrine disorders of the ovaries and female reproductive tract include disorders of the ovary, menstrual disorders, anatomical disorders of the uterus, fallopian tubes, or cervix disorders of the vagina and external genitalia as well as disorders of the breasts and nipples.

Glucose and lipid metabolism disorders comprise diabetes mellitus, hypoglycemia and primary disturbances of lipoprotein metabolism. Calcium and phosphate metabolism disorders range from

transient neonatal hypocalcemia, permanent hypocalcemia, rickets, rickets-like conditions, soft tissue calcification, and conditions associated with altered bone mass as well as hypercalcemia.

Salt and water regulation conditions encompass disorders characterized by polydipsia and polyuria, disorders other than diabetes insipidus characterized by hypernatremia and disorders characterized by hyponatremia.

Finally, syndromes with endocrine features span from numerical chromosomal abnormalities, dysmorphic syndromes, non-dysmorphic syndromes and syndromes with multiple neoplasia. Notably these syndromes may affect several other body systems while manifesting endocrine abnormalities[7].

Figure 1 below gives a summary of various endocrine hormones produced by the glands and tissues in a human body while table 1 is a summary of the literature review.

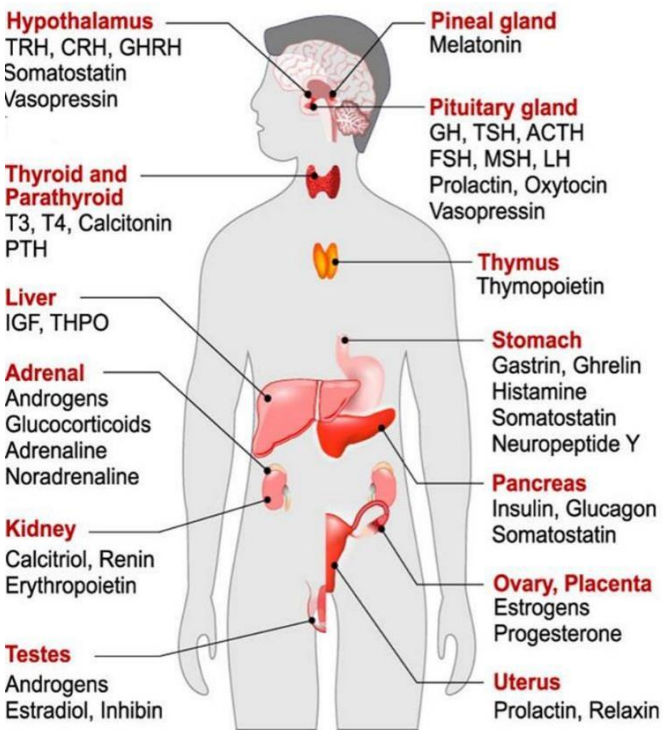


Figure 1-1 Diagrammatic representation of the various endocrine hormones produced by the glands and tissues in a human body[8]

Table 1:1 Summary of Literature Review

Author	Title	Study Design	Source	Findings
Nasir et al (2012)[9]	Spectrum of endocrine disorders at the pediatric endocrine clinic, King Khalid University hospital, Riyadh	10-year Retrospective study (1999-2009)	Journal of Taiban University Medical Sciences	Nutritional rickets was the most common disorder followed by ambiguous genitalia secondary to CAH in 46 XX genetic females. Familial shorts stature and nutritional obesity were the 3rd and 4th commonest endocrine disorder. An increasing prevalence of T1DM. They indicated the need for more trained pediatricians.
Jaja et al (2019)[10]	Pattern of pediatric endocrine disorders according to ICD-10 classification in a tertiary center in Southern Nigeria	Descriptive cross-sectional study (Jan 2013-Aug 2017)	Asian Journal of Pediatric Research.	A total of 178 patients were studied with female preponderance and a mean age of 6.9 years. Pubertal disorders, DM, thyroid disorders, calcium metabolism and bone disorders were the most common at 17%, 14%, 12%, 11% and 11% respectively. Most were middle social class and faced challenges with cost of tests and drugs.
Ayotunde et al (2019)[11]	Spectrum of endocrine disorders as seen in a tertiary health facility in Sagamu, Southwest Nigeria.	Retrospective 3-year study (Dec 2016-Dec 2018)	Nigerian Medical Journal	There was a female preponderance. Diabetes mellitus type 2 was the most common disorder followed by thyroid and metabolic syndrome. This study involved mainly adults aged between 16 to 88 years.
Osei et al (2017)[12]	Spectrum of endocrine disorders in Central Ghana	Retrospective 3-year study (2011-2015)	International Journal of Endocrinology	Type 2 diabetes mellitus, thyroid disorders and adrenal disorders were most common at 79%, 13% and 2.2% respectively. Findings implied the need for well-trained endocrinologists.
Belloto et al (2020)[13]	Patterns and features of pediatric endocrinology referrals	Retrospective study (Nov 2012-2019)	Frontiers in Pediatrics	Out of 2165 referrals, slow growth, precocious puberty, and obesity formed the bulk of the visits. There was a male preponderance more so in growth disorders and delayed puberty. Thirty-five percent had pathological endocrine findings and 67% had more than one follow up visit. Precocious puberty was assigned "urgent" on priority ranking while hypothyroidism was assigned "deferrable". There was a 33% loss to follow up. The study highlighted the need for medical training of primary physicians on appropriate referrals.

Thomsett et al. (2010)[14]	The spectrum of clinical pediatric endocrinology: 28 years of referrals to an individual consultant.	28-year retrospective study	Journal of Pediatric Child Health.	Short stature, TIDM, and pubertal disorders accounted for most of the disorders at 29%, 20%, 12% respectively followed by thyroid disorders, obesity, tall stature and hypothalomo-pituitary disorders. There was male preponderance especially amongst cases of short stature and delayed puberty. There were notable increasing cases of T1DM. They recommended neonatal screening for CAH as well as more resources in managing the increasing cases of diabetes mellitus.
Jarett et al (2013)[20]	Pediatric endocrine disorders at the university College hospital, Ibadan.	Retrospective study (2002-2009)	Annals of Ibadan Post graduate Medicine	110 children were found to have various endocrine disorders with a male preponderance. Their ages ranged from 2 weeks to 15 years. Rickets and metabolic disorders were the leading conditions followed by DM, adrenal and pubertal disorders while obesity was the least common. Sixty percent were lost to follow up.

2. RESEARCH GAP

A review of studies done in Africa reveal that common pediatric endocrine disorders are Type 1 diabetes mellitus, thyroid disorders, diseases of bone and calcium metabolism and partly pubertal disorders. A few studies done in non-developing countries, however, consistently show that slow growth or short stature, pubertal disorders and obesity form the bulk of pediatric endocrine diagnoses. We seek to describe data from the local and major referral hospital that would present an accurate picture locally for policy action. The results will hopefully and subsequently form a basis to seek answers as to why the discrepancy exists between the countries.

2.1 Study Justification and Utility

There is no similar study in Kenyatta National Hospital or other similar institutions in Kenya. It is imperative that knowledge on pediatric endocrine disorders is sought to inform policy makers on equipping human resource including diabetes education nurses, pediatric endocrinologists, geneticists, psychologists, and nutritionists with relevant skills to manage the increasing endocrine cases.

This being a limited resource setting, information from this study will be used to guide policymakers on allocation of resources towards endocrine investigations which are expensive and beyond the reach of many of our patients. In addition, an understanding of the pattern of referrals will guide on areas of focus for continuous medical education for primary healthcare providers and pediatricians to avoid inappropriate or delayed referrals. It will also serve as a basis for further research on specific endocrine conditions.

3. RESEARCH QUESTIONS

1. What is the pattern of endocrine disorders in children and adolescents seen at the Pediatric Endocrinology Unit in Kenyatta National Hospital?
2. What is the clinical presentation of endocrine disorders in these children?
3. What are the characteristics of these children regarding age at diagnosis, gender, source of referral and place of residence?
4. What is the time interval between onset of symptoms and actual visit at the Pediatric Endocrinology clinic?
5. What is the percentage of patients who are lost to follow up?

3.1 Broad Objective

- To describe the clinical spectrum of endocrine disorders in children and adolescents seen at the Pediatric Endocrinology Unit in Kenyatta National Hospital for the last 14 years.

3.2 Specific Objectives

1. To determine the pattern of endocrine disorders in children and adolescents seen at the Pediatric Endocrinology Unit in Kenyatta National Hospital.
2. To characterize the presenting complaints of endocrine disorders in these children.
3. To illustrate the characteristics of these children regarding to age at diagnosis, gender, source of referral and place of residence.
4. To determine the time interval between onset of symptoms and actual visit at the Pediatric Endocrinology clinic.
5. To find out the percentage of patients who are lost to follow up.

4. METHODOLOGY

4.1 Study Design and Study Area

This study was a hospital-based retrospective, descriptive study carried out in the Pediatric Endocrinology Unit at Kenyatta National Hospital, Nairobi, Kenya. The hospital is a tertiary referral and teaching institution that serves as a major patient referral facility receiving patients from all the 47 counties in Kenya as well as walk-in patients from Nairobi City and its environs. However, patients seen in this clinic are specifically referral cases from clinics within Kenyatta National Hospital or from level 4 and 5 county hospitals in the country. The clinic is run every Tuesday by pediatric endocrinologists and has an attendance of approximately thirty clients per day. It also serves as a teaching clinic for medical students, pediatric resident doctors, and pediatric endocrinology fellows.

4.2 Study Population

This study comprised of children and adolescents below 25 years who had been seen and received treatment in the Pediatric Endocrinology clinic at the Kenyatta National Hospital between January 2008 and December 2021

4.3 Inclusion Criteria

All children and adolescents aged 25 years old and below with endocrine disorders seen between January 2008 and December 2021.

4.4 Exclusion Criteria

Patient files with major missing data.

4.5 Expected Study Outcomes

The study endeavored to achieve the following outcomes:

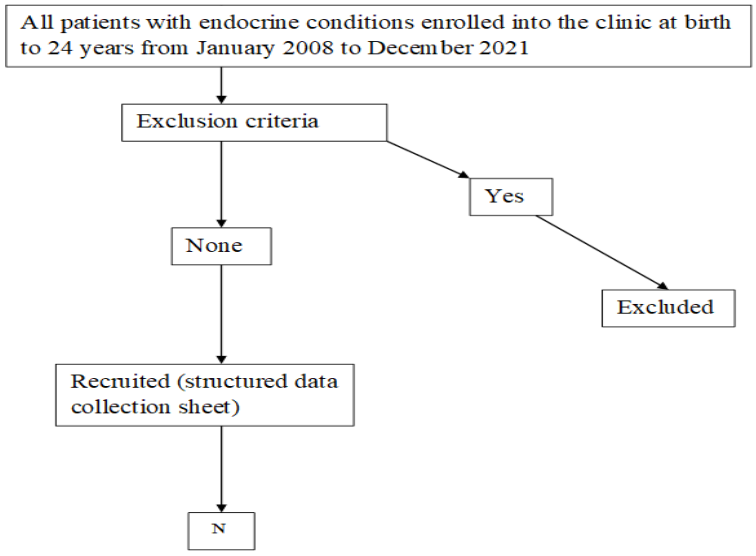
- Determination of the pattern of endocrine disorders in children and adolescents seen at the Pediatric Endocrinology Unit in Kenyatta National Hospital.
- Characterization of the presenting complaints of endocrine disorders in these children.
- Illustration of the characteristics of these children regarding age at diagnosis, gender, source of referral and place of residence.
- Determination of time interval between onset of symptoms and actual visit.
- Determination of the percentage of patients who are lost to follow up.

4.6 Sampling Procedure

A search was conducted in the hospital records department using the ICD coding system. This search yielded patient registration numbers which was used to obtain patient files. For confidentiality purposes, codes were used instead of full names for identification. A systematic review of patient files was carried out. Data of all cases of children and adolescents with endocrine conditions aged from birth to 24 years seen between January 2008 and December 2021 were obtained from patients' files by the principal investigator as seen in the pediatric endocrinology clinic using a structured data collection instrument.

All patient files that met the inclusion criteria of the study were selected for the study. Files that lacked a diagnosis, presenting complaints, patient's age and gender were excluded from the study sincethese constituted major data. Minor data included caregivers' bio data, anthropometric measurements,and source of referral. Missing minor data was indicated in the data collection tool as "unstated" and subsequently analyzed. Presenting complaints comprised mainly of the first three for every endocrine condition. Final diagnosis was determined from either the consultants' clinical criteria and/or the requested confirmatory tests. Six months' duration of non-visit from the last clinical review indicated that the patient was lost to follow up. Referral source was either from counties, self-referral or from internal clinics or departments at Kenyatta National Hospital.

4.7 Screening and Recruitment



4.8 Sample Size Determination

All files of children and adolescents below the age of 24 years who received treatment between January 2008 and December 2021 and met the inclusion criteria of the study formed the final sample size.

4.9 Recruitment And Consenting Procedures

Patient files were sorted according to the year of attendance and outpatient number. Medical data as per the data collection tool was mined from a secured office. Respective files were marked "seen" and returned to the records office. Since this was a retrospective study dealing with patient files, consent from study participants was not necessary because the data was collected as part of routine care and no biological sample was obtained. We did not also investigate experimental or new protocols.

4.10 Data Analysis and Presentation

Data collected via the questionnaire was checked for completeness and free of error prior to entering into the Microsoft Excel 2017 spreadsheet. Thereafter the data was exported to the Statistical Package for Social Science (SPSS) version 23.0 for analysis. Demographic characteristics of the patients were summarized as frequencies and percentages for categorical data and as means with standard deviations or median with interquartile range for continuous data. The pattern of endocrine disorders in children and adolescents seen at the Pediatric Endocrinology Unit in Kenyatta National Hospital was analyzed and presented as frequencies and percentages. The presenting complaints of endocrine disorders in these children was analyzed and presented as frequencies and percentages. The characteristics of these children with regard to age at diagnosis, gender, source of referral and place of residence was analyzed and presented as frequencies and percentages. The time interval between onset of symptoms and actual visit at the Pediatric endocrinology clinic was calculated as the difference between the time of onset of symptoms and the time of actual visit at the Pediatric endocrinology clinic and categorized into time intervals where the results were presented as frequencies and percentages, as well as a mean with standard deviation. The percentage of patients who were lost to follow-up were the proportion of patients who were marked as lost to follow up over the total sample size and presented as a percentage.

4.11 Materials – Equipment, Supplies

Materials that were required were data collection instruments, stationery (pen and files/books) and computer for data storage, analysis, and dissemination.

4.12 Ethical Considerations and Approval

Approval of this study was obtained from the Ethics Committee of the University of Nairobi and Kenyatta National Hospital.

4.13 Declaration of Conflict of Interest

The authors had got no conflict of interest to declare.

SOURCE OF FUNDING

This study was funded by ELMA foundation under the Kenya Pediatric Fellowship Program (KPFP) as part of the funding for the entire 2-year fellowship program under the University of Nairobi.

5. RESULTS

5.1 Pattern of endocrine disorders.

Table 5:1 Spectrum of Diseases

Diagnosis	**Number of cases**	**% Cases recorded**
Calcium and phosphate metabolism disorders	788	35.20%
Glucose and lipid metabolism disorders	381	17.02%
Growth Disorders	321	14.30%
Testes and male reproductive tract conditions	252	11.2%
Thyroid Disorders	169	7.55%
Syndromes with endocrine features	103	4.60%
Sex development and gender disorders	67	2.99%
Endocrine disorders of the ovaries and female reproductive tract	26	1.16%
Inborn errors of metabolism	26	1.16%
Puberty Disorders	25	1.11%
Obesity	21	0.93
Pituitary, Hypothalamus, CNS disorders	20	0.89%
Disorders of the adrenal glands	20	0.89%
Salt and water regulation conditions	17	0.75%
TOTAL	**2238**	100%

Calcium and phosphate metabolism disorders formed the bulk of all endocrine disorders at 35.2% followed by glucose and lipid metabolism disorders, growth disorder, testes and male reproductive tract conditions, thyroid disorders, syndromes with endocrine features and sex development and gender disorders at 17.02%, 14.3%, 11.2%, 7.55%, 4.6% and 2.99% respectively. Other infrequent disorders reviewed and managed in the endocrine unit were endocrine disorders of the ovaries and female reproductive tract; inborn errors of metabolism; puberty disorders; pituitary, hypothalamus, CNS disorders; disorders of the adrenal gland; obesity and salt and water regulation conditions in the decreasing order.

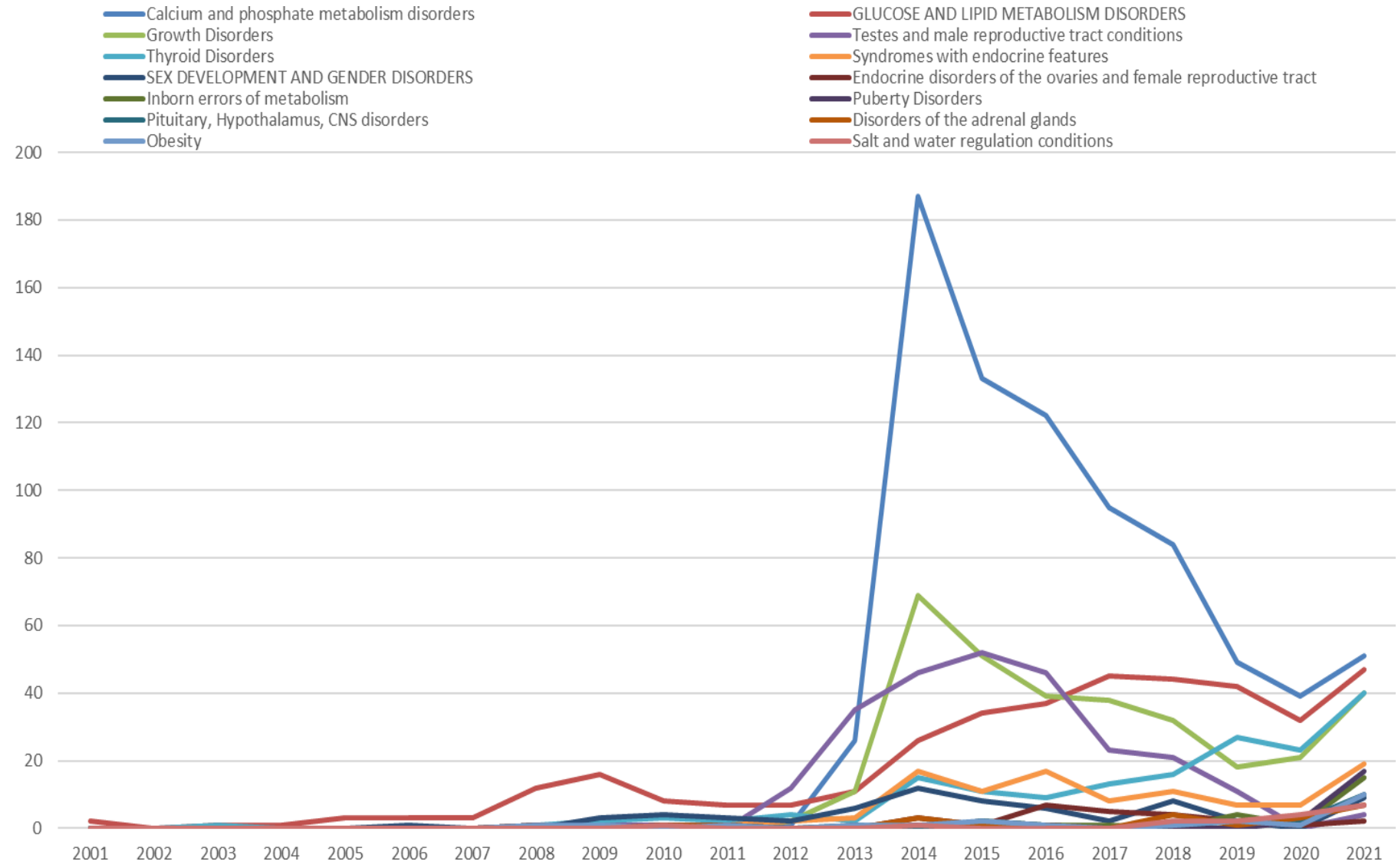


Fig 7.1 Annual incidence trend

There is a declining trend of calcium and phosphate metabolic disorders as well as growth disorders but an increasing trend in glucose and lipid met disorders and hypothyroidism as shown in figure 7.1 above. There is dip in all cases in the year 2020. There were several missing files between the year 2008 and 2012.

5.1.1 Calcium and Phosphate Metabolism Disorders.

There is a declining trend of calcium and phosphate disorders over the last eight years as shown in the Figure 7-1 below with a plunge in cases in the year 2020.

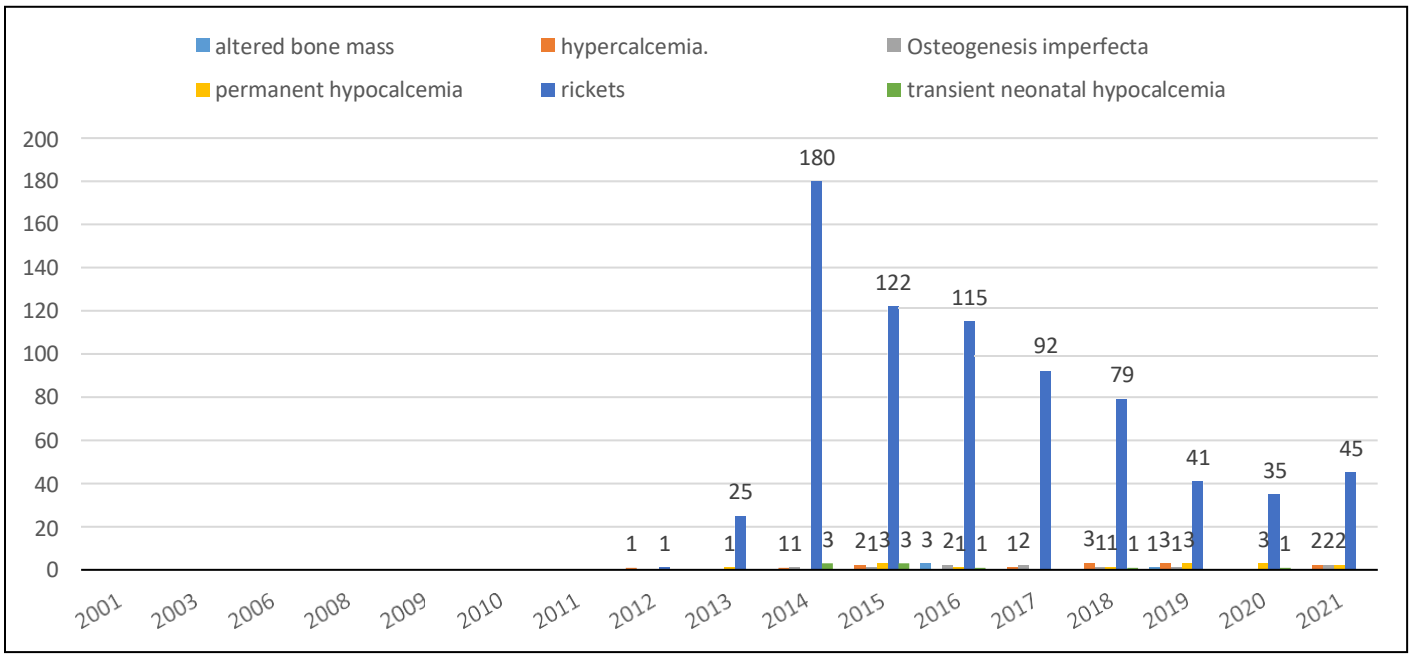


Figure 5-1 Annual incidence of Calcium and Phosphate Metabolism Disorders

Rickets constituted the majority of these disorders followed by permanent hypocalcemia from unspecified causes and hypercalcemia at 93% (n=735), 1.8% (n=14) and 1.6%(n=13) respectively. Osteogenesis imperfecta accounted for 1.3% (n=10) while transient neonatal hypocalcemia and conditions with altered bone mass comprised 0.1% (n=9) and 0.05% (n=4) respectively

5.1.2 Glucose and Lipid Metabolism Disorders

There is an increasing annual incidence of Type 1 Diabetes mellitus cases seen at Kenyatta National Hospital from 2014 to December 2021 as depicted in figure 7.2 below.

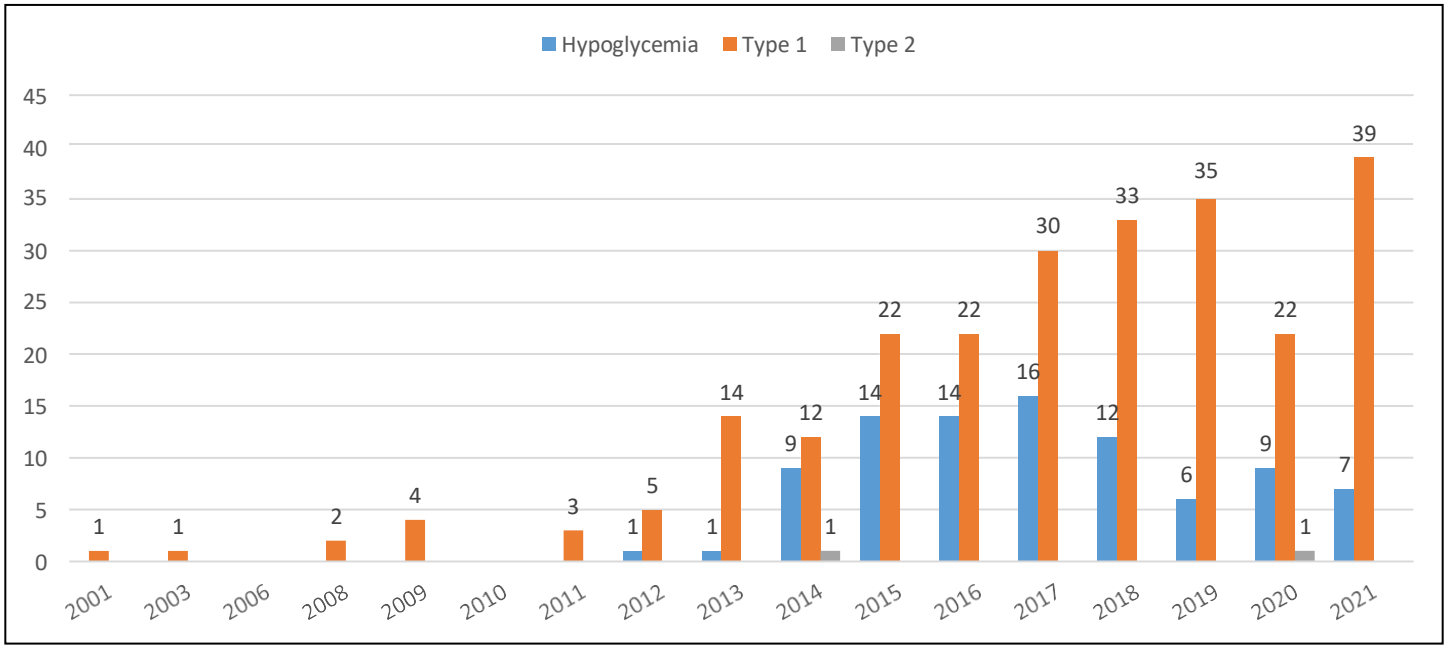
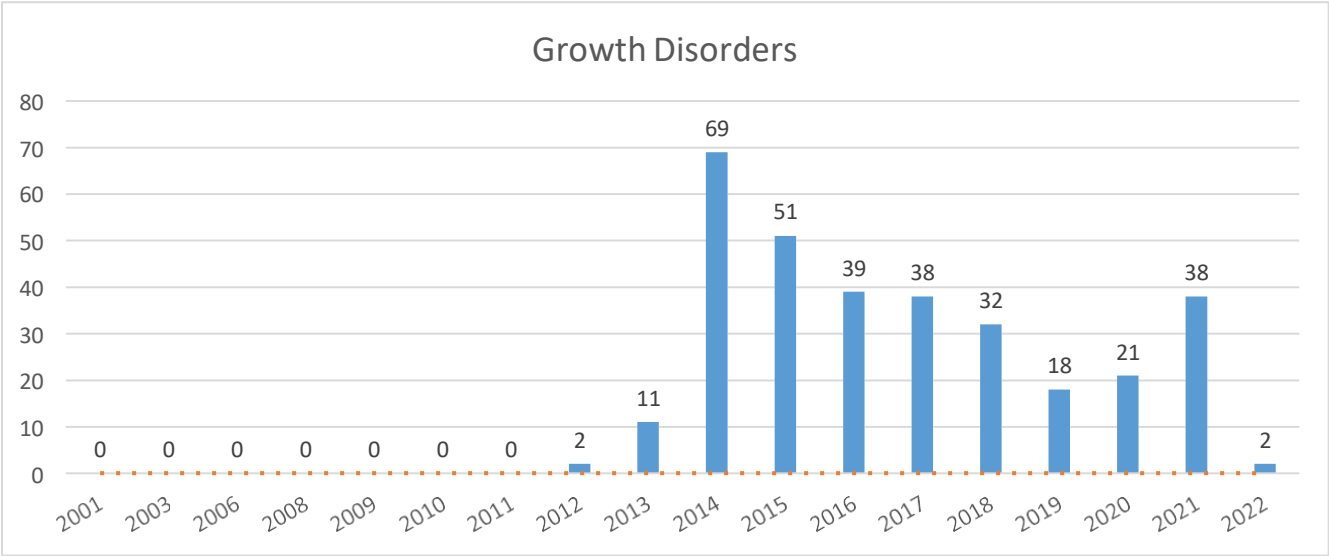


Figure 5-2 Annual incidence of Glucose and Lipid Metabolism Disorders

Out of the 381 cases of glucose and lipid metabolism disorders, Type 1 diabetes mellitus was the leading followed by cases of hypoglycemia at 73% (n=288) and 26% (n=90) respectively with just 1% (n=2) type 2 diabetes mellitus. Most cases of hypoglycemia were transient neonatal forms from mainly infants of diabetic mothers. A few cases were persistent hypoglycemia from causes ranging from pituitary, adrenal insufficiency to glycogen storage disorders and fatty acid oxidation disorders. There was a notable increasing annual incidence trend amongst cases of type 1 diabetes except in the year 2020 which recorded fewer cases than the preceding years.

5.1.3 Growth Disorders

Figure 5-3 Yearly incidence of Growth Disorders



There is a 6-year decreasing trend of growth disorders from the year 2014 to 2019 as depicted in figure 7.3 above. Short stature forms the majority of these conditions at 98.8% (n=317) followed by tall stature at 1.2% (n=4).

5.1.3.1 Tall Stature

All the 4 cases of tall stature were secondary to other conditions for instance precocious puberty and hyperthyroidism

5.1.3.2 Short Stature

Approximately 90% (n=285) of children diagnosed with short stature had failure to thrive secondary to various medical conditions while primary causes of short stature, secondary short stature, syndromic short stature and constitutional delay of growth and puberty comprised 1.6% (n=5), 4.4% (n=15), 2.2%(n=7) and 1.3%(n=4). Notably there was no single diagnosis of familial short stature. Primary causes of short stature were mainly growth hormone deficiency and two cases of pycnodysostosis. Secondary short stature comprised conditions like adrenal hormone deficiency or excess, hypothyroidism and pituitary tumors.

5.1.4 Testes and Male Reproductive Conditions.

A higher percentage of these patients were seen in the years 2013 to 2017 as shown in figure 7.4 below. Most of these patients were first seen in pediatric surgical clinics and wards.

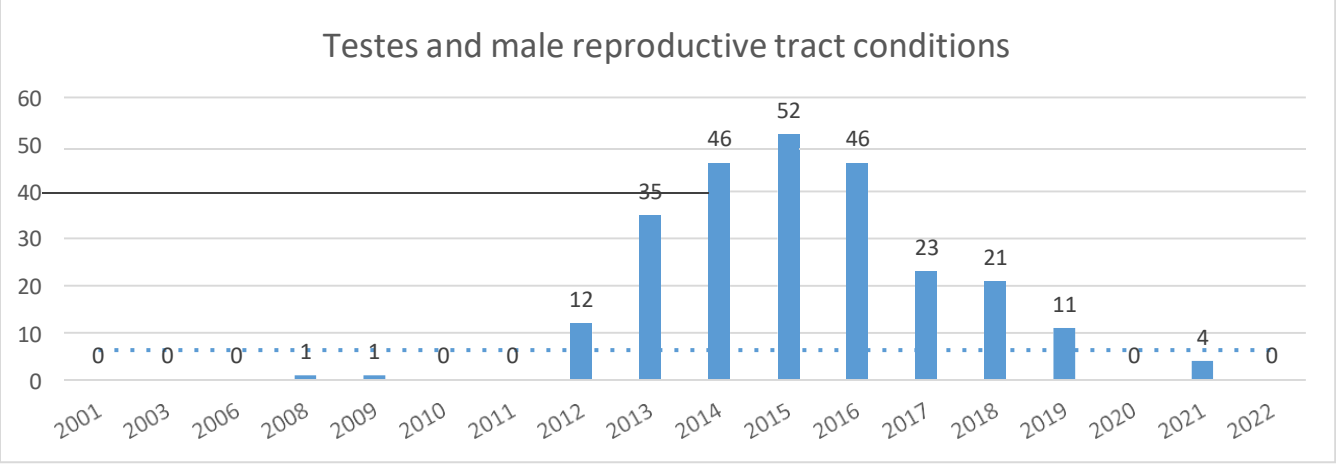


Figure 5-4 Yearly incidence of Testes and Male Reproductive Conditions

Maldescended testes formed majority of testes and male reproductive conditions followed by disorders of the penis at 65% (n=163) and 28% (n=73) respectively. Most of these patients were seen between the years 2013 and 2017. Notably, there was no single recorded case in the year 2020. Unilateral undescended testis was the commonest presentation at 50% followed by bilateral undescended testes at 43%. Almost all the penile disorders were hypospadias and epispadias of varying degrees with or without chordee. Some patients comprising 3.2%(n=8) presented with both maldescended testes and hypospadias while disorders of the scrotum and tumors of the testes comprised 0.8% (n=2) and 1.2% (n=3) respectively.

5.1.5 Thyroid Disorders

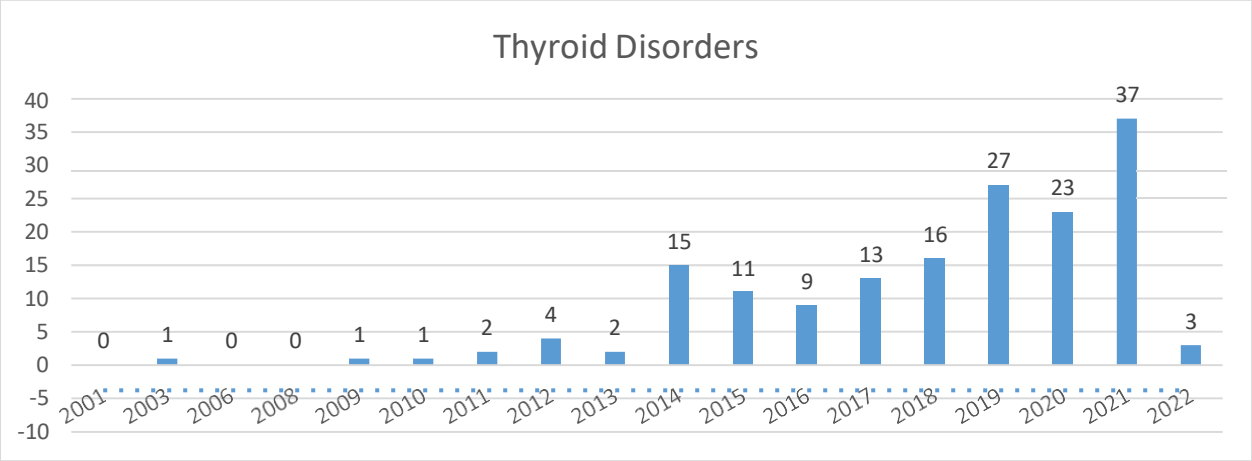


Figure 5-5 Yearly incidence of Thyroid disorders

There is a gradual increasing trend in thyroid disorders over the past 7 years, a dip in the year 2020 and a notable highest frequency in the year 2021, figure 7.5 above. Hypothyroidism was the leading condition at 84% (n=142) followed by hyperthyroidism and thyroid tumors at equal frequency of 5.9% (n=10). Patients who presented with goitre comprised 4.1% (n=7).

5.1.5.1 Hyperthyroidism

Majority of patients diagnosed with hyperthyroidism had Grave's hyperthyroidism comprising 80% (n=8) of the total hyperthyroid conditions.

5.1.5.2 Hypothyroidism

Subclinical hypothyroidism was the most commonly occurring condition among hypothyroid disorders at 60.5% (n=86) followed by overt primary hypothyroidism and central hypothyroidism at 25.3% (n=36) and 13.3% (n=19) respectively.

5.1.6 Syndromes with Endocrine Features.

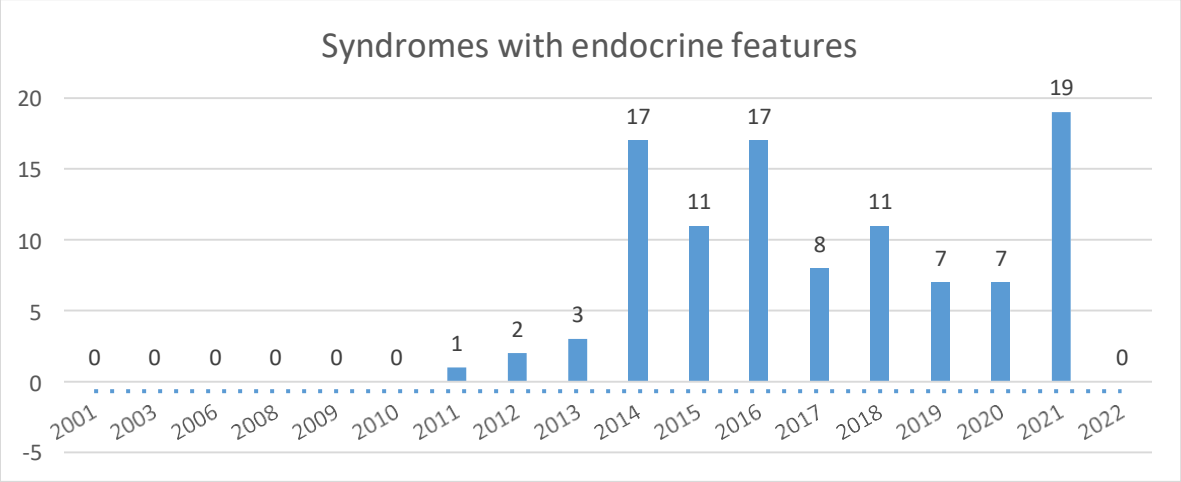


Figure 5-6 Annual incidence of Syndromes with Endocrine Features

Highest incidence of syndromes with endocrine features was noted in the year 2021 as depicted in figure 7.6 above.

Patients with numerical chromosomal abnormalities comprised 76.4% (n=78) followed by cases of dysmorphic features at 22.5% (n=23). Non dysmorphic syndromes had only one case while multiple endocrine neoplasia syndromes recorded no single case.

5.1.6.1 Numerical chromosomal abnormalities

Most of the cases seen with numerical chromosomal abnormalities had Down syndrome at 97% (N=76) with just one single case of Turner's syndrome.

5.1.7 Sex Development and Gender Disorders

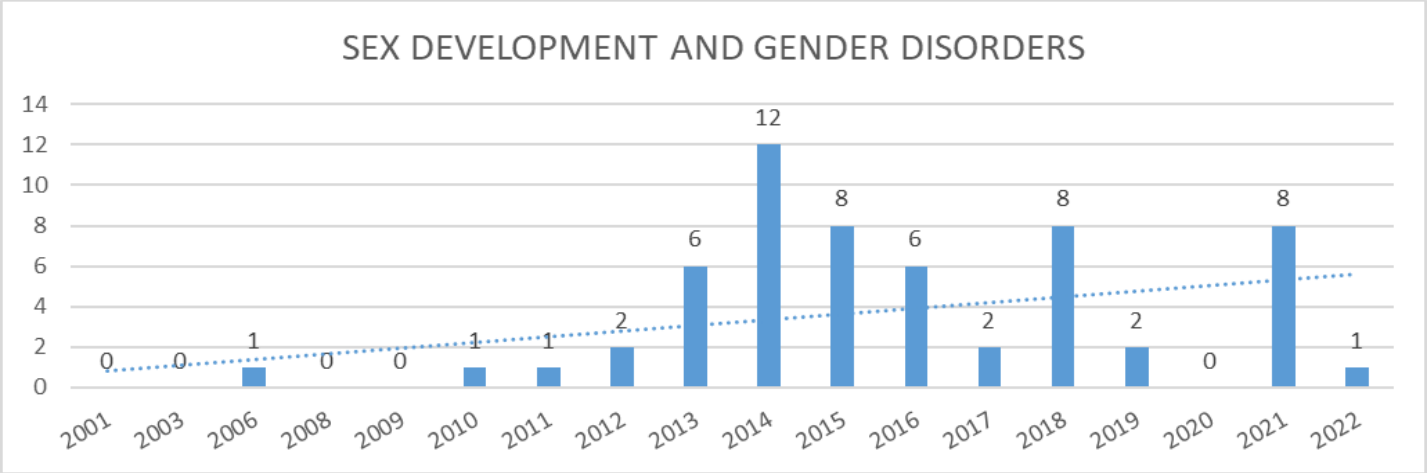


Figure 5-7 Yearly incidence of Sex development and gender disorders

Majority of the cases of sex development and gender disorders were seen between the year 2013 to 2016. These disorders showed no particular trend over the years. However, it is noteworthy that the year 2020 recorded no single case as show in figure 7.7 above.

Disorders of sexual differentiation, DSD, comprised all cases of Sex development and gender disorders. This condition constituted 2.67% of the total endocrine cases seen in Kenyatta national hospital.

5.1.8 Obesity

Most cases of obesity were nutritional in nature at 38% (n=8) followed by obesity from iatrogenic causes, central nervous system conditions and genetic causes at 28.5% (n=6), 23.8% (n=5) and 9.5 % (n=2) correspondingly. Iatrogenic causes were mainly as a result of excessive use of corticosteroids as part of chemotherapy in oncology patients and steroid replacement in hormone deficiency following cases such as pituitary tumor resection.

5.1.9 Puberty Disorders.

Precocious puberty was the leading condition among puberty disorders at 41% (n=11) followed by delayed puberty, non-pathological sexual variations and contrasexual development of sexual variations at 26% (n=7), 22% (n=6) and 11.5% (n=3) respectively.

5.1.9.1 Delayed Puberty

Constitutional delay in growth and puberty constituted majority of cases under delayed puberty at 86% (n=6). Delayed puberty as a result of pathological causes had only one case that presented with pituitary hormone deficiency.

5.1.9.2 Non pathological sexual variations (PT/PA)

Patients with premature adrenarche and premature thelarche presented at an equal frequency of three cases each.

5.1.10 Pituitary, Hypothalamus, CNS Disorders

Deficiency of pituitary hormones and acquired pituitary disorders constituted the most common conditions under this category at 43% (n=9) each followed by congenital CNS malformations at 14.2% (n=3). All the nine acquired pituitary disorders were as a result of tumors.

5.1.11 Disorder of the Adrenal Glands

Primary adrenal insufficiency was the most common condition among disorders of adrenal glands at 50% (n=11) followed by secondary adrenal hormone excess and secondary adrenal insufficiency at 41% (n=9) and 9% (n=2) correspondingly. All cases of primary insufficiency were due to congenital adrenal hyperplasia.

5.1.11.1 Adrenal hormone excess

Adrenal tumors was the most common condition among cases of secondary adrenal hormone excess at 75% (n=6).

5.1.12 Endocrine Disorders of the Ovaries and Female Reproductive Tract.

Ovarian disorders, mainly comprising of cysts were the most common disorders constituting 37% (n=10) followed by anatomical defects.

5.1.13 Salt and Water Regulation Conditions.

A half of the cases, (n=8), in the category of salt and water regulation conditions were cases of hypernatremia followed by hyponatremia and diabetes insipidus at equal frequency of 25% (n=4) each.

5.1.14 Inborn Errors of Metabolism.

Inborn errors of metabolism have clinical presentations that cut across several fields of pediatric practice. However, a few tend to be domiciled in the pediatric endocrinology clinic. Out of these, unspecified cases, Hunter's disease and Gaucher's disease constituted 61% (n=16), 23% (n=6) and 15% (n=4) respectively. Majority, 65%, of these cases were identified in the year 2021, figure 7.9 below. Unspecified cases are those that were clinically suspected to be inborn errors of metabolism and follow up metabolic tests were performed without enzymatic or genetic confirmation. Galactosemia was the commonly suspected condition in this group.

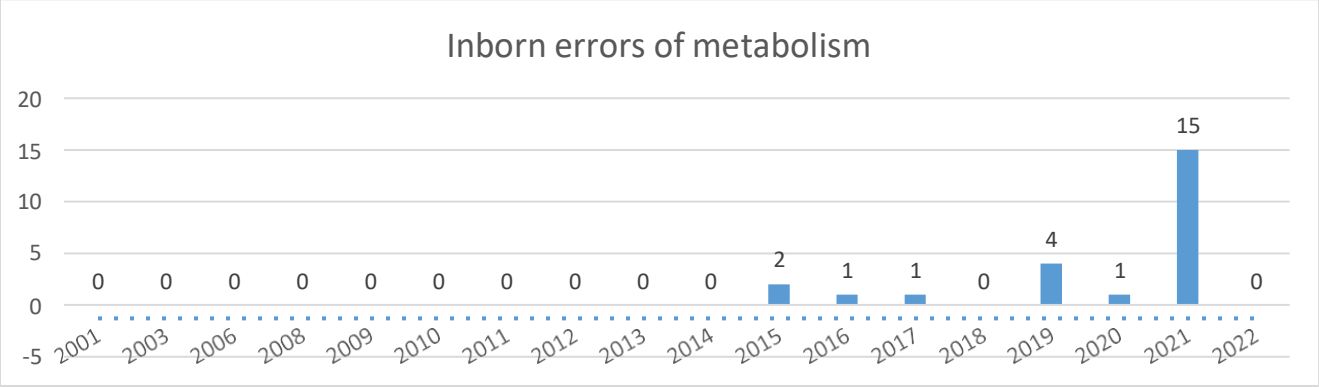


Figure 5-8 Annual incidence of Inborn Errors of Metabolism

5.2 Top presenting clinical complaints of endocrine disorders

5.2.1 Calcium and phosphate metabolism disorders.

a) Altered bone mass

The two patients who were diagnosed with altered bone mass had pycnodysostosis. These patients presented with short stature, head enlargement, recurrent fractures and an open widened anterior fontanelle at 5 and 3 years of age respectively.

b) Hypercalcemia

Patients that were diagnosed with hypercalcemia predominantly presented with generalized pain and irritability followed by polyuria and vomiting at 50% (n=7), 29% (n=4) and 21% (n=3) respectively.

c) Osteogenesis imperfecta

Poor growth and multiple recurrent fractures were the main presentation at equal frequency, n=7, in patients who had osteogenesis imperfecta.

d) Permanent hypocalcemia

Convulsions were the leading presenting complaints followed by delayed milestones and poor growth at 55% (n=11), 25% (n=5), 20% (n=4) respectively in children diagnosed with permanent hypocalcemia.

e) Rickets

Most children with rickets presented with predominance of pneumonia followed by delayed milestones and hotness of body at 35% (n=267), 33% (n=251), 32% (n=239) respectively.

f) Transient neonatal hypocalcemia

Convulsions ranked first followed by respiratory distress and irritability in children who had transient neonatal hypocalcemia in the order of 69% (n=9), 23% (n=3), 8% (n=1) respectively.

5.2.2 Glucose and Lipid Metabolism Disorders.

a) Hypoglycemia

Convulsions were the major presenting symptom amongst children diagnosed with hypoglycemia at 55% (n=48). Approximately 29% (n=25) were infants of diabetic mothers while 16% (n=14) were macrosomic.

b) Type 1 diabetes mellitus

Majority, 90.2% (n=438) of children diagnosed with type 1 diabetes mellitus had diabetic keto-acidosis as the initial presenting complaint. This presentation overlapped closely with weight loss 21% (n=103) and often fever 16% (n=78) from various infections including pneumonia, vaginal candidiasis, urinary tract infections as well as ear infections. A few patients presented with concomitant polyphagia 2.7% (n=13) and secondary enuresis 2% (n=10) while approximately 2% (n=10) of the patients presented with classical symptoms of polyuria, polydipsia and hyperglycemia without acute complications.

c) Type 2 diabetes mellitus

Type 2 diabetes mellitus was only diagnosed in 2 patients and they all presented with polyuria, polyphagia and polydipsia in the background of obesity. These patients were first seen in outpatient clinic without acute diabetic complications.

5.2.3 Growth Disorders

a) Short Stature

Children who had short stature as a result of failure to thrive had delayed milestones as the top presenting complaint at 40% (n=171) followed by malnutrition 31% (n=133) and convulsions 28% (n=120) respectively

b) Tall Stature

Most children who were diagnosed with tall stature presented with penile enlargement at 50% (n=4) followed by acne, 25% (n=2) and pubic hair, 25% (n=2) correspondingly as a result of precocious puberty.

5.2.4 Testes and Male Reproductive Tract conditions.

a) Disorders of penis

Hypospadias with or without chordee constituted the leading presenting complaint among children with penile disorders at 88% (n=61). The rest of the patients presented with ambiguous genitalia and undescended testis as well at 6% (n=4) each.

b) Disorders of scrotum

The only patient who was diagnosed as having disorders of the scrotum presented with respiratory symptoms and a congenital hydrocele was picked out as a secondary symptom.

c) Maldescended testes

Unilateral undescended testes were the commonest presentation at 50% (n=68) followed by bilateral undescended testes at 43% (n=59). Inguinal hernia as a presentation of maldescended testes constituted 6% (n=9) of the total complaints.

d) Tumors of testes

The infrequent testicular tumors had undescended testes and poor growth as the main presentation at 67% (n=2), 33% (n=1) respectively.

5.2.5 Thyroid Disorders.

a) Goitre

Neck swelling was the most common presentation amongst patients who had goiter followed by pains on swallowing and weight loss at 70% (n=7), 20% (n=2), 10% (n=1) respectively.

b) Hyperthyroidism

Amongst patients who were diagnosed with hyperthyroidism, weight loss and palpitations were the leading complaints at equal frequency of 38.5% (n=5) each followed by neck swelling at 23% (n=3).

c) Hypothyroidism

Most patients who had hypothyroidism presented with features of heart failure at 37.5% (n=80). This which was later identified to be as a result of pericardial effusion, cardiomyopathy or congenital heart disease. This was followed by poor growth and pneumonia at 20% (n=47) each. Some of the children who presented as having pneumonia were later found to have a heart condition. Delayed milestones constituted approximately 17% (n=39) of the common presenting complaints.

d) Thyroid tumor

Patients who were diagnosed with thyroid tumor had neck swelling as the commonest complaint followed by weight loss and odynophagia at 54% (n=6), 27% (n=3) and 18% (n=2) respectively.

5.2.6 Syndromes with endocrine features

a) Dysmorphic syndromes

Most dysmorphic syndromes with endocrine features presented with difficulty breathing and convulsions at 61% (n=14) and 39% (n=9) respectively.

b) Non-dysmorphic syndromes

The only patient who was diagnosed with non-dysmorphic syndromes had cough, vomiting and fever as presenting complaints.

c) Numerical chromosomal abnormalities

Congestive heart failure, poor growth and features of pneumonia characterized the presentation in children who were diagnosed with numerical chromosomal abnormalities at 45% (n=42), 32% (n=30) and 23% (n=22) respectively.

5.2.7 Sex Development and Gender Disorders.

a) Disorders of sexual differentiation (DSD)

Most, 84.8% (n=56) children diagnosed with DSD presented as having ambiguous genitalia at birth followed by either hypospadias, undescended testis or micropenis at 15% (n=10).

5.2.8 Endocrine disorders of the ovaries and female reproductive tract.

a) Anatomical defects

Most patients with anatomical defects of female reproductive tract presented with abdominal mass at 56% (n=5) followed by cyclical abdominal pain at 33% (n=3) with pelvic pain at 11% (n=1). These were girls who either had imperforate hymen or vaginal atresia.

b) Disorders of breasts and nipples

Breast enlargement was the only presentation in this category.

c) Menstrual disorders

Excessive per vaginal bleeding and anemia constituted the commonest complaints at 40% (n=2) each followed by weight gain at 20% n=1) in patients who had polycystic ovarian syndrome.

d) Ovarian disorders

Abdominal mass constituted 80% (n=4) of complaints in ovarian disorders followed by abdominal pain at 20% (n=1).

e) Ovarian disorders with menstrual abnormalities mmm

A few cases were diagnosed with menstrual abnormalities as a result of ovarian disorders. Anemia in this category of patients was the most common complaint at 50% (n=5) followed by heavy menses at 30% (n=3) and abdominal mass at 20% (n=2) correspondingly.

5.2.9 Puberty Disorders.

a) Contra-sexual development of sexual characteristics

This disorder had a single male gender case that presented with breast enlargement.

f) Delayed Puberty

All of the cases that presented with delayed puberty were male with most complaining of small penile length followed by lack of erections at 57 % (n=4) and 43% (n=3) respectively.

g) Non pathological sexual variations (PT/PA)

Acne, body odor, pubic hair and breast enlargement were the most common presentations at equal frequencies in children who either were diagnosed with premature adrenarche or premature thelarche respectively (n=3).

h) Precocious puberty

Children with precocious puberty commonly complained of pubic hair and penile enlargement at a frequency of 35% (n=5) each followed by testicular enlargement at 30% (n=4).

5.2.10 Obesity

Children who were diagnosed with central obesity had convulsions and difficulty in breathing as the most common complaints followed by delay in milestones whereas those who had genetic or polygenic obesity presented with mental retardation, convulsions and body weakness besides faster weight gain. Those with iatrogenic obesity manifested with rapid weight gain, mood changes besides other features

of underlying disorder like anemia. Nutritional obesity mostly manifested as rapid weight gain at 71% (n=5) with non-specific symptoms like easy fatigability and breathing problems.

5.2.11 Pituitary, Hypothalamus, CNS disorders

a) Acquired pituitary disorders

Half of the patients with acquired pituitary disorders presented with headache followed by vomiting and testicular enlargement in equal frequencies.

b) Deficiency of pituitary hormones

Poor growth and undescended testes constituted 2 major presenting complaints at equal frequencies of 37.5% (n=3) followed by convulsions at 25 % (n=2) in patients who were diagnosed with deficiency of pituitary hormones.

c) Vasopressin deficiency

Children and adolescents diagnosed as having vasopressin deficiency presented with weight loss, polydipsia and polyuria at equal frequencies.

5.2.12 Disorders of the adrenal glands.

a) Primary adrenal insufficiency

Ambiguous genitalia was the leading presentation in patients who had primary adrenal insufficiency followed by acne and penile enlargement at 58% (n=7), 25% (n=3) and 16% (n=2) respectively.

b) Secondary adrenal hormone excess

Palpitations and sweating were the dominant symptoms at 37.5% (n=3) each followed by abdominal pain at 25% (n=2) in patients who had secondary adrenal hormone excess.

c) Secondary adrenal insufficiency

The patient who was diagnosed with the infrequent secondary adrenal insufficiency presented with visual blurring, convulsions and headache.

5.2.13 Salt and water regulation conditions

a) Diabetes insipidus

Polyuria, polydipsia and headache constituted symptoms in children with diabetes insipidus at equal frequency of n=2.

b) Hypernatremia

Patients diagnosed with hypernatremia were more likely to have presented with poor feeding, fever and oliguria in the order of 44% (n=7), 31% (n=5) and 25% (n=4) respectively.

c) Hyponatremia

Convulsions were the leading complaints followed by vomiting and poor feeding at 60% (n=3); 20% (n=1); 20% (n=1) respectively in children who were diagnosed with low body sodium levels.

5.2.14 Inborn errors of metabolism.

a) Unspecified cases of inborn errors of metabolism

Convulsions ranked as the first presenting complaint followed by poor growth and delayed milestones at frequencies of 50% (n=11); 27% (n=6); 23% (n=5) correspondingly in children who were suspected to have unspecified inborn errors of metabolism.

b) Gaucher's disease

Common presenting symptoms in patients with Gaucher’s disease were massive splenomegaly, hepatosplenomegaly and pancytopenia at 33% (n=3), 44% (n=4) and 22% (n=2) respectively.

c) Hunter's disease

Poor growth and upper airway obstruction characterized the most common presentation in children with Hunter’s disease at equal frequencies at 35% (n=6) followed by joint deformities at 30% (n=5) respectively.

5.3 Demographic Characteristics

5.3.1 Admitted vs Outpatient

5.3.1.1 Calcium, phosphate metabolism and growth disorders

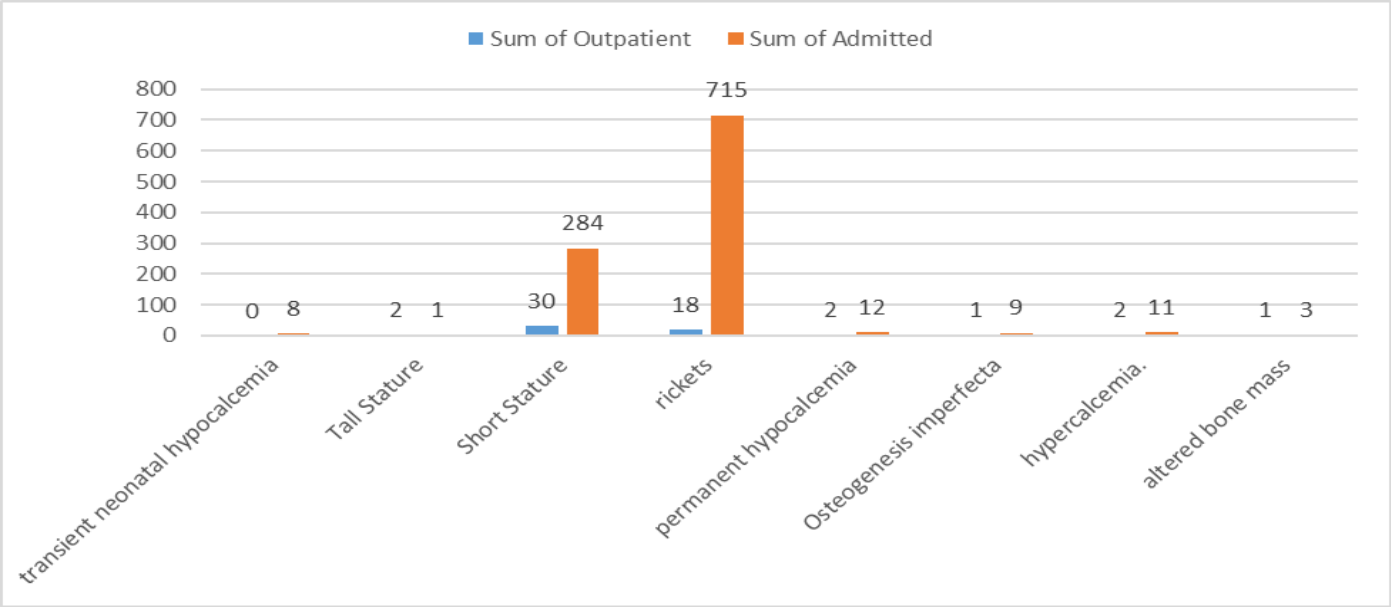


Figure 5-9 Calcium, phosphate metabolism and growth disorders for Admitted vs Outpatient

Majority of patients with rickets, 97.5% and short stature, 90.4% were diagnosed as inpatients as shown above. Similarly, all patients with hypocalcemia, hypercalcemia were admitted as shown in figure 7.9 above.

5.3.1.2 Glucose and Lipid metabolism disorders and Testes and male reproductive tract disorders

Majority, 90% of children with type 1 diabetes and all children with hypoglycemia were first treated as inpatients. Similarly, majority of patients diagnosed with disorders of penis and maldescended testes were seen as inpatients as shown in figure 7.10 below.

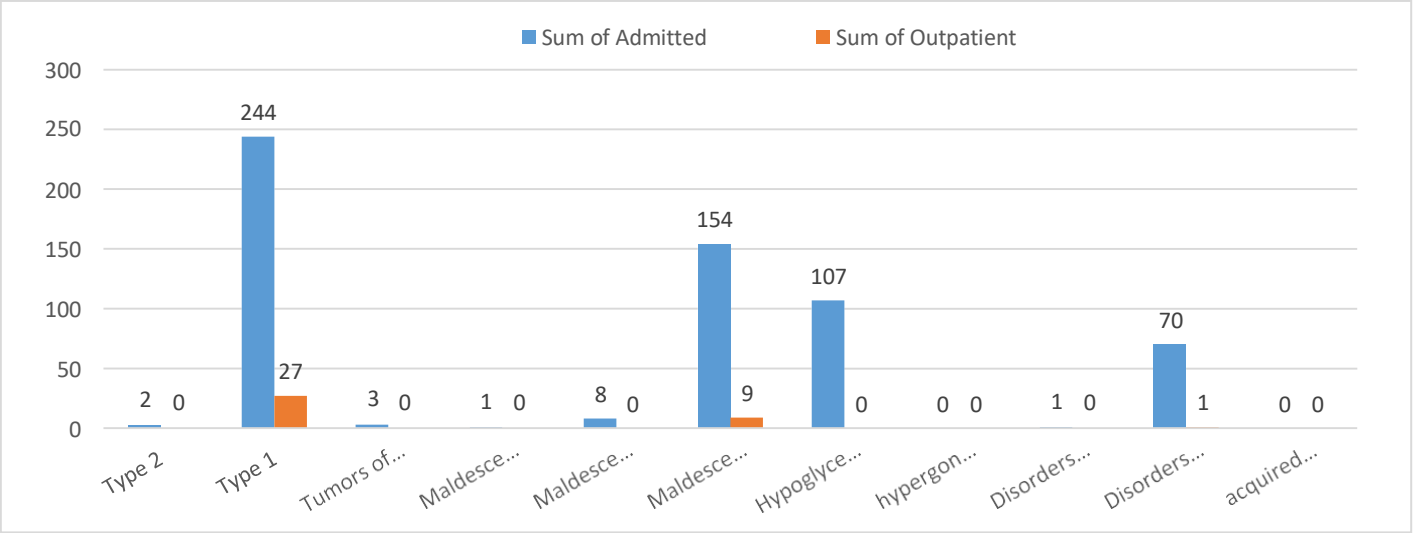


Figure 5-10 Glucose and Lipid metabolism disorders and Testes and male reproductive tract disorders for Admitted vs Outpatient

5.3.1.3 Thyroid Disorders and Syndromes with endocrine features

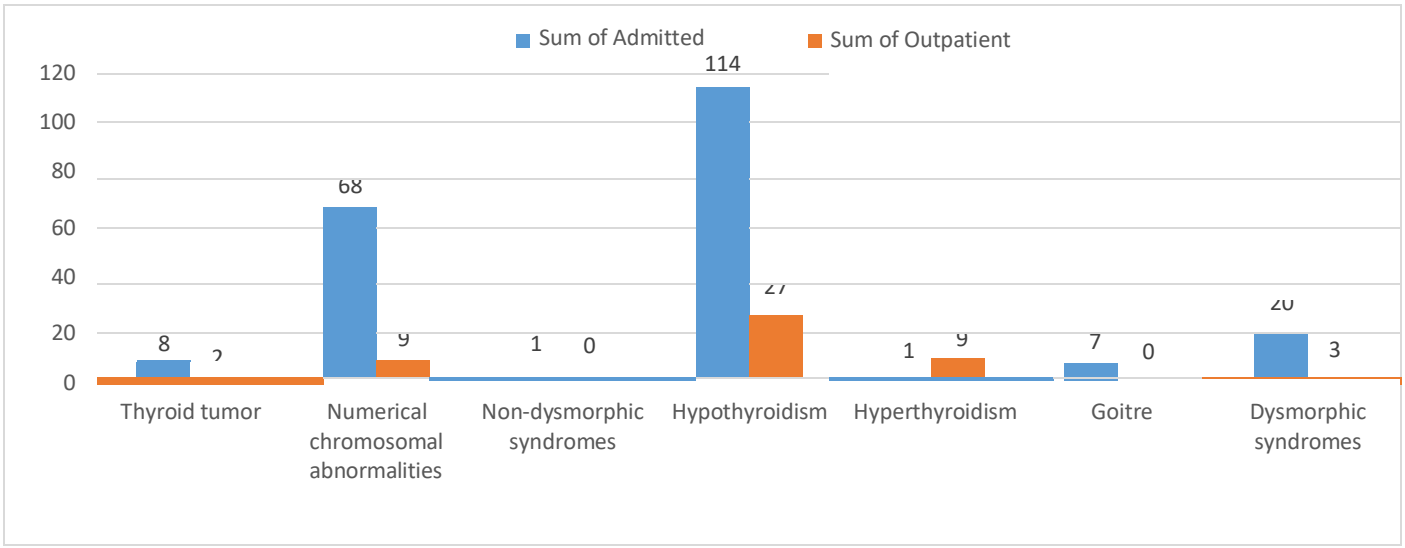


Figure 5-11 Thyroid Disorders and Syndromes with endocrine features

Majority of patients diagnosed with thyroid disorders with an exception of hyperthyroidism were initially admitted in the wards. Likewise, patients with numerical chromosomal disorders and dysmorphic syndromes were first treated as inpatients before getting booked for outpatient follow up, figure 7.11.

5.3.1.4 Pituitary, Hypothalamus, CNS Disorders & Disorders of the adrenal glands. & Salt and water regulation conditions. & In-born metabolism disorders.

Majority of patients who presented with adrenal and pituitary disorders of either hormonal excess or deficiency were admitted while patients who had inborn errors of metabolism showed a mixed pattern. All patients with Gaucher's disease were admitted initially while most patients with Hunter's disease were first seen as outpatients. Those with unspecified causes of metabolic disorders were first managed both at outpatient level and inpatient at a ratio of 1:1 as shown in figure 7.12 below.

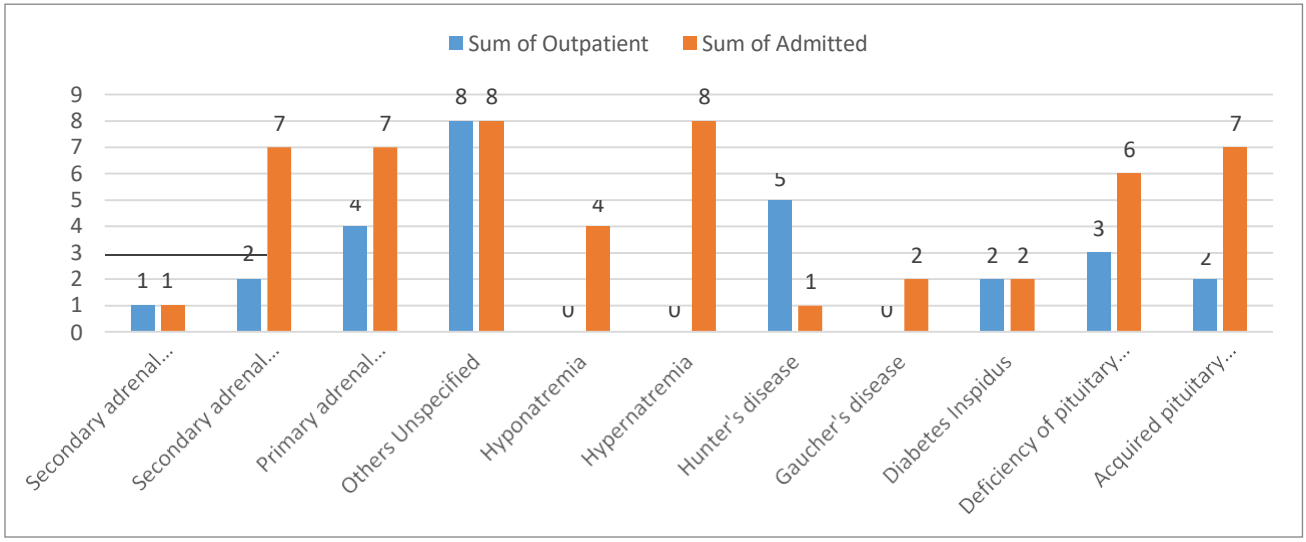


Figure 5-12 Pituitary, Hypothalamus, CNS Disorders & Disorders of the adrenal glands. & Salt and water regulation conditions & In-born metabolism disorders

5.3.1.5 Obesity & Sex Development and Gender Disorders & Puberty Disorders & Endocrine disorders of the ovaries and female reproductive tract.

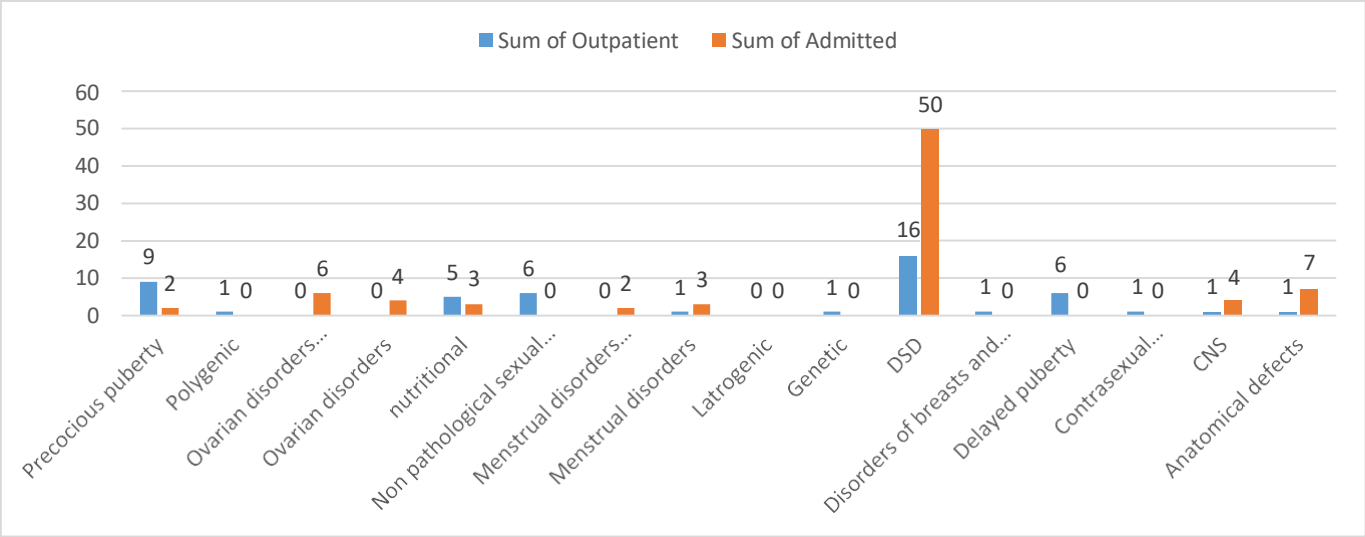


Figure 5-13 Obesity & Sex Development and Gender Disorders & Puberty Disorders & Endocrine disorders of the ovaries and female reproductive tract.

Puberty disorders were commonly seen as outpatient cases while 75% of disorders of sexual differentiation were first reviewed while in the wards as inpatients as depicted in figure 7.13 above. Children and adolescents who presented with ovarian and menstrual disorders were most commonly admitted initially. However, patients who had obesity were either diagnosed first while in the wards or as outpatients depending on the cause. For instance, nutritional obesity cases were mainly first seen as outpatients while CNS obesity cases were commonly seen as inpatients.

5.3.2 Referral Source

Majority, 1217 (54.3%) of cases got referred by various counties followed by self-referral at 711 (31.7%) and internal referrals from other KNH clinics, 300 (13.4%). Rickets was an exception in that most, 54.1%, came in as self-referral as shown in table 7.70 below.

Table 5:2 Referral Sources

Sub-diagnosis	**County**	**Other KNH Clinics**	**Self**
Rickets	305	28	398
Type 1 diabetes	171	8	94
Short Stature	171	31	113
Maldescended testes	82	59	30
Hypothyroidism	93	31	18
Numerical chromosomal abnormalities	46	26	6

Hypoglycemia	64	12	30
DSD	45	21	0
Disorders of penis	52	20	0
Dysmorphic syndromes	13	4	7
permanent hypocalcemia	11	2	1
Contrasexual development of sexual characteristics	0	1	0
Delayed puberty	6	0	0
Non pathological sexual variations(PT/PA)	6	0	0
Precocious puberty	7	4	0
CNS	5	0	0
Genetic	0	1	0
Iatrogenic	5	1	1
Nutritional	7	1	0
Polygenic	1	0	0
Goitre	7	0	0
Hyperthyroidism	10	0	0
Thyroid tumor	8	2	0
Acquired pituitary disorders	5	4	0
Deficiency of pituitary hormones	5	4	0
Primary adrenal insufficiency	9	2	0
Secondary adrenal hormone excess	6	2	1
Secondary adrenal insufficiency	1	1	0
Disorders of scrotum	0	0	1
Tumors of testes	2	0	1
hypergonadotropichypogonadism (HH)	0	0	0
acquired testicular without HH	0	0	0
Anatomical defects	4	4	0
Disorders of breasts and nipples	0	1	0
Menstrual disorders	4	2	0
Ovarian disorders	6	4	0
Type 2	1	1	0
Altered bone mass	4	0	0
Hypercalcemia.	4	5	4
Osteogenesis imperfecta	9	1	0
Transient neonatal hypocalcemia	9	0	0
Diabetes Insipidus	4	0	0
Hypernatremia	8	0	0
Hyponatremia	4	0	0
Non-dysmorphic syndromes	1	0	0
Tall Stature	2	1	0
Gaucher's disease	4	0	0
Hunter's disease	4	2	0
Others Unspecified	8	7	0

Referrals from other KNH clinics constituted a considerable percentage amongst patients diagnosed with DSD, hypothyroidism, disorders of the penis, maldescended testes, numerical chromosomal abnormalities, Hunter's disease and unspecified cases of inborn errors of metabolism at frequencies of 31.3%, 21.8%, 27.7%, 41.8%, 33.3%, 33.3% and 46.6% respectively.

5.3.3 Sub-Diagnosis with County of Residence.

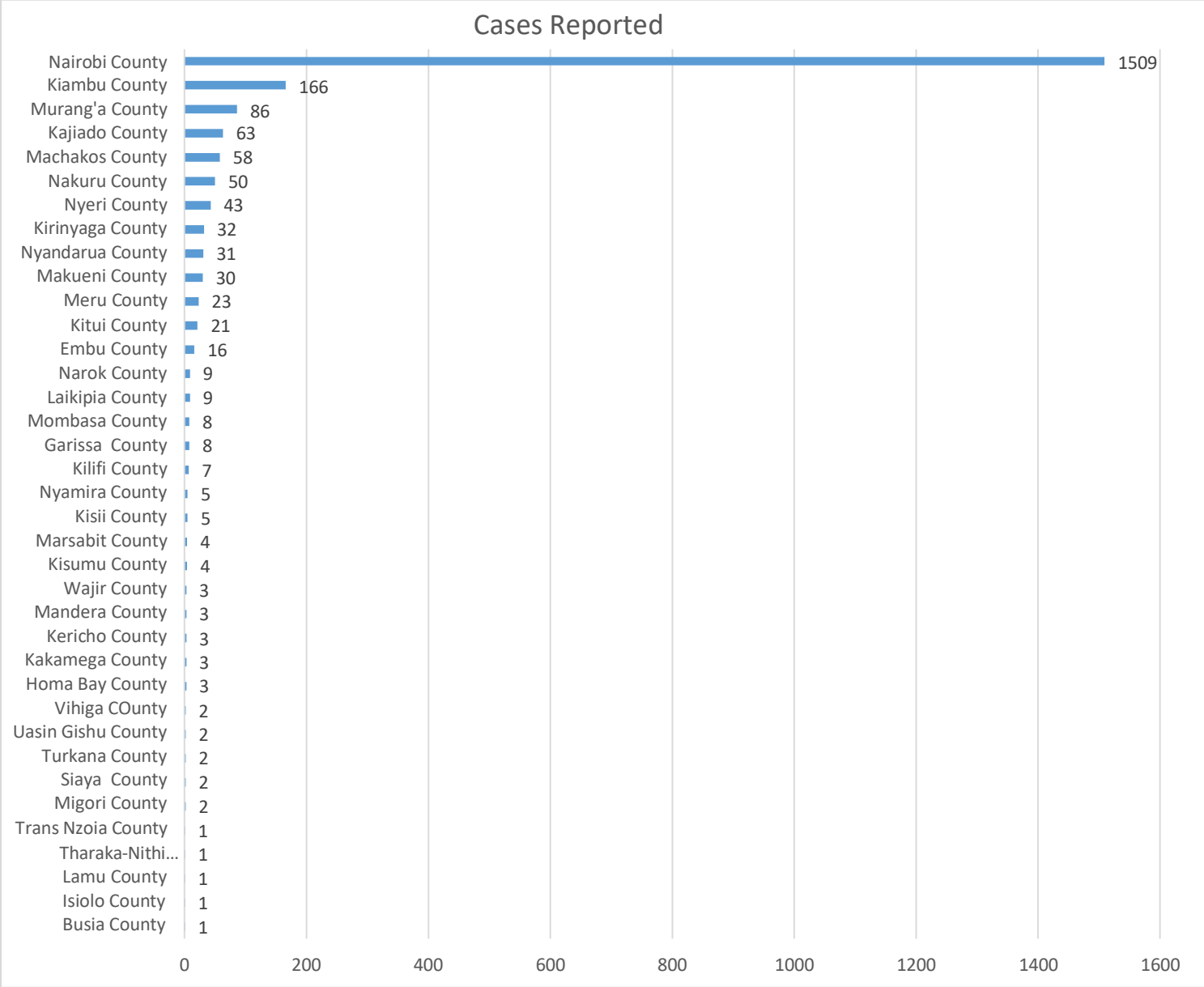


Figure 5-14 Sub-Diagnosis with County of Residence

Over 68% of all pediatric endocrine cases seen at Kenyatta National Hospital came from Nairobi County followed by Kiambu county at 7.4%, Murang'a county at 3.9%, Kajiado county at 2.8%, Machakos county at 2.6%, and Nakuru county at 2.2% as depicted in figure 7.14 above.

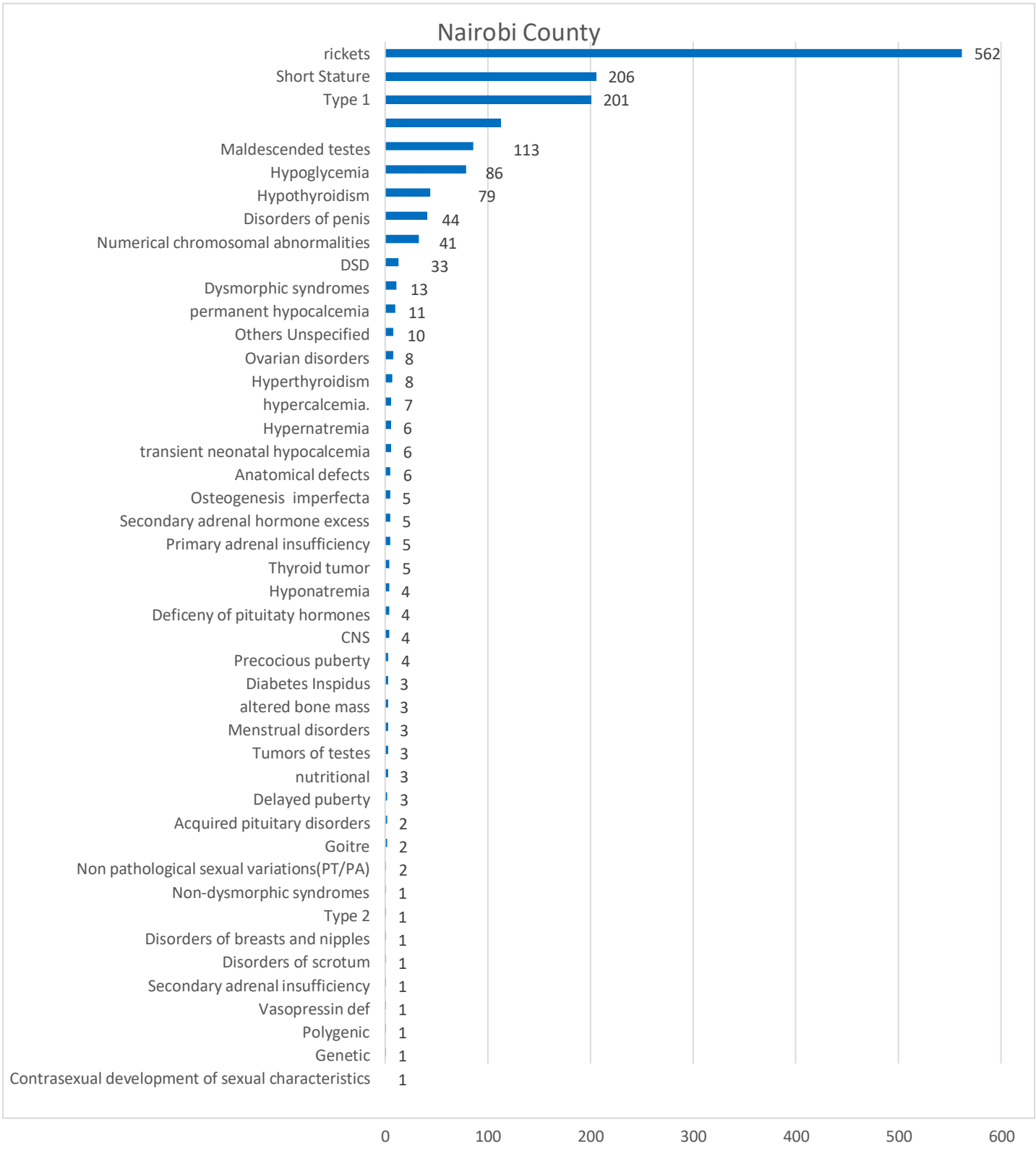


Figure 5-15 Sub-Diagnosis: Nairobi County

Nairobi county recorded most of the conditions that were seen at Kenyatta national hospital. Out of these, rickets was the leading referred condition at 37.2% followed by short stature and type 1 diabetes at 13.6% and 13.3% respectively. Of the total corresponding cases seen at the tertiary hospital from this county, rickets constituted 76% while short stature and type 1 diabetes comprised 65% and 82% respectively. Maldescended testes and hypothyroidism constituted 69% and 56.8% of the respective total cases, figure 7.15 above.

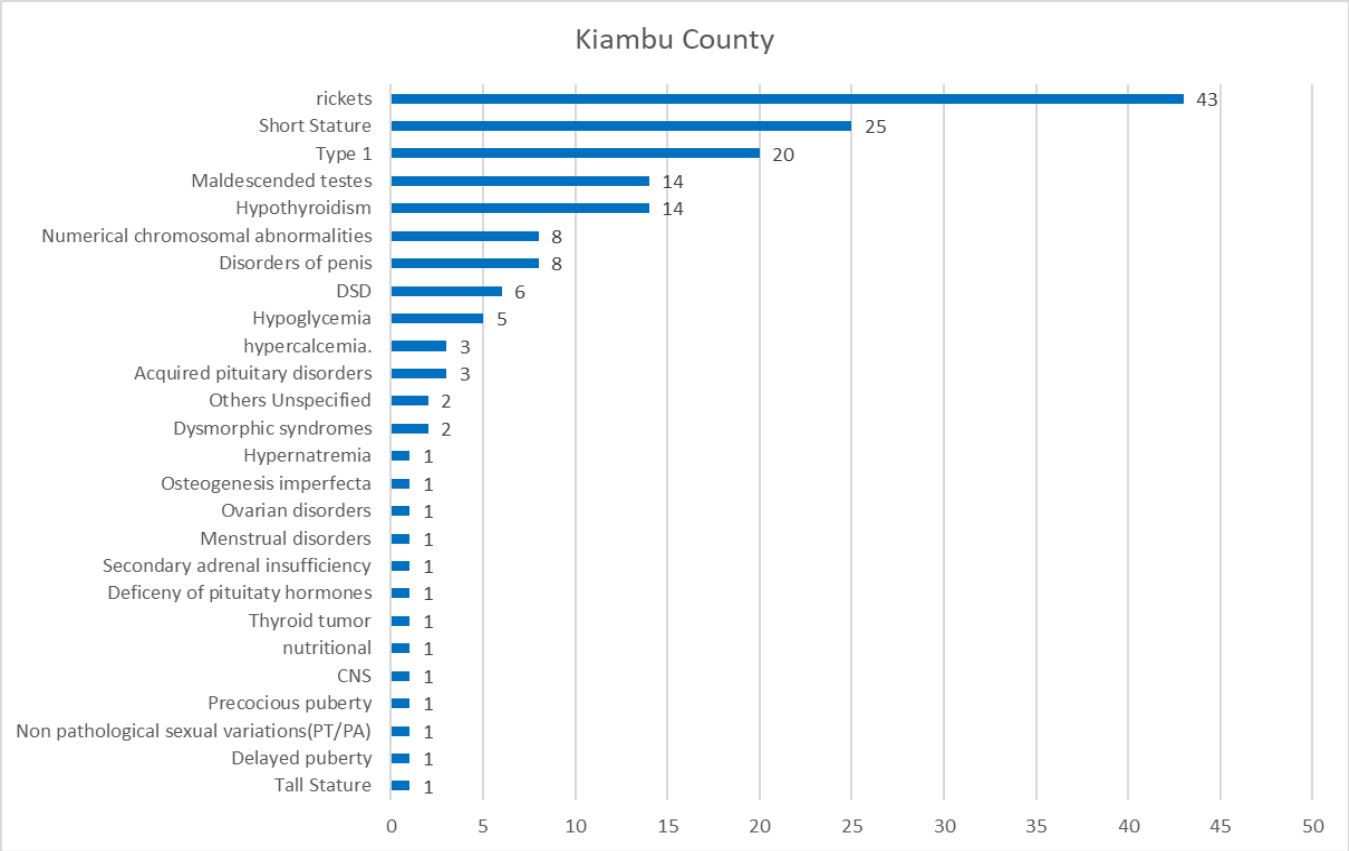


Figure 5-16 Sub-Diagnosis: Kiambu County

Majority of children who were referred from Kiambu county had rickets followed by short stature as a result of failure of thrive, type 1 diabetes, hypothyroidism and maldescended testes at 26%, 15%, 12%, 8.4%, 8.4% respectively, figure 7.16. Rickets, short stature, type 1 diabetes and hypothyroidism cases comprised 5.9%, 7.9%, 8.1% and 10% of all cases seen at Kenyatta hospital.

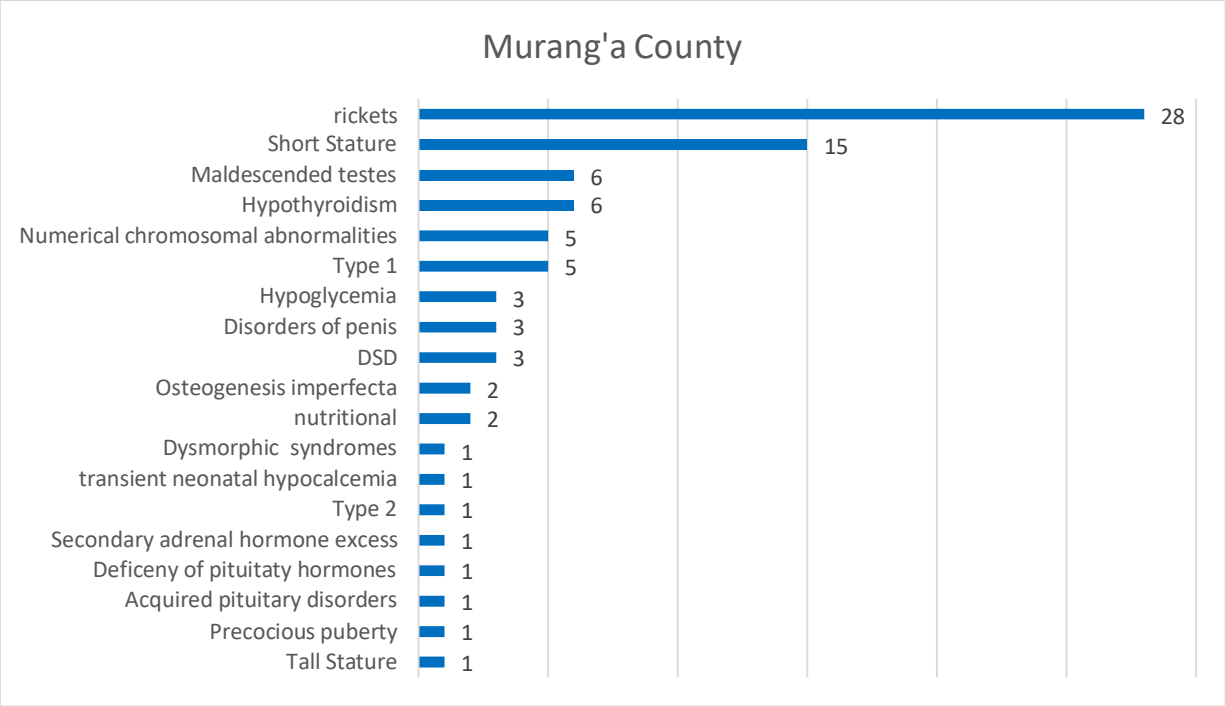


Figure 5-17 Sub-Diagnosis: Murang'a County

Rickets, short stature, hypothyroidism, maldescended testes, numerical chromosomal abnormalities and type 1 diabetes formed the most frequent diagnoses referred from Murang'a county at 33%, 17%, 7%, 7%, 5.8%, 5.8% respectively, figure 7.17. Rickets, short stature and hypothyroidism from this county comprised 3.8%, 4.7% and 4.3% of all cases seen at Kenyatta hospital respectively. Type 1 diabetes on the other hand formed 2% of the cases seen at Kenyatta hospital.

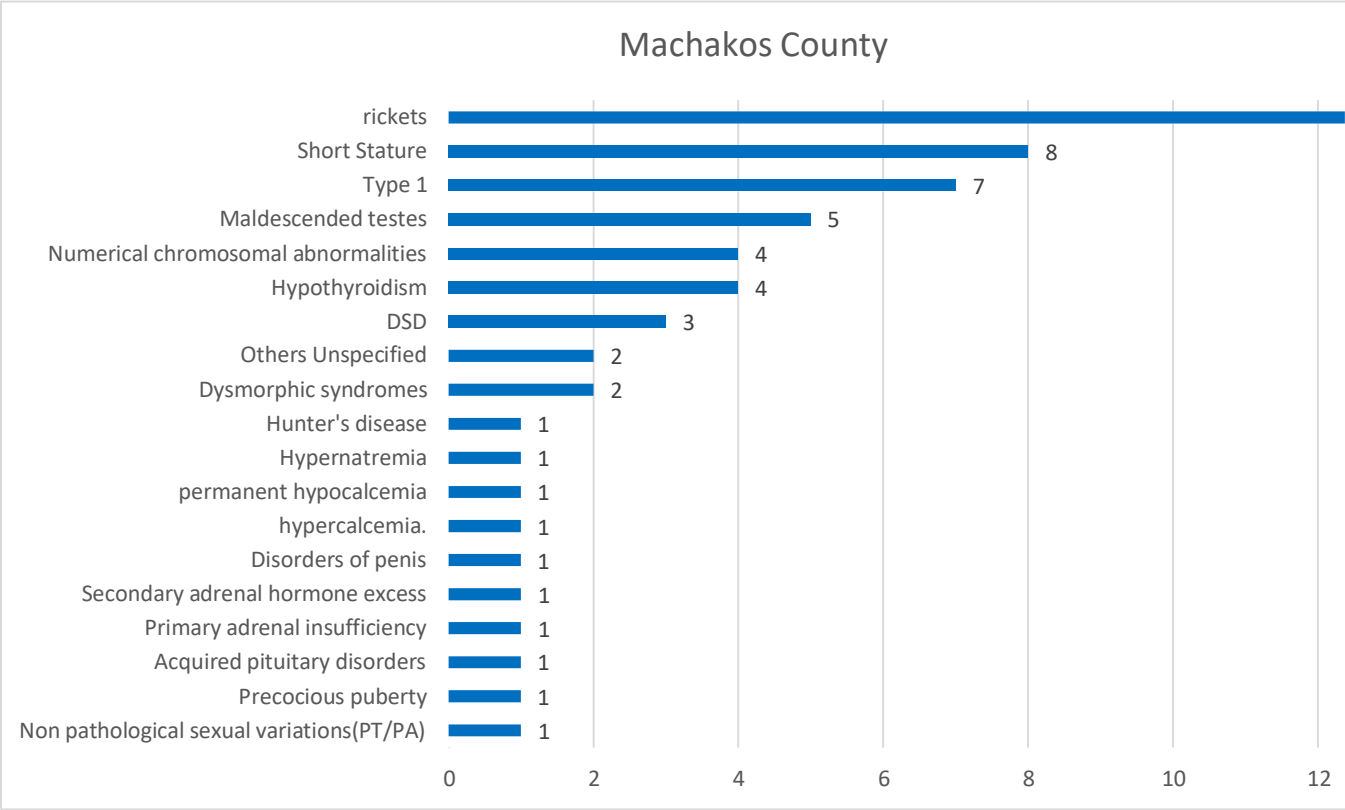


Figure 5-18 Sub-Diagnosis: Machakos County

Rickets, short stature and type 1 diabetes comprised the bulk of referred cases from Machakos county at a frequency of 22%, 13.8% and 12% respectively, figure 7.19. Out of the respective total cases seen at Kenyatta hospital, rickets formed 1.8% while short stature and type 1 diabetes formed 2.5% and 2.4% respectively.

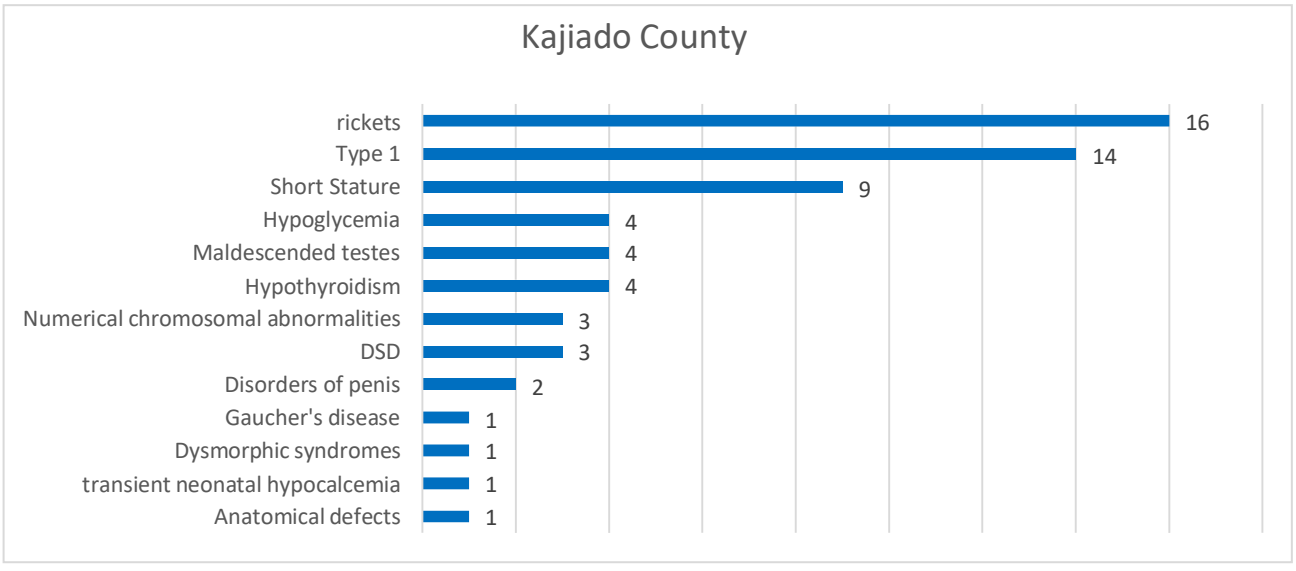


Figure 5-19 Sub-Diagnosis: Kajiado County

Rickets, type 1 diabetes and short stature formed the bulk of pediatric endocrine cases that were referred from Kajiado county at a frequency of 25%, 22%, 14% respectively, figure 7.18. Rickets cases as referred from Kajiado county comprised 2% of all rickets cases seen at Kenyatta national hospital while type 1 diabetes and short stature formed 5% and 2.8% respectively.

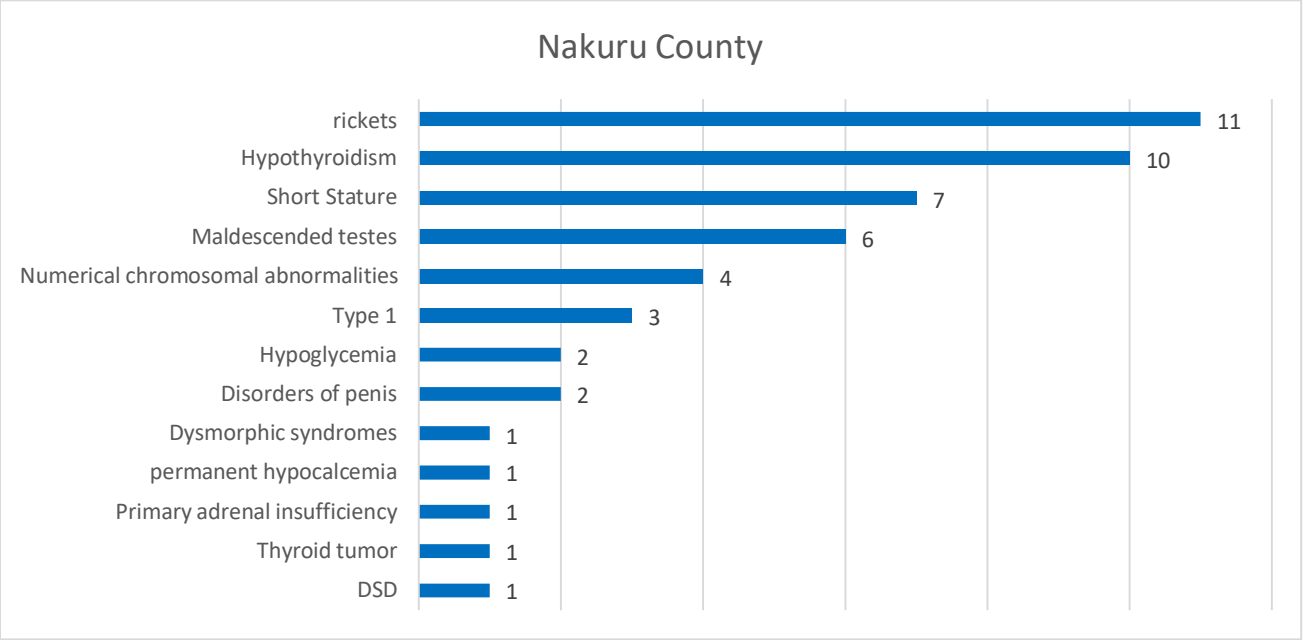


Figure 5-20 Sub-Diagnosis: Nakuru County

Rickets, hypothyroidism and short stature were the commonly referred cases from Nakuru county at a frequency of 22%, 20% and 14% respectively, figure 7.20. Rickets cases from this county constituted 1.5% of all cases seen at Kenyatta hospital while hypothyroidism, short stature and type 1 diabetes formed 7%, 2.2% and 1% of the total respective cases correspondingly.

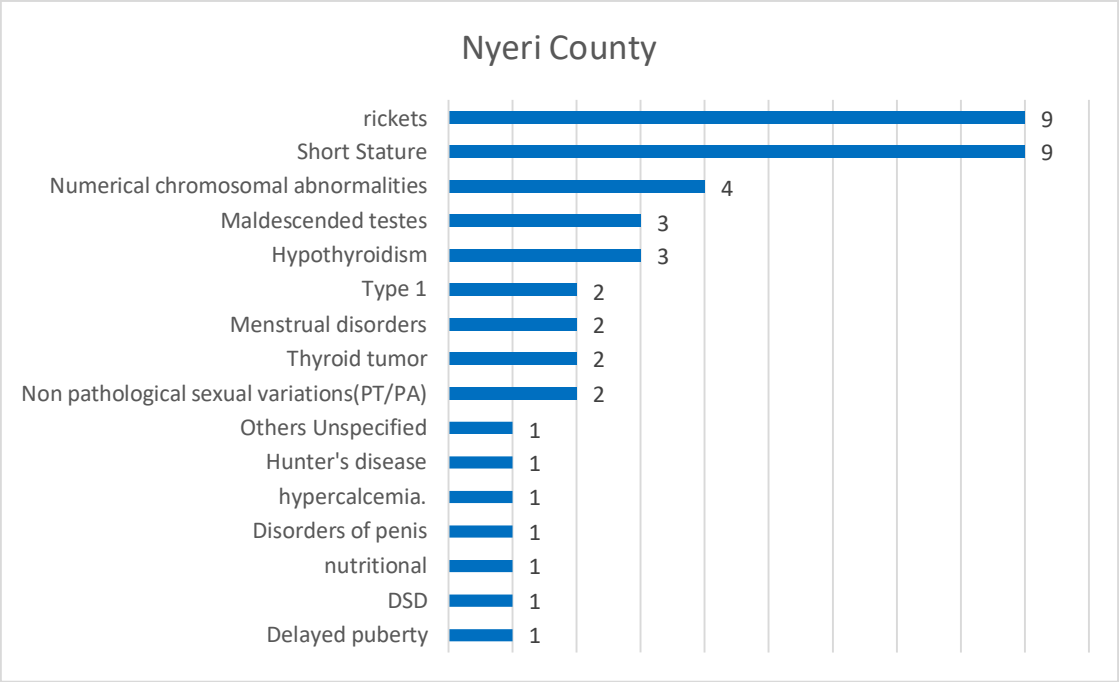


Figure 5-21 Sub-Diagnosis: Nyeri County

Nyeri county frequently referred cases of rickets, short stature and numerical chromosomal abnormalities at a rate of 21%, 21% and 9.3% specifically, figure 7.21. Cases of rickets from Nyeri County formed 1.2% of respective cases seen at Kenyatta hospital while short stature and numerical chromosomal abnormalities comprised 2.8% and 5.1% correspondingly.

Rickets was the leading cause of referral from Kirinyaga county at a frequency of 25% followed by short stature, hypothyroidism and disorders of the penis at an equal frequency of 9.4% each, figure 7.22. Rickets from this county comprised approximately 1% of the corresponding cases seen at Kenyatta while short stature, hypothyroidism and penile disorders formed 0.9%, 2.2% and 4.2% respectively. Notably, there was no single case of type 1 diabetes referred from this county.

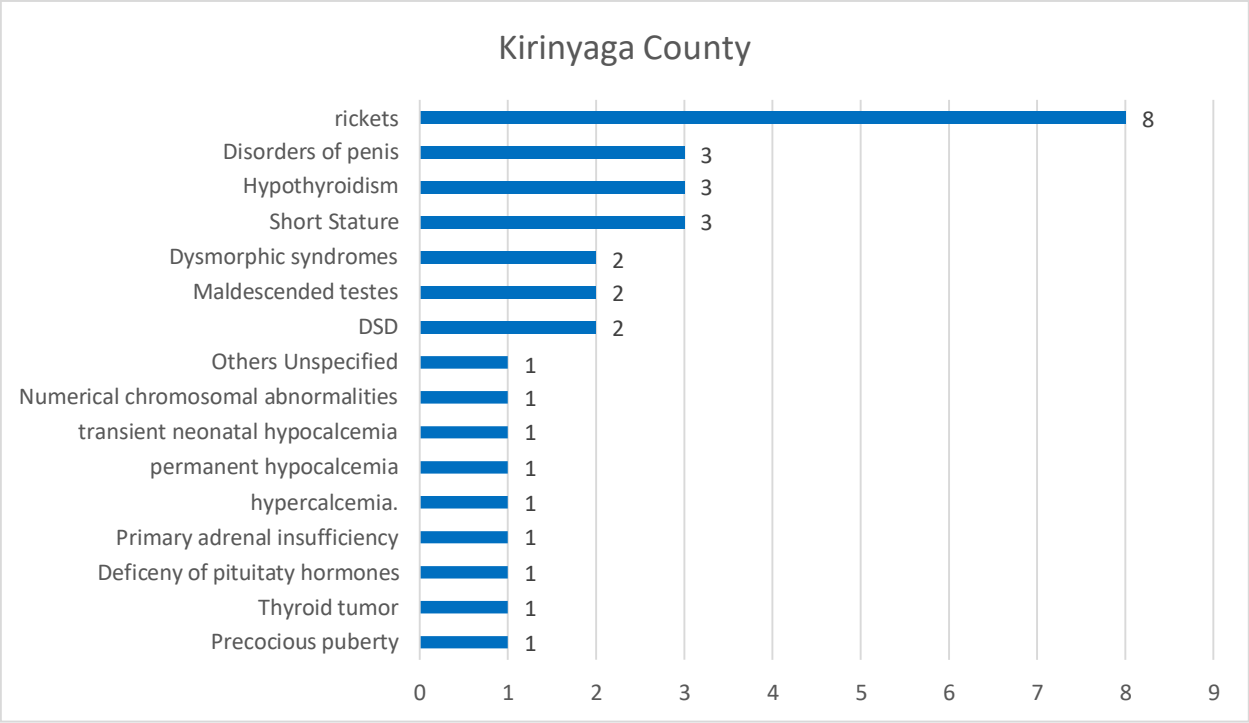


Figure 5-22 Sub-Diagnosis: Kirinyaga County

Short stature was the leading cause of referral from Makueni county followed by rickets and disorders of sexual differentiation at a frequency of 27%, 23.3% and 13.3% respectively, figure 7.23. Out of the corresponding cases seen at the tertiary referral hospital, short stature from this county constituted 2.5% while rickets and disorders of sexual differentiation formed 1% and 6.9% respectively. Hunter's disease from this county constituted 50% of total cases in KNH.

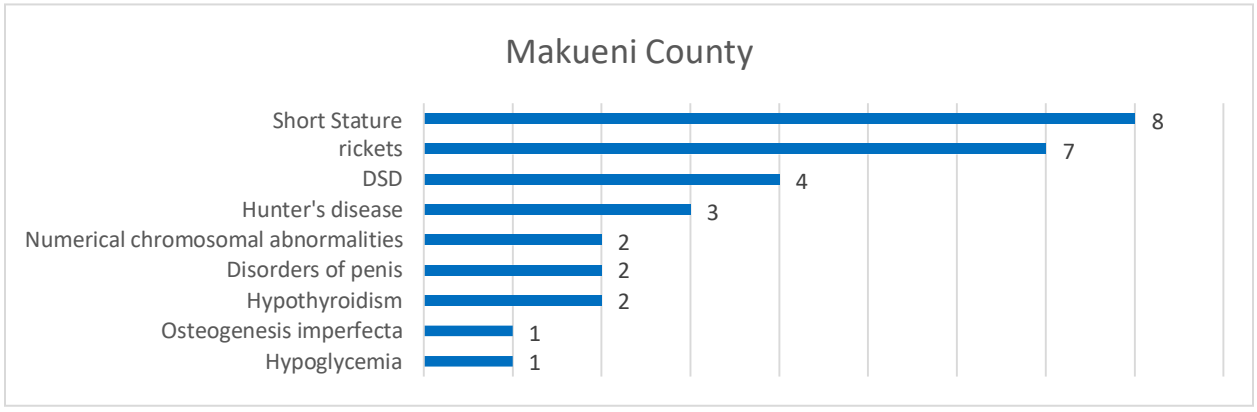


Figure 5-23 Sub-Diagnosis: Makueni County

Nyandarua county frequently referred cases of rickets and short stature at 25.8% and 16.1% specifically, figure 7.24. These were followed by type 1 diabetes, maldescended testes and hypothyroidism at an equal frequency of 12.9% each. Rickets constituted 1% of specific cases referred from this county to Kenyatta hospital while short stature, type 1 diabetes, maldescended testes and hypothyroidism formed 1.6%, 1.6%, 2.5% and 2.9% respectively.

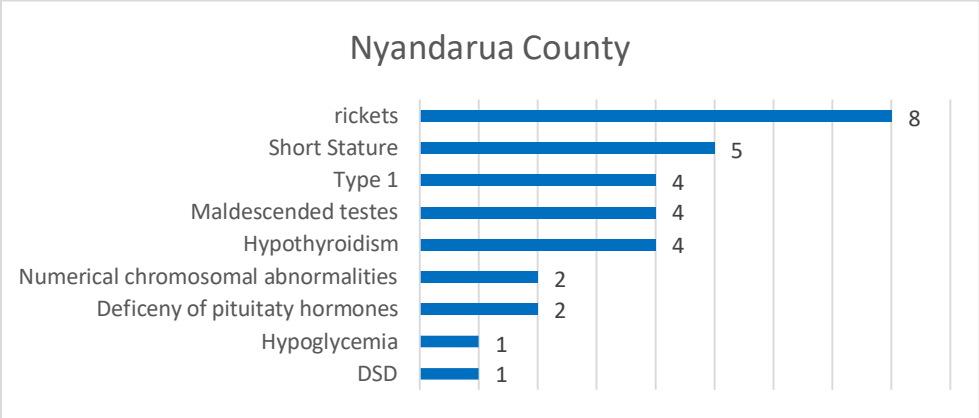


Figure 5-24 Sub-Diagnosis: Nyandarua County

Meru county commonly referred cases of rickets and short stature at 22% and 17.3% respectively followed by type 1 diabetes and hypothyroidism at an equal frequency of 13% each, figure 7.25. Out of the corresponding total cases seen at Kenyatta national hospital, these conditions constituted 0.7%, 1.3%, 1.2% and 2.2% respectively.

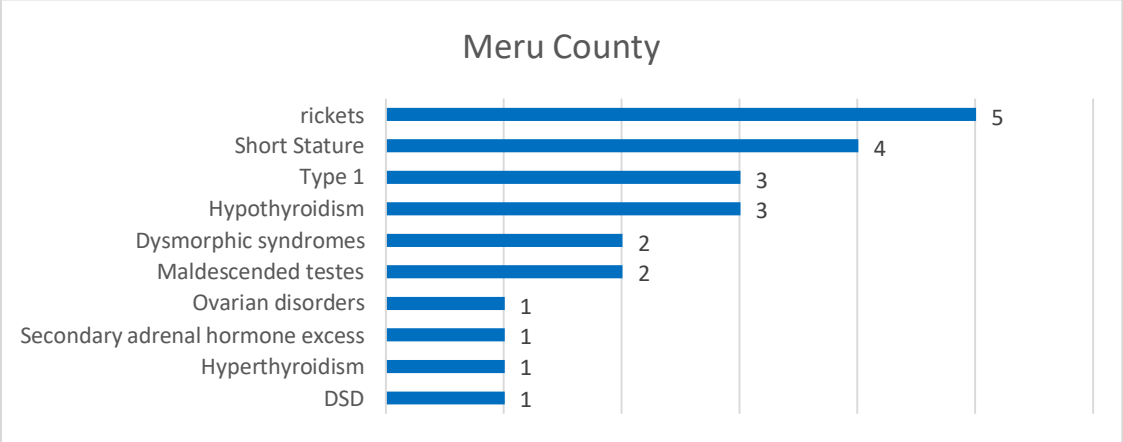


Figure 5-25 Sub-Diagnosis: Meru County

The most commonly referred conditions from Kitui county were rickets and short stature at a frequency of 19% and 14.1% respectively, figure 7.26. These were followed by type 1 diabetes, hypoglycemia

and hypothyroidism at an equal frequency of 9.5% each. Rickets and short stature comprised 0.5% and 0.9% of the corresponding cases seen at Kenyatta hospital. Type 1 diabetes, hypoglycemia and hypothyroidism similarly formed 0.8%, 2.2% and 1.4% respectively.

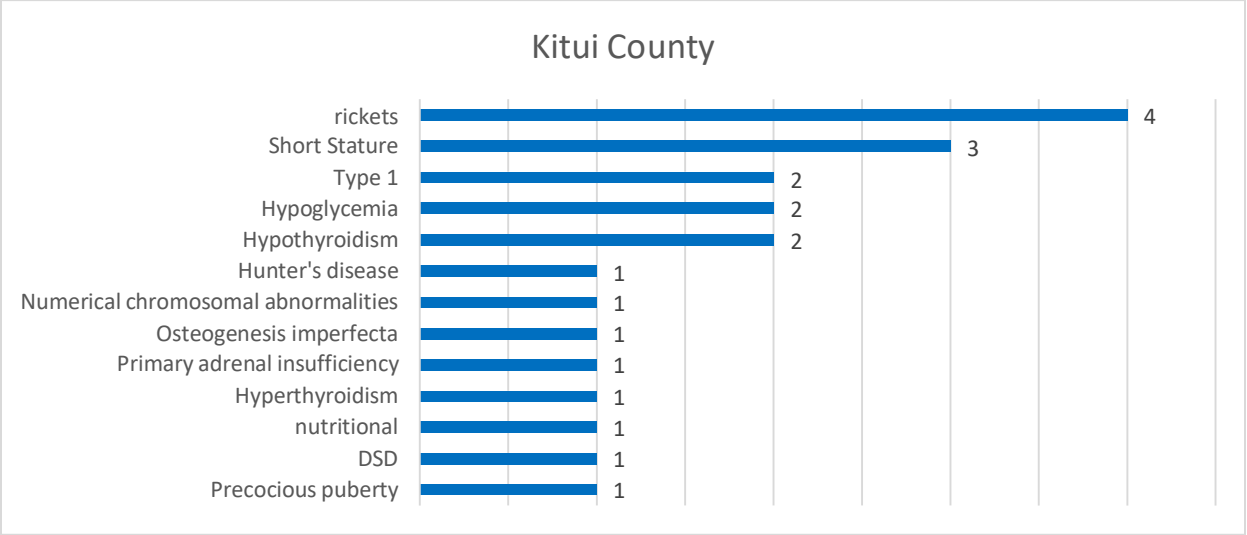


Figure 5-26 Sub-Diagnosis of Kitui County

5.3.4 Gender Characteristics

5.3.4.1 Growth Disorders & Calcium and phosphate metabolism disorders

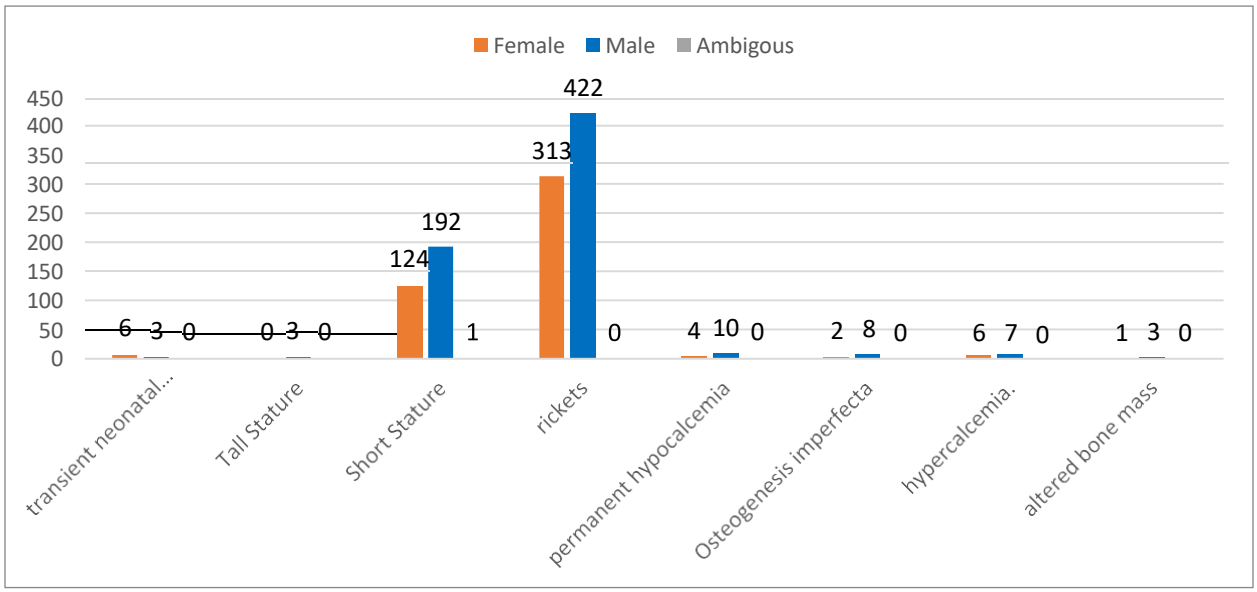


Figure 5-27 Growth Disorders & Calcium and phosphate metabolism disorders

More males were diagnosed with rickets, permanent hypocalcemia, hypercalcemia, osteogenesis imperfecta, altered bone mass and short stature at frequencies of 57.8, 71.4%, 53.8%, 80%, 75% and 60.5% correspondingly. All children with tall stature were male. One child with short stature had ambiguous genitalia, figure 7.27.

5.3.4.2 Thyroid Disorders & Syndromes with endocrine features.

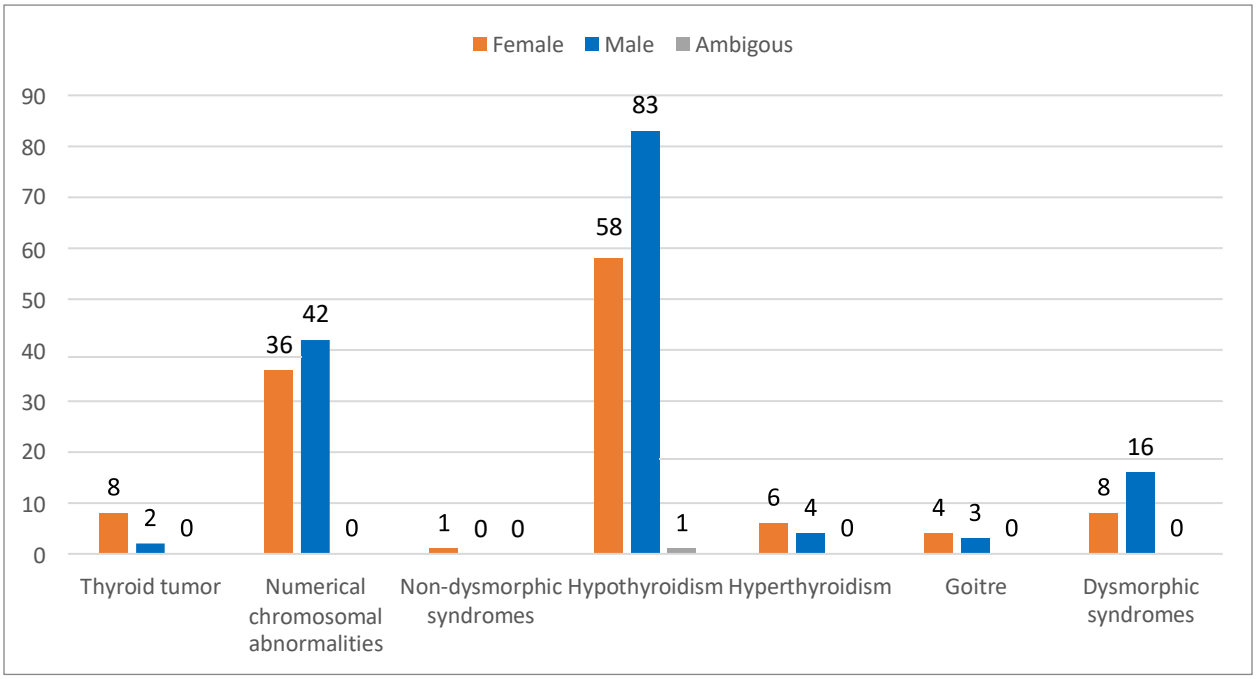


Figure 5-28 Thyroid Disorders & Syndromes with endocrine features

Numerical chromosomal abnormalities as well as dysmorphic syndromes had a slight male preponderance at 53.8% and 66.5%. However, children who were diagnosed with hyperthyroidism and goitre were mainly female at a frequency of 60% and 57% respectively. Children and adolescents diagnosed with hypothyroidism had a male to female ratio of 1.4: More females were diagnosed with thyroid tumor at 80% of the total cases., figure 7.28.

5.3.4.3 Glucose and Lipid metabolism disorders and Testes and male reproductive tract disorders.

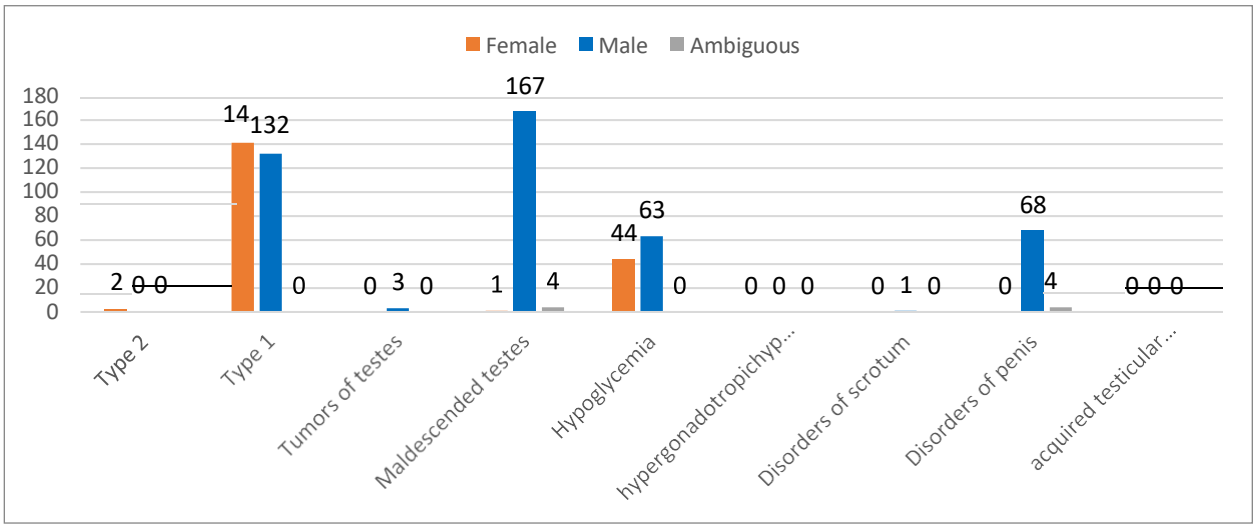


Figure 5-29 Glucose and Lipid metabolism disorders and Testes and male reproductive tract disorders

Type 1 diabetes had a slight female to male preponderance at a ratio of 1.07:1. Children who presented with hypoglycemia were mainly male at 58.8% while all the two patients who presented with type 2 diabetes were female. 2.3% and 5.6% of children diagnosed with maldescended testes and disorders of the penis correspondingly had ambiguous genitalia, figure 7.29.

5.3.4.4 Obesity & Sex Development and Gender Disorders & Puberty Disorders & Endocrine disorders of the ovaries and female reproductive tract.

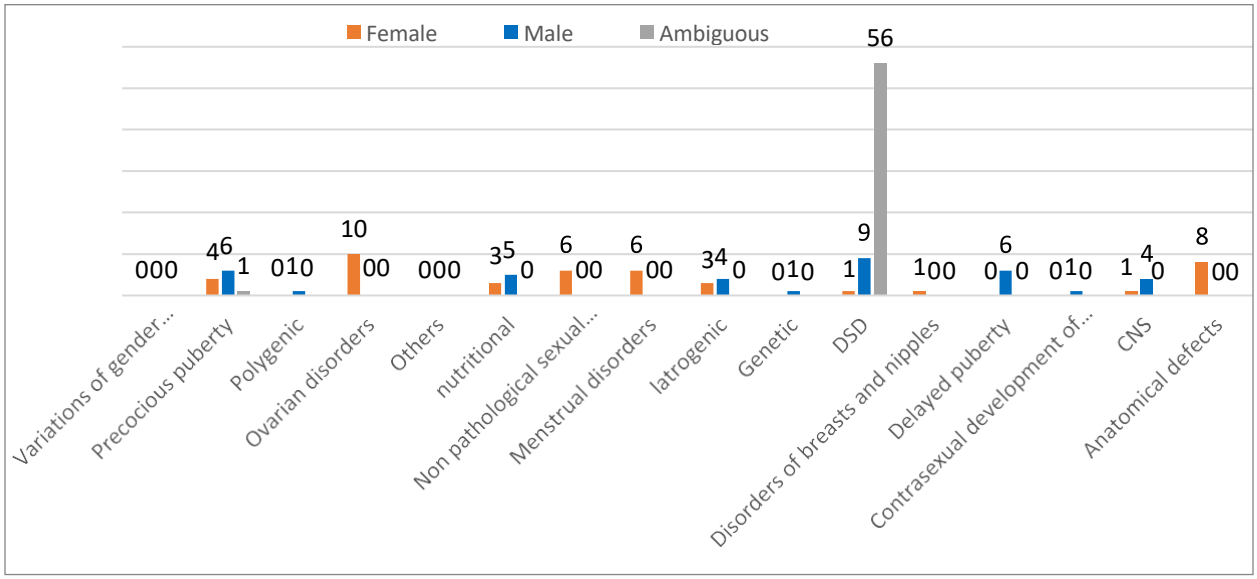


Figure 5-30 Obesity & Sex Development and Gender Disorders & Puberty Disorders & Endocrine disorders of the ovaries and female reproductive tract

More males than females were diagnosed with various forms of obesity as well as precocious puberty. All patients who had delayed puberty were male. Amongst children and adolescents diagnosed to have disorders of sexual differentiation, 13.6% had initially been labelled as male while one case had been labelled as female, figure 7.30.

5.3.4.5 Pituitary, Hypothalamus, CNS Disorders. & Disorders of the adrenal glands. & Salt and water regulation conditions. & Inborn metabolism disorders.

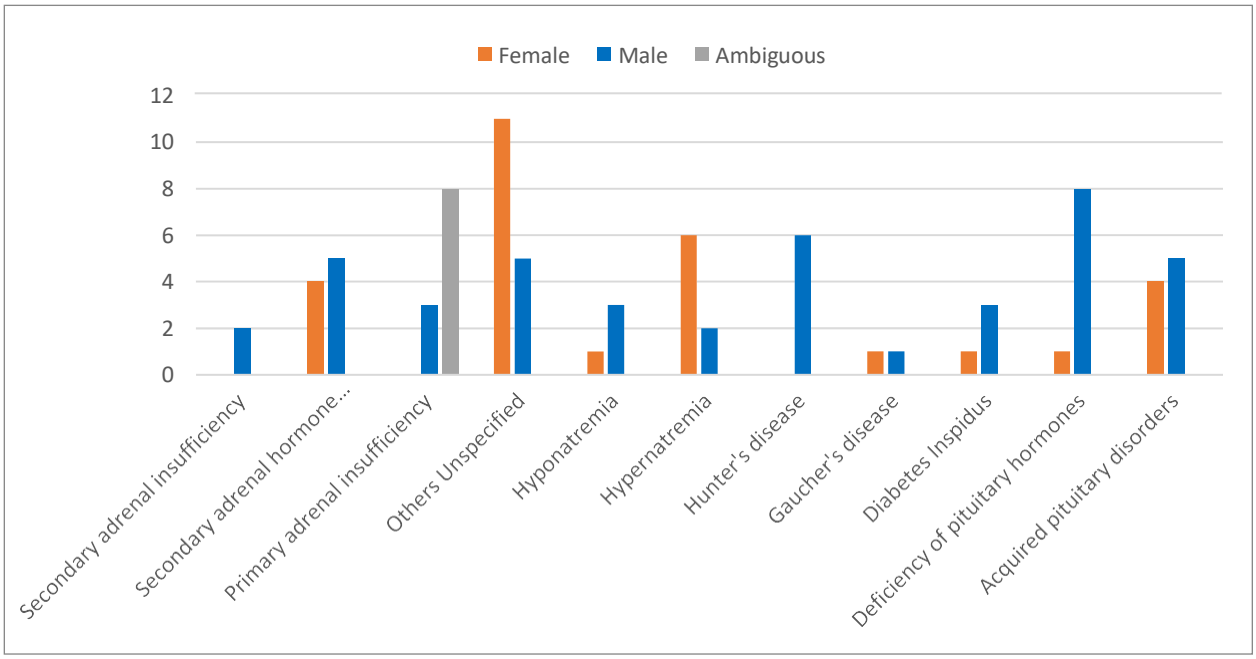


Figure 5-31 Pituitary, Hypothalamus, CNS Disorders. & Disorders of the adrenal glands. & Salt and water regulation conditions. & Inborn metabolism disorders

There was a male to female preponderance amongst cases with deficiency of pituitary hormones as well as acquired pituitary disorders at frequencies of 89% and 56% respectively. Similarly, patients diagnosed to have secondary adrenal hormone excess had a Male to female ratio of 1.25:1. 72.7% of patients who were diagnosed with primary adrenal insufficiency were male while all the ones with secondary adrenal insufficiency were male as well. All children with Hunter's disease were male while those who had unspecified inborn errors of metabolism had a female to male preponderance at a ratio

of 2.2:1. There were more males amongst the cases of diabetes insipidus at a frequency of 75%, figure 31.

5.3.5 Age of the Patient at Diagnosis

5.3.5.1 Growth Disorders & Calcium and phosphate metabolism disorders.

Most, 87.4%, of the children with short stature, more so, failure to thrive were diagnosed between the first month of life and two years of age followed by two to five years at 4.4%. A few children, 2.2%, with poor growth were picked out within the first one month of life. 95.5% of children with rickets were diagnosed between the first month and two years of life while only 2.7% got diagnosed between two and five years of life. Children with permanent hypocalcemia got identified frequently during the first one month of life and two years and occasionally, 1.4%, between two and five years of life, figure 7.32.

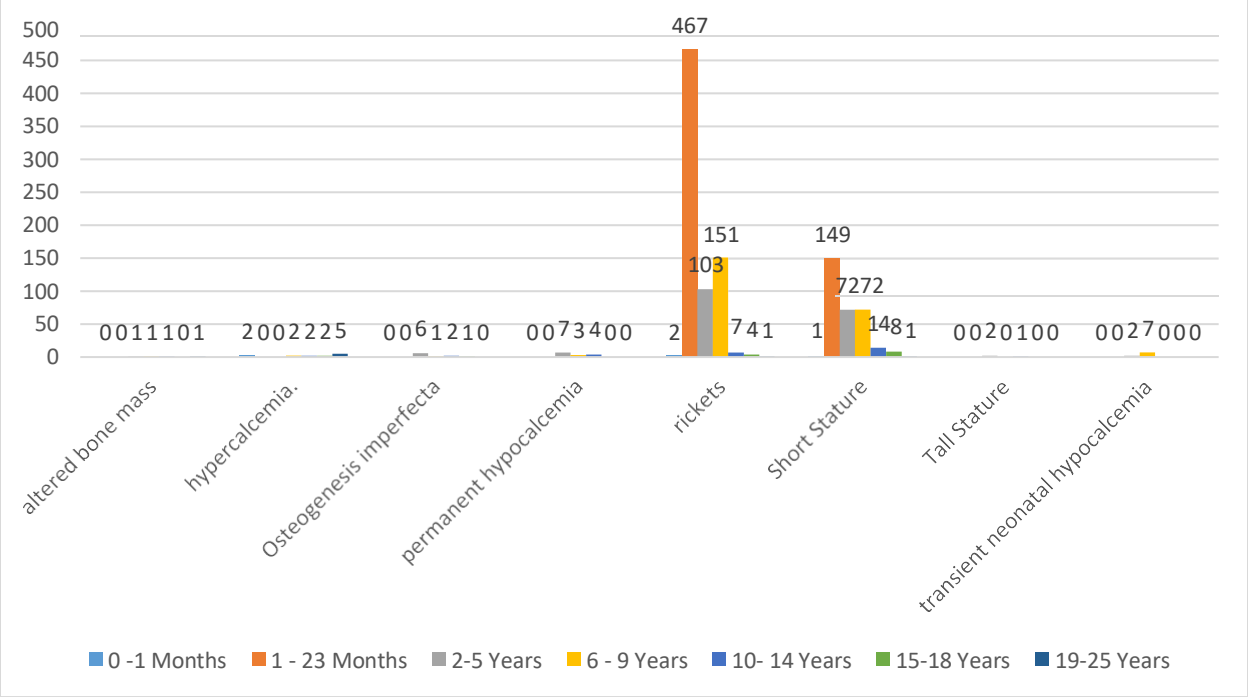


Figure 5-32 Growth Disorders & Calcium and phosphate metabolism disorders

5.3.5.2 Thyroid Disorders & Syndromes with endocrine features.

A significant number of patients diagnosed with hypothyroidism, 66.9%, were identified between 1 to 23 months of life followed by 0 to 1 month, 2 to 5 years, 4 to 9 years at 18.3%, 7%, 4.9% respectively and an equal frequency of 1.4% between the ages of 6 to 9 years and 15 to 18 years. Hyperthyroid patients on the other hand commonly presented between the ages of 6 to 9 years and 10 to 14 years at a frequency of 30% each followed by 20% getting diagnosed at 1 to 23 months with the least frequency of 10% between the ages of 2 to 5 years and 0 to 1 month each. 50% of patients diagnosed to have goitre presented between 10 to 14 years of life while 33% got diagnosed at 6 to 9 years of age. Close association was noted amongst patients diagnosed with thyroid tumor where the majority, 40%, got picked out between 19 to 25 years, 30% between 10-14 years with the least at 20% getting diagnosed between 15 to 18 years, figure 7.33.

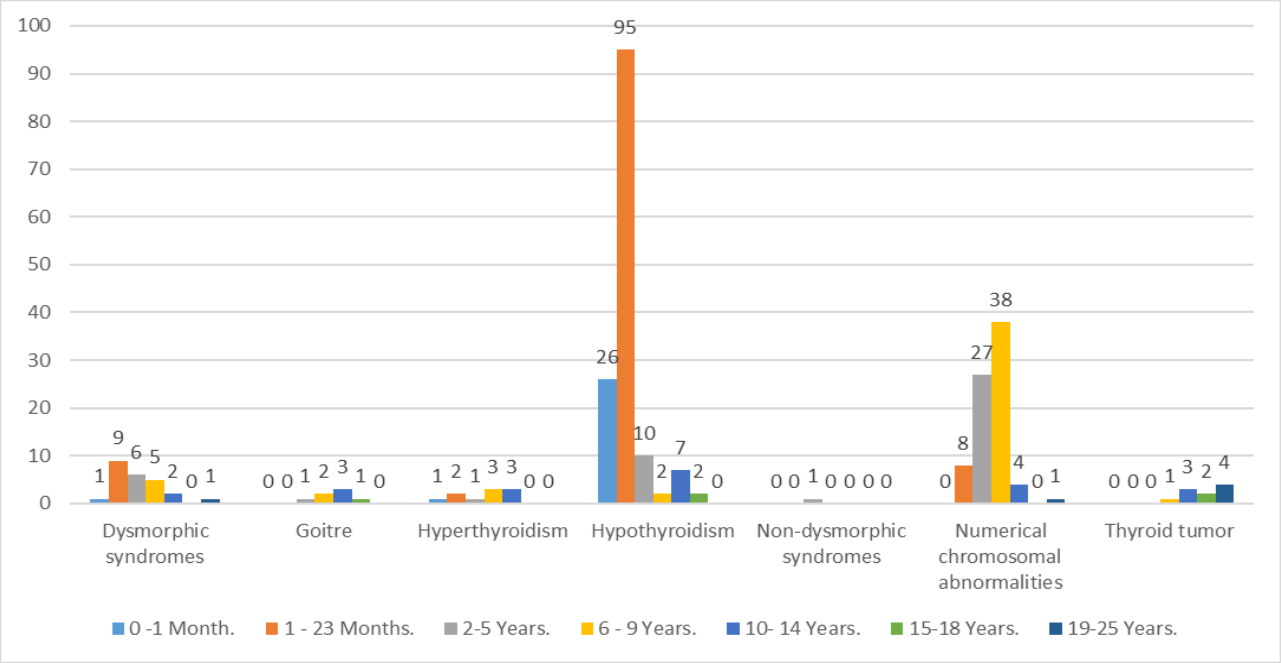


Figure 5-33 Thyroid Disorders & Syndromes with endocrine features

Children and adolescents with numerical chromosomal abnormalities got diagnosed frequently, 49.3%, between 6 and 9 years followed by 2 to 5years, 1 to 23 months and 10 to 14 years at 35%, 10.3% and 5.19% respectively. Children with dysmorphic syndromes on the other hand tended to be diagnosed earlier on in life with a decreasing frequency with increasing age as follows: 41%, 20.8% and 8.3% at the ages of less than 2 years, 2 to 5 years and 6 to 9 years respectively, figure 7.33.

5.3.5.3 Glucose and Lipid metabolism disorders and Testes and male reproductive tract disorders.

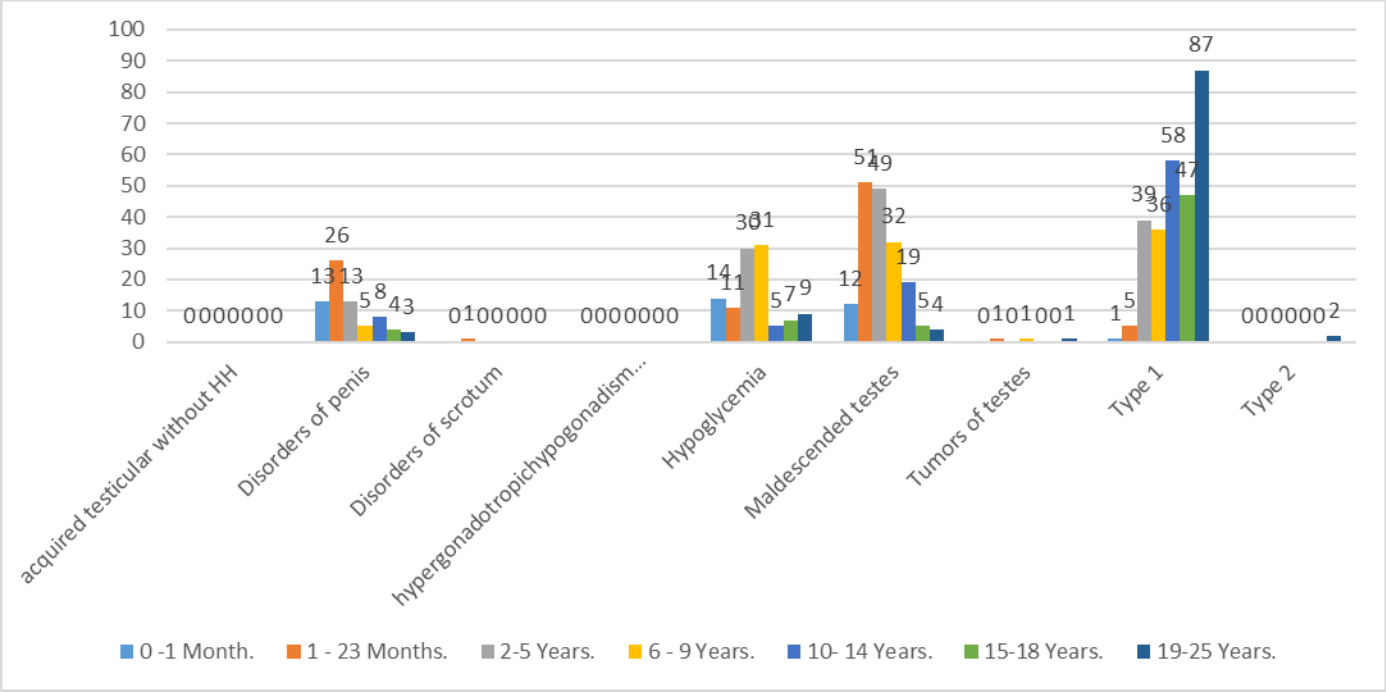


Figure 5-34 Glucose and Lipid metabolism disorders and Testes and male reproductive tract disorders

All patients with type 2 diabetes were diagnosed at the age of 19 to 25 years. Most, 36.4%, of type 1 diabetes on the other hand got diagnosed within the ages of 10 to 18 years with 20.1% falling within 10-to-14-year age group and 16.3% within 15 to 18 years. 30% of these patients got diagnosed between 19 to 25 years, 12.5% within 6 to 9 years, 13.5% within 2 to 5 years while 2% were diagnosed within the first 2 years of life. Out of the 107 patients diagnosed to have hypoglycemia, 28.9%, 28% and 23.3% got identified within the age groups of 6 to 9 years, 2 to 5 years and less than 2 years respectively. Most, 36.5%, of the patients with maldescended testes were diagnosed within the first 2 years of life although only 6.9% were picked out early within the first month of life. 28.5%, 18.6%,11% and 5.2% were identified at the ages of 2 to 5 years, 6 to 9 years, 10 to 14 years and between 15 to 25 years respectively. Similarly, most disorders of the penis were diagnosed in the first 2 years of life at 54.1% within which, 18% got identified in the first month of life. 18%, 6.9%, 11.1% and 9.3% were diagnosed at the ages of 2 to 5 years, 6 to 9 years, 10 to 14 years and 15 to 25 years respectively, figure 7.34.

5.3.5.4 Obesity & Sex Development and Gender Disorders & Puberty Disorders & Endocrine disorders of the ovaries and female reproductive tract.

Most children diagnosed with precocious puberty were identified at 2 to 5 years of age followed by 6 to 9 years at 54.5% and 36.3% respectively. On the contrary, children and adolescents who presented with constitutional delay in growth and puberty were mainly diagnosed within the ages of 10 to 14 years and 15 to 18 years at 66.6% and 33.3% respectively. Those who had ovarian disorders were majorly, 50%, diagnosed at 15 to 18 years followed by 10 to 14 years at 20%. Girls with menstrual disorders were first identified at 19-25 years of age at 66.6% followed by 15 to 18 years at 33.3%. Children and adolescents with disorders of sexual differentiation were frequently, 68.6%, diagnosed below 2 years of age with 35.8% getting diagnosed within the first one month of life. Similarly, the frequency diagnosis decreased with increasing age as follows: 14.9% and 4.4% got diagnosed within the age groups of 2 to 5 years and 6 to 9 years respectively and an equal frequency of 2.9 % for 10 to 14 years, 15-18 years and 19 to 25 years each. Girls with anatomical defects of the reproductive system were mostly, 75%, diagnosed between the ages of 15 to 25 years with only 25% getting picked out within 10 to 14 years of age. Obesity showed a variation in age at diagnosis depending on suspected etiology as follows: 25% each of the children with nutritional obesity were diagnosed within the first 2 years of life, between 2 to 5 years and 10 to 14 years of life while 12.5% got diagnosed between 10 to 14 years and 19 to 25 years of life each. Iatrogenic causes of obesity mainly had the diagnosis made within 6 to 9 years followed by 15 to 18 years at 42.5% and 28.5% respectively. Lastly, obesity from CNS causes were frequently diagnosed within the first 2 years of life followed by 2 to 5 years of age at 60% and 40% respectively, figure 7.35.

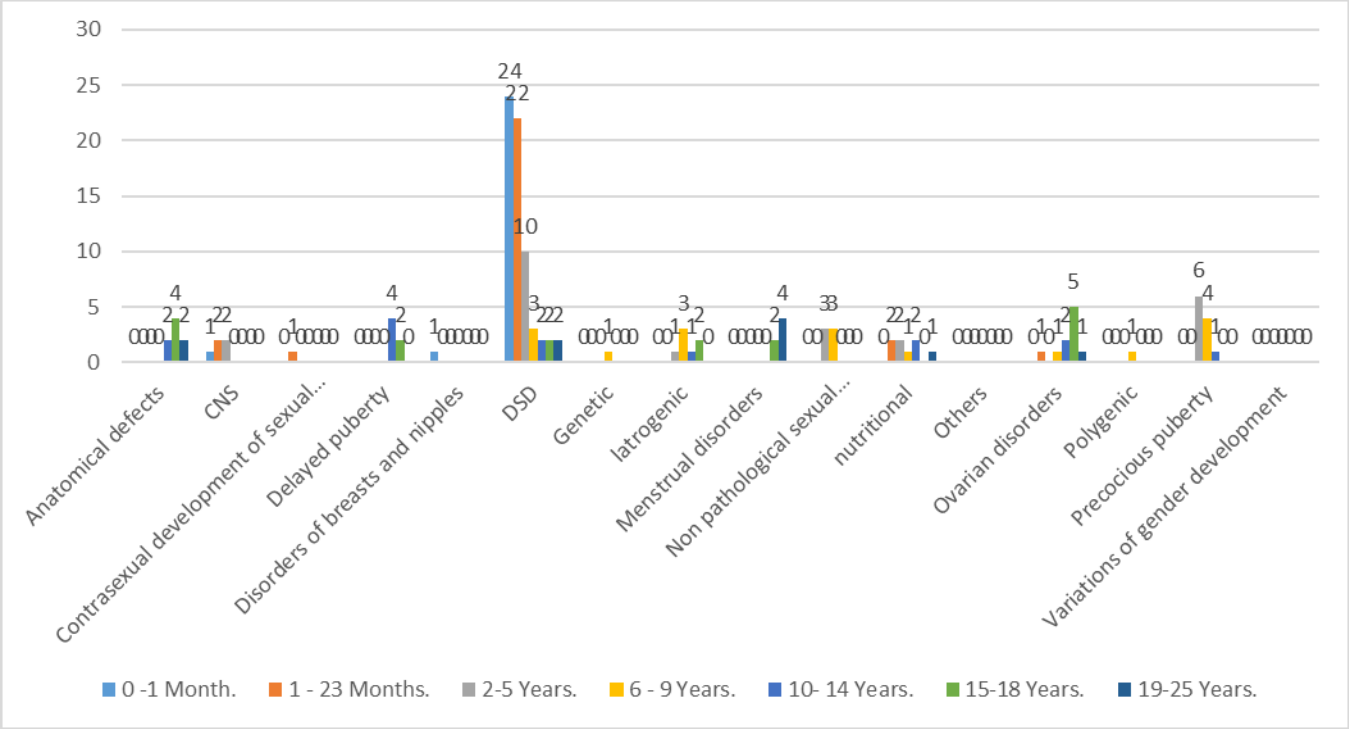


Figure 5-35 Obesity & Sex Development and Gender Disorders & Puberty Disorders & Endocrine disorders of the ovaries and female reproductive tract

5.3.5.5 Pituitary, Hypothalamus, CNS Disorders. & Disorders of the adrenal glands. & Salt and water regulation conditions. & Inborn metabolism disorders

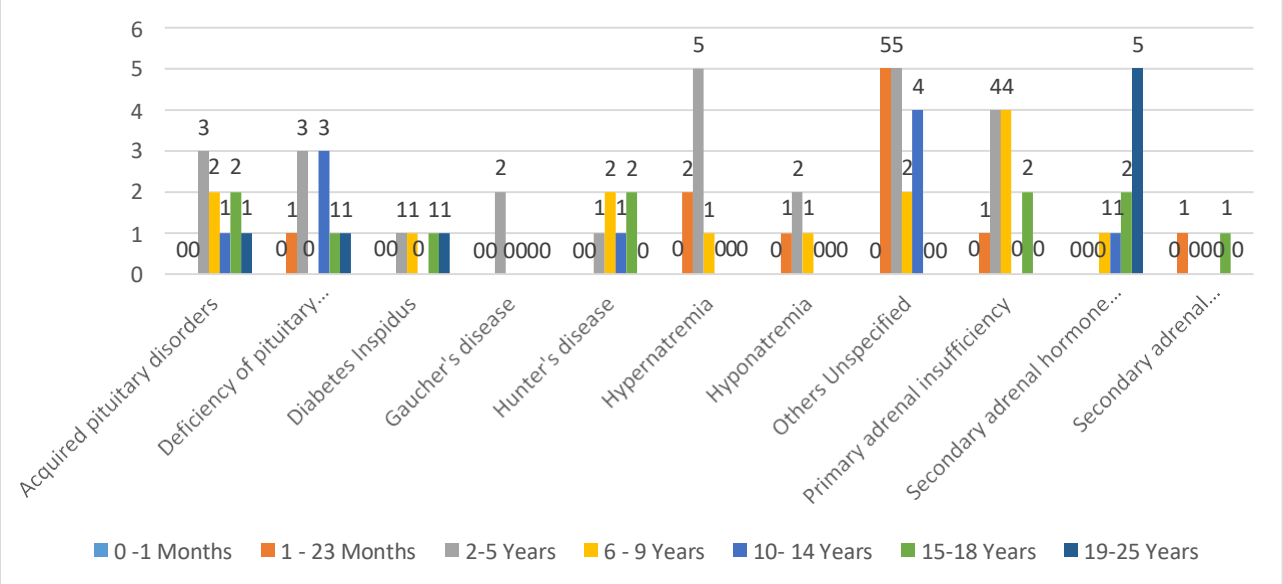


Figure 5-36 Pituitary, Hypothalamus, CNS Disorders. & Disorders of the adrenal glands. & Salt and water regulation conditions. & Inborn metabolism disorders

Patients with adrenal hormone excess were mainly diagnosed between the ages of 19-25 years and the rest between 6 to 18 years. None got diagnosed within the first 5 years of life. In contrast, those who got diagnosed with primary adrenal insufficiency were first identified mainly between the ages of 1 to 23 months and 2 to 5 years each at 45% followed by 15 to 18 years at 18% Children who had non specified inborn errors of metabolism were mainly picked out within 1 to 23 months and 2 to 5 years at 31.5% each while 25% and 12,5% constituted those who got diagnosed within the age groups of 10 to 14 years and 6 to 9 years respectively. Children and adolescents with Hunter's disease were frequently diagnosed within 6 to 9 year and 15-to-18-year age groups at frequencies of 33.3% each. On the other hand, those with Gaucher's were diagnosed within 2 to 5 years of age. Lastly, most patients diagnosed with disorders of the pituitary gland mainly got diagnosed within 2 to 5 years of age followed by 10 to 14 years of age, figure 7.36.

5.4 **Duration between symptom onset and presentation to the hospital**

Table 5:3 Duration between symptom onset and presentation to the hospital

Sub-diagnosis	***Average duration (in Days)***	***Max duration (in Days)***	***Min duration (in Days)***
Tall Stature	583	900	400
Short Stature	121	4500	7
CNS	152	365	30
Genetic	1500	1500	1500
Iatrogenic	240	400	30
Nutritional	464	1800	75
Polygenic	180	180	180
Primary adrenal insufficiency	332	2100	17
Secondary adrenal hormone excess	423	1500	30
Secondary adrenal insufficiency	235	410	60
Anatomical defects	279	1500	45
Disorders of breasts and nipples	26	26	26
Menstrual disorders	346	700	35
Ovarian disorders	263	1800	45
Hypoglycemia	56	3200	1
Type 1	80	8000	2

Type 2	183	300	65
altered bone mass	539	1500	21
hypercalcemia.	69	365	2
Osteogenesis imperfecta	486	1500	19
permanent hypocalcemia	86	850	3
Rickets	23	300	1
transient neonatal hypocalcemia	12	21	3
Gaucher's disease	330	500	160
Hunter's disease	1925	4500	300
Others Unspecified	335	1500	17
Contrasexual development of sexual characteristics	90	90	90
Delayed puberty	508	1200	300
Non pathological sexual variations(PT/PA)	142	240	60
Precocious puberty	404	900	3
DSD	724	6500	1
Goitre	363	1500	9
Hyperthyroidism	156	365	7
Hypothyroidism	79	1650	3
Thyroid tumor	124	380	24
Acquired pituitary disorders	279	900	75
Deficiency of pituitary hormones	372	1200	21
Disorders of penis	1244	8000	14
Disorders of scrotum	21	21	21
Maldescended testes	629	7000	7
Tumors of testes	140	240	60
Diabetes Inspidus	815	1200	258
Hypernatremia	14	18	10
Hyponatremia	16	17	15
Dysmorphic syndromes	229	3000	7
Non-dysmorphic syndromes	30	30	30
Numerical chromosomal abnormalities	84	1200	8

Figure 5-37 7.3.5.5 Pituitary, Hypothalamus, CNS Disorders. & Disorders of the adrenal glands. & Salt and water regulation conditions. & Inborn metabolism disorders

Patients diagnosed with rickets, hypocalcemia and hypercalcemia had a shorter duration of less than a month between symptom onset and presentation to the hospital or clinic in contrast with those who had other bone abnormalities like osteogenesis imperfecta and altered bone mass. These two conditionstook almost one and a half years to be diagnosed. Children and adolescents who had tall stature had alonger duration with a mean of over one and a half years compared to 121 days amongst those who were diagnosed with short stature.

Children and adolescents with hypothyroidism took averagely 2 and a half months between symptom onset to clinic presentation with a median age of one month while hyperthyroid patients took a longer period of averagely 5 months and a median of 3 months. Patients with goitre and thyroid tumor took averagely a year and 4 months respectively to present to the clinic. Children diagnosed with numerical chromosomal abnormalities averagely took almost 3 months with a median of 45 days to present to clinic after symptom onset in contrast to those with dysmorphic syndromes that took almost 8 months and a median age of 28 days.

Patients diagnosed to have type 2 diabetes took averagely 3 months to present to the clinic as opposed to an average of 2.5 months and a median age of 18 days amongst those with type 1 diabetes. Hypoglycemic patients took averagely 2 months to visit the endocrine clinic. Patients with disorders of testes and male reproductive tract took a much longer period with those with maldescended testes averagely taking close to 2 years with a median age of 280 days while those with disorders of the penis taking much longer at almost 3 years and a median of one year.

Patients who were diagnosed with puberty disorders averagely took 1.1 to 1.3 years with a median age of one year, those with DSD averagely took 1.9 years and a median age of 3 months, obesity cases had an average of between 0.4 to 11.2 years depending on the cause while girls who had ovarian disorders, menstrual disorders and anatomical defects took an average of 0.7 years to 1 year to present to the hospital or endocrine clinic since symptom onset.

Children and adolescents who got diagnosed with disorders of adrenals and pituitary glands took 0.7 to 1.1 years on the average while those with Hunter's disease took 5 years averagely with a median of 4.1 years to present to endocrine clinic from the time of symptom onset. Patients with Gaucher's disease on the other hand had an average of 0.9 years with a similar median, table 7.71.

5.5 Loss to follow-up

A considerable percentage, 29.9% (n=669) of patients with pediatric endocrine conditions seen at Kenyatta National hospital were lost to follow up.

5.5.1 Growth Disorders & Calcium and phosphate metabolism disorders.

Most, 50.6%, of patients diagnosed with short stature were discharged while 29.6% got lost to follow up. Similarly, majority, 66.1%, of children with rickets were discharged and 23.9% got lost to follow up. 71.4% of those who had suspected permanent hypocalcemia were lost to follow up, figure 7.38.

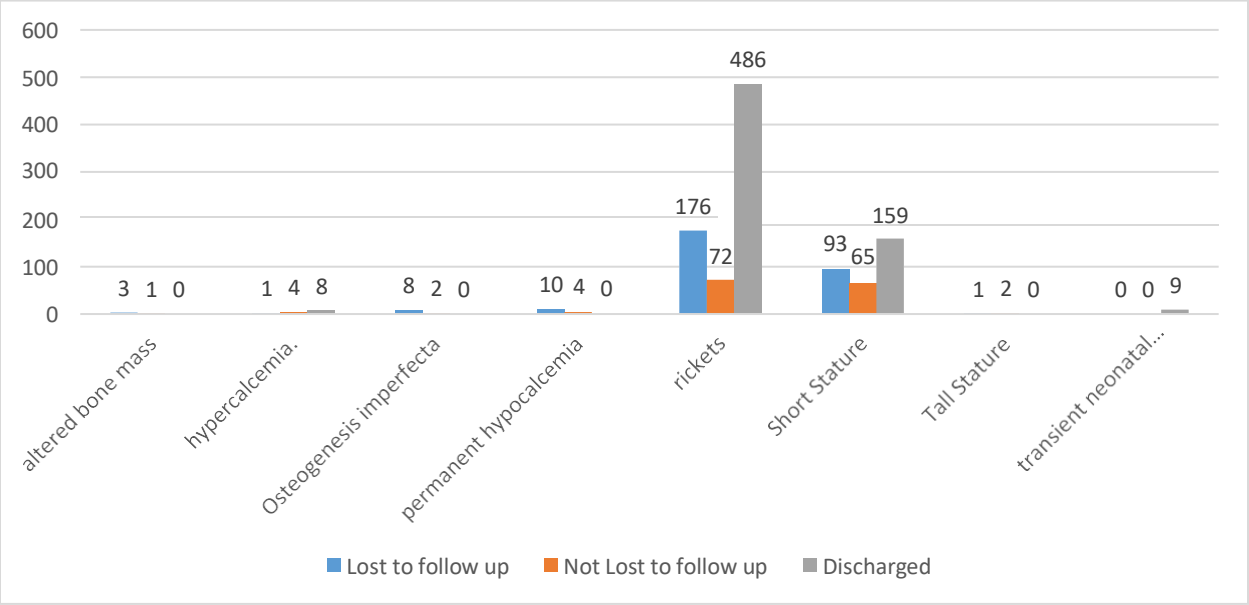


Figure 5-38 Growth Disorders & Calcium and phosphate metabolism disorders

5.5.2 Thyroid Disorders & Syndromes with endocrine features.

Out of the total patients diagnosed with hypothyroidism, 50% were lost to follow up and only 6.3% got discharged from the clinic. Contrastingly, only 1 patient, 10%, with hyperthyroidism was lost to follow up and another one case got discharged from the clinic. Most children, 45%, with numerical chromosomal disorders were lost to follow up while 11% got discharged from the clinic. Correspondingly, 39.1% of children with dysmorphic endocrine disorder were lost to follow up and 34.7% got discharged, figure 7.39.

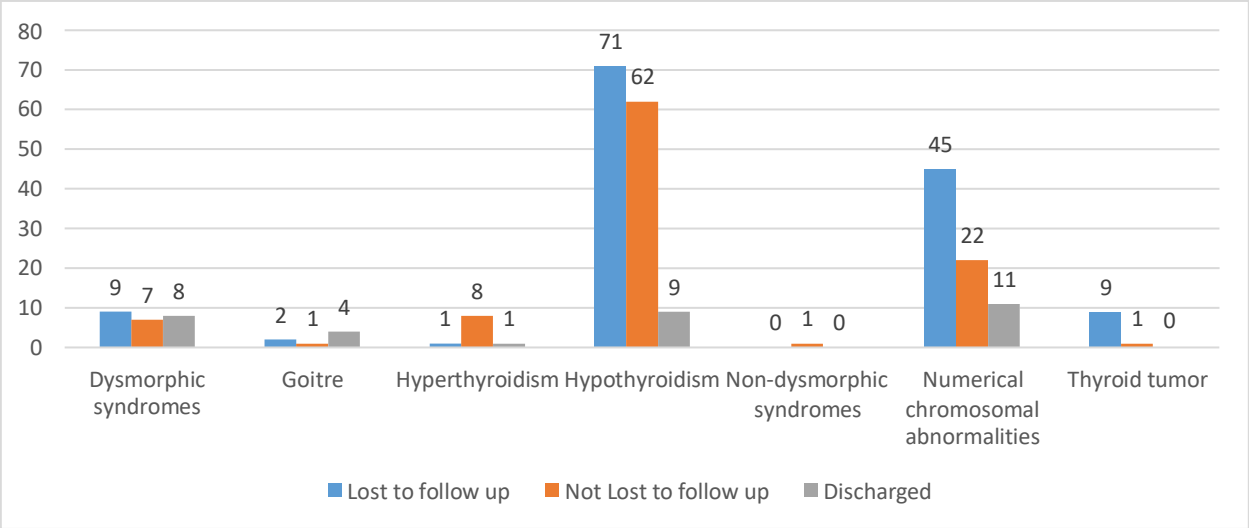


Figure 5-39 Thyroid Disorders & Syndromes with endocrine features

5.5.3 Glucose and Lipid metabolism disorders and Testes and male reproductive tract disorders.

Out of the 272 cases of type 1 diabetes, 31.25% were lost to follow up while both the 2 patients with type 2 diabetes got lost to tracking. Majority of patients with hypoglycemia, 63.5% were discharged from the clinic while approximately 15% got lost to follow up. A great percentage, 90.1%, of children and adolescents diagnosed with maldescended testes were discharged from the clinic while 7.5% got lost to follow up. Closely related to that, 77.7% of those who had disorders of the penis, mainly hypospadias, were discharged from follow up while 19.4% were lost to tracking, figure 7.40.

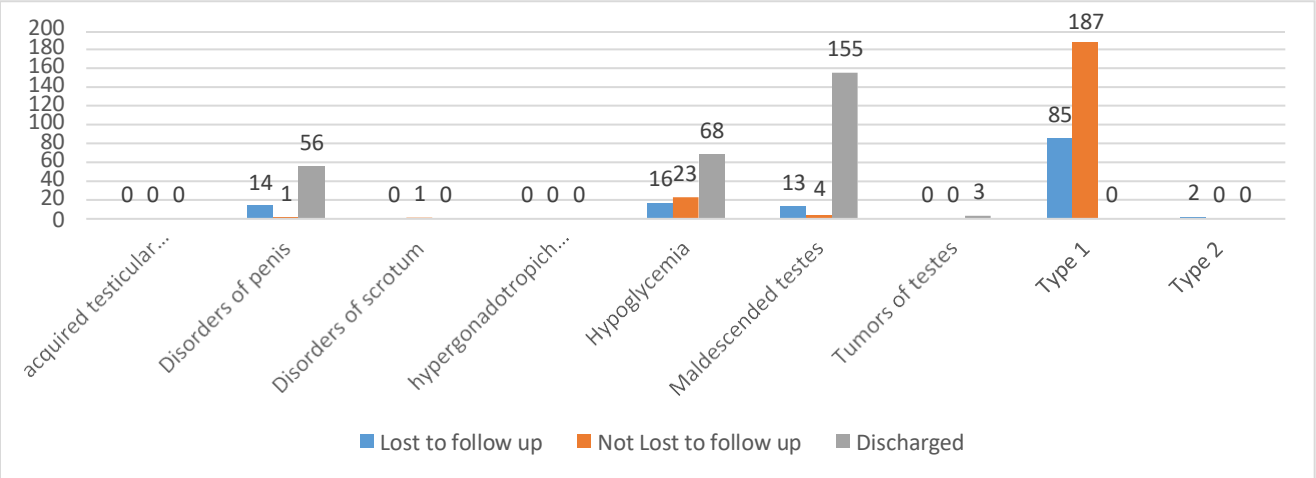


Figure 5-40 Glucose and Lipid metabolism disorders and Testes and male reproductive tract disorders

5.5.4 Obesity & Sex Development and Gender Disorders & Puberty Disorders & Endocrine disorders of the ovaries and female reproductive tract.

Approximately 36% of patients who were diagnosed to have precocious puberty got lost up while none with delayed puberty and non-pathological sexual variations was lost. Majority, 77.6%, of children and adolescents with disorders of sexual differentiation were lost to follow up, figure 7.41.

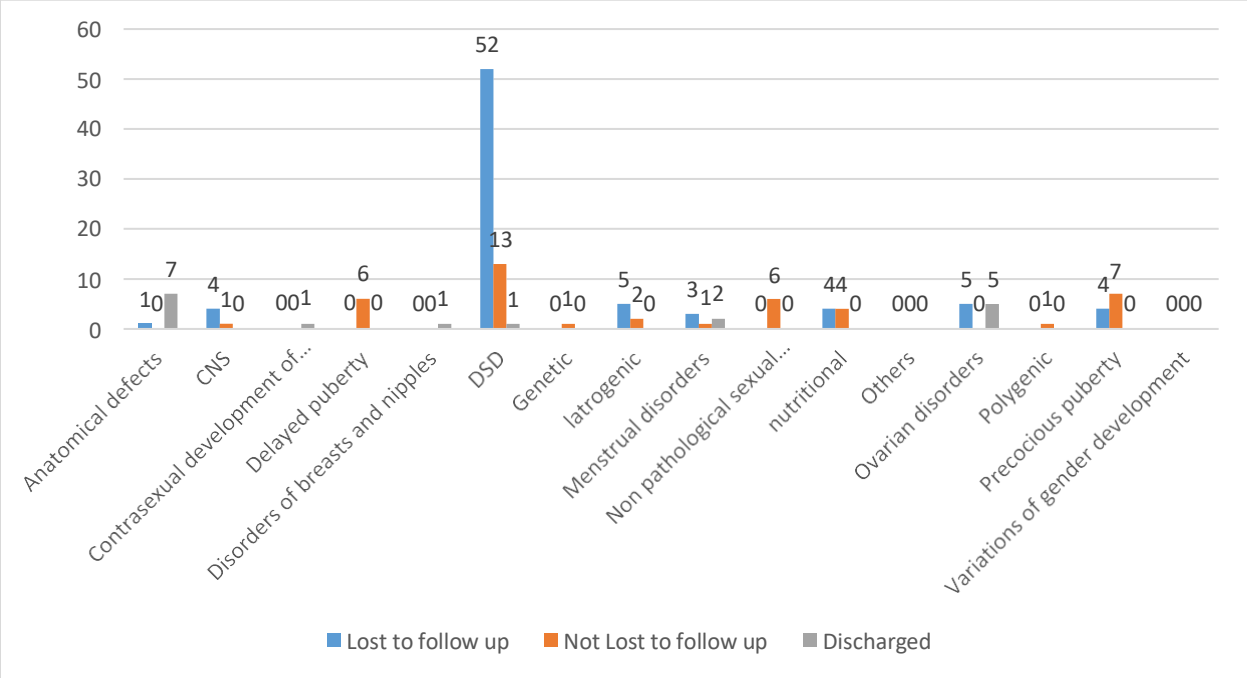


Figure 5-41Obesity & Sex Development and Gender Disorders & Puberty Disorders & Endocrine disorders of the ovaries and female reproductive tract

5.5.5 Pituitary, Hypothalamus, CNS Disorders & Disorders of the adrenal glands & Salt and water regulation conditions & Inborn metabolism disorders.

None of the patients diagnosed with Hunter's disease, secondary adrenal insufficiency got lost to follow up nor was discharged from the clinic. However, 75%, 44.4%, 22.2%, 56%, 72.7% of children with diabetes insipidus, acquired pituitary disorders, deficiency of pituitary hormones, unspecified cases of inborn errors of metabolism and primary adrenal insufficiency got lost to up respectively, figure 7.42.

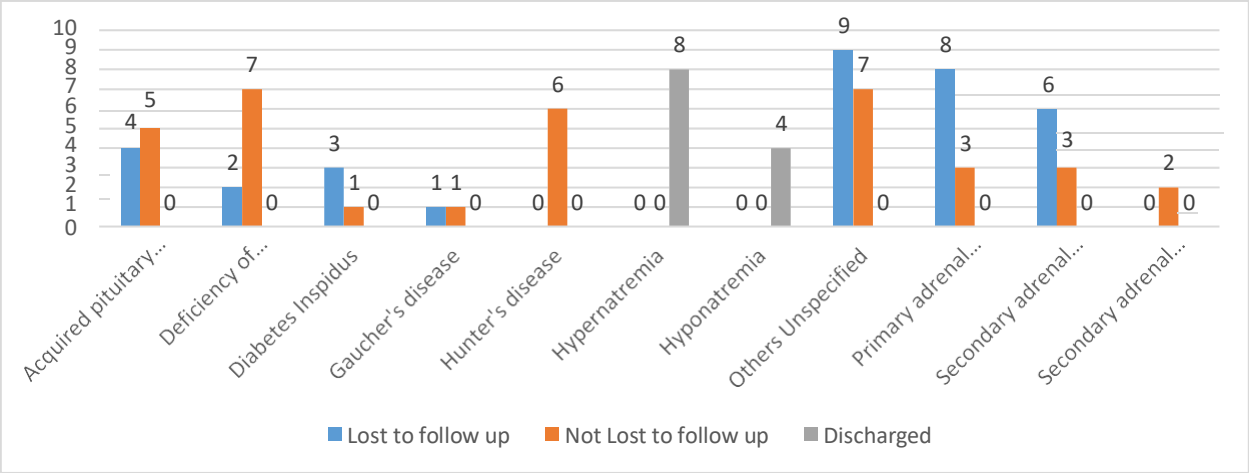


Figure 5-42 Pituitary, Hypothalamus, CNS Disorders & Disorders of the adrenal glands & Salt and water regulation conditions & Inborn metabolism disorders

6. DISCUSSION

Pediatric endocrine disorders among children and adolescents aged 0 to 25 years in Kenyatta national hospital within the period of January 2008 and December 2021 were found to be 2238. This number is less compared to Thomsett et al [14] who illustrated a total of 9062 patients in 28 years and Belloto etal [13] 2168 in a 6-year duration. This could be attributed to missing files largely from the year 2008 to 2013. However, this was much more than the studies done in Africa by Jarett et al [20] and Jaja et al [10] perhaps due to the size of the tertiary hospitals. There was notable increase in total pediatric endocrine conditions over the years perhaps attributed to increased awareness of the condition by the primary healthcare workers and resident doctors hence appropriate referrals. However, a general plunge in all the cases was noted in the year 2020. This dive in the cases seen at the hospital could have been due to restrictions of hospital visitations as well as general movements of people as a result of Covid-19.

Calcium and phosphate metabolic disorders

Calcium and phosphate metabolic disorders comprised the bulk of endocrine disorders in these patients at 35.25%. This is comparable to the study done by Nasir et al[9] that looked at the spectrum of endocrine disorders at the Pediatric Endocrine Clinic in King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia in a 10-year retrospective study as well as the study by Jarrett et al who conducted a 7-year study in Ibadan, Nigeria and looked at the burden of pediatric endocrine disorders [20.] Rickets is a disease that essentially affects the growing bones of children due to poor mineralization hence causing bone deformities and widespread systemic symptoms[21, 22.] It has diverse causes including nutritional deficiency of calcium and or vitamin D, renal causes, hereditary causes among others[23]. Nutritional rickets due to vitamin D deficiency is shown to be the most common and this is in line with most studies done worldwide and in Africa [24, 25]. Inasmuch as nutritional causes have been found to be the major cause especially in developing countries[23], recent studies have shown that it could affect children in developed countries[23]. This study together with the ones conducted by Nasir et al and Jaret et al therefore show that rickets may not entirely be a disease of developing countries. There was a male to female preponderance at 57% (1:1.4) in line with a study done by Ashwin et al[24] and Mohanna et[25] that revealed higher male figures at 53.7% and 70% respectively. However, most studies done previously show no specific gender bias[26.] Similarly, to the two studies by Ashwin and Mohanna et al, our study showed that majority at 96% of the children with rickets presented in the first two years of life, a time when most children are either still exclusively breastfeeding and or getting introduced to

complementary feeds and risk getting enough vitamin D from the mother's milk [27, 28]. This study finding therefore validates the need for adequate nutritional supplementation as well as sun exposure.

Majority, of children with rickets were brought to the hospital as self-referral perhaps reflecting the acute nature of accompanying symptoms like seizures, breathing problems and fever. Additionally, Kenyatta national hospital is proximal to several major urban low settlement areas within the city of Nairobi where majority of these children reside. Previous local studies have shown increased prevalence of rickets in the urban areas[29]. Nairobi county constituted majority of referrals followed by Kiambu county not only due to the proximity but also the urban high-rise buildings that have been shown to be risk factor of vitamin D deficiency[30].

The most common clinical presentations in these children were difficult in breathing, fever, poor growth and delayed milestones. The fever and difficulty in breathing have been attributed to infections like pneumonia as a result vitamin D deficiency which has been shown to modulate immune system[28-35]. Furthermore, there are several studies that have shown a positive correlation between vitamin D deficiency and recurrent respiratory infections[34]. Breathing difficulty may as well be due to dilated cardiomyopathy as a result of longstanding effects of severe hypocalcemia on the heart muscle[35]. Poor growth and malnutrition have been noted in various studies[36] to be due to poor bone mineralization and phosphate metabolism[37].

There is a declining trend of cases of rickets from the year 2013 up to dec 2021 in this study. However, this trend seems to contrast studies in developed countries that indicate an increasing trend in the last decade[38, 39]. This is despite the efforts that had been put in place overtime to reduce the burden of nutritional rickets like food fortification and vitamin D supplementation to exclusively breast fed infants[40]. There are however no published studies in developing countries that have looked at the recent trend of rickets in children. This declining trend among these cases at Kenyatta national hospital could perhaps also be attributed to policy change at Kenyatta national hospital that could have led to stringent measures on referrals from county hospitals as well as an increase in consultation and admission fees hence barring admissions of some of these cases. Population studies may be needed to correlate these results.

The average time taken by children diagnosed with rickets from symptom onset to presentation to hospital is twenty-three days with a median of 14 days. However, they may have presented with other

more acute conditions like pneumonia or fever before the diagnosis of rickets in the hospital. Majority, 66%, of these children got discharged from our clinics indicating that nutritional rickets is more common and is largely treatable. Nonetheless, a significant percentage, 24%, got lost to follow up. More data on the reasons for loss to follow up may be crucial in reducing this number and ensuring effectiveness during follow up of patients.

Glucose and lipid metabolism disorders

Glucose and lipid metabolism disorders were the second leading pediatric endocrine disorders at 381 forming 17.03% of the total cases. Out of these, type 1 diabetes formed the bulk at 64.3% followed by hypoglycemia at 23.3%. Only 2 patients were identified to have type 2 diabetes. This study correlates with several studies, namely Jaret et al[20], Thomsett et al[14] and Jaja et al[10]that found that type 1 diabetes was the second leading pediatric endocrine disorder in their studies. There is an overall increasing trend of type 1 diabetes in the period 2008 and 2021 in this study. This trend correlates with global reports of worsening numbers in pediatric type 1 diabetes[41-43] as well as studies done by Thomsett et al [14] and Nasir et al [9]. It is known that development of type 1 diabetes is a factor of genetic predisposition, immunological factors, lifestyle and environmental insults[44-48]. Nevertheless, factors that could be driving the increase are still under study but could be attributed to change in environmental factors owing to the similar increase in other autoimmune disorders[49]. Increased awareness of the condition by the general public may be a contributing factor as well. There was a female preponderance correlating with Ayotunde et al[11]. We however didn't stratify the gender into different age groups like the Swedish and Italian studies that showed different findings of male preponderance but only amongst patients with type 1 diabetes aged 0 to 14 years [50,51]. In these studies,they attributed the effect of male hormones on insulin resistance[50]. Some studies nevertheless found no gender differences beyond 15 years[50] while others observed the male gender preponderance only inthe population with high incidence rate[51].

Majority, 36.4%, of the patients with type 1 diabetes in our study were diagnosed between the age of 10 to 18 years within which the 10-to-14-year age group having a greater frequency than the 15-to-18-year age group. The high incidence of the 10- to 14-year-olds has been noted in a number of studies[52-53] and this is thought to be as a result of the effect of sex steroid hormones on insulin resistance[54]. Adolescents aged 19 to 25 years formed the second leading group in Type 1 diabetes frequency at 30%. Generally, population studies have showed that the incidence rate beyond puberty tend to attain

a plateau between 15 to 29 years[55]. A considerable number, 28%, of children below 9 years in this study were found to have type 1 diabetes and this implies a longer duration and burden of the disease as well as a more immediate challenge of caring for a young child with new onset type 1 diabetes[56].

Nairobi county contributed a significant percentage of children with type 1 diabetes followed by Kiambu and Kajiado counties perhaps due to proximity to Kenyatta national hospital. Great majority, 90.2%, of children and adolescents with type 1 diabetes presented in diabetic ketoacidosis at diagnosis. Diabetic ketoacidosis at diagnosis has been shown to be an indicator of inadequate awareness of symptoms of diabetes, delayed access to health care, poor education amongst primary healthcare workers and low socioeconomic status[57]. Our finding contrasts studies done in developed countries that have for instance shown a decreased incidence to below 20% in Scandinavian countries[58] and an incidence rate of 38.9% in United states[59]. However, in certain states like Carlifonia, Washington and Colorado, the incidence has been increasing over time up to 46.5% amongst the youth possibly due to lack of access to health insurance[59-61]. Diabetic ketoacidosis at presentation essentially means the diagnosis of type 1 diabetes is delayed. Various studies have shown that delayed diagnosis of type 1 diabetes increases complications and risk of death[62], prolongs hospitalization time, reduces chances of entering clinical remission, it is associated with poor future metabolic control and eventually increases the risk of long-term microvascular and macrovascular complications[63-66]. There is paucity of data on the incidence of diabetic ketoacidosis at diagnosis in developing countries, nevertheless, some studies have shown high mortality rates and increased duration of hospital stay amongst these children at Kenyatta national hospital[67]. In a systematic review, DKA rates varied from 14.7% (Denmark) to 79.8% (Saudi Arabia)[68]. Diabetic ketoacidosis is a preventable disease especially amongst the youth who classically present with polyuria, polydipsia and sometimes weight loss. The second commonest presenting complaint was weight loss followed by fever from various febrile illnesses. Weight loss is as a result of the catabolic nature of the disease owing to inadequate insulin[69]. A number of patients presented with febrile illness and this could have triggered them into the acute state of diabetic ketoacidosis. Polyphagia wasn't a common presentation in these cohort of patients as is usually seen in type 2 diabetes[70]. Few patients presented with the classical symptoms of polyuria, polydipsia and weight loss without Diabetic ketoacidosis implying that most may not be aware of typical symptoms of diabetes that necessitate early hospital visitation.

Considerable number of patients, 31.5%, got lost to follow up. There are no local similar studies on loss to follow up in type 1 diabetes but a study done in Uganda recently showed a high percentage, 93%, of loss to follow up amongst type 2 diabetes patients[71]. More studies are needed to stratify the kind of patients getting lost to follow up and reasons thereof.

Average time taken between symptom onset and presentation to the clinic was eighty days, with a median age at 18 days varying between 1 to 8000 days. This differs with findings by Rashed et al[72] in Saudi Arabia who found an average of 15 days, varying between 1 to 365 days and a median of 14 days. This wide variation in our study means that possibly some of these patients were being treated for some different medical condition or they passed through other medical facilities for initial management of type 1 diabetes before getting referred to KNH. There therefore needs a further study to get more information on the delay.

Around 90% of patients with type 1 diabetes were admitted, majority because of DKA, validating previous studies that have reported increased medical costs in management of these patients[64].

Thyroid disorders

Thyroid disorders constituted 7.65% of the total pediatric endocrine cases, forming the 5th commonest endocrine disorder seen at Kenyatta national hospital. This closely reflects the study findings by Thomsett et al[14], Jaja et al[10], Jaret et al[20] that found that thyroid disorders were the 4th, 3rd, and 6th leading pediatric endocrine disorder respectively. The incidence of thyroid disorders has gradually increased in the last five years with the highest incidence in the year 2021**.(fig..).** This increase reflects the general reported rise in autoimmune conditions in the recent past[73]. It may also reflect increased awareness by the primary doctors on the condition although more studies would help confirm or refute this. Hypothyroidism constituted the majority of cases at 84% while hyperthyroidism and goitre formed 5.9% each. This is in keeping with a study done at a tertiary hospital in India that found that hypothyroidism comprised 93% of all thyroid disorders while hyperthyroidism had 6% and goitre was rare[74,75]. Oyenusi et al in Nigeria found congenital hypothyroidism to have a prevalence of 46.7% with a total thyroid disorder being 13.6% of all the pediatric endocrine disorders[76]. Subclinical hypothyroidism, defined as mild thyroid failure with normal peripheral hormones but slightly elevated thyroid stimulating hormone[77] was the commonest amongst hypothyroid conditions at 60.5% followed by overt primary hypothyroidism and central hypothyroidism at 25.3% and 13.3% respectively. These

findings are in keeping with two studies done in India[78,79] that found that subclinical hypothyroidism is the commonest in the general population. This condition often goes unrecognized and may progress to overt hypothyroidism with clinical consequences. Children and adolescents diagnosed with hyperthyroidism commonly presented with weight loss, palpitations, tachycardia and goitre. These clinical presenting complaints are as a result of the increased effect of excess peripheral thyroid hormones on metabolism. Goitre is a universal finding in Grave's disease as a result of activation of thyroid stimulating hormone receptor on the thyroid gland hence diffuse swelling[79].

Patients with hypothyroidism on the other hand had features of congestive cardiac failure, poor growth and delayed milestones as the top three clinical presenting complaints and majority of these patients were admitted initially to stabilize them. These presenting complaints likely point to longstanding effect of underactive thyroid on general metabolism[83], heart muscle[81] and skeletal maturation and growth[82]. However, congestive cardiac failure may also be due existing comorbid congenital heart disease as reported in an Indian study[74] as well as close association with children with down syndrome who are likely to have both hypothyroidism and cardiac defect[75]. These findings correlate with Oyenusi et al[76] that also found out that poor growth and delayed milestones were the commonest presenting complaints of children with congenital hypothyroidism. With neonatal screening of congenital hypothyroidism and early diagnosis, these complications are likely to be avoided[84].

Most of the thyroid disorders were referred from Nairobi County followed by Kiambu county respectively at 56% at 9.8%. This may be due to the proximity to the national referral hospital. However, Nakuru county was third commonest referring region at 7% inasmuch as it is quite a distance from Kenyatta national hospital compared to Murang'a, Kajiado and Machakos which recorded much lower referred cases. Referrals from other clinics in the study hospital were second most common besides counties and these mainly came from pediatric cardiac clinic after patients have initially been sent for an echo from congestive cardiac failure. A smaller proportion of children were brought in as self-referrals possibly due to other acute comorbid conditions like difficult breathing. Hyperthyroid patients however were all referred from Nairobi County.

There was a male preponderance amongst children and adolescents with hypothyroidism at 1.4:1 and most frequent, 66.7%, age at presentation was 1 to 23 months, followed by 0 to 1 month, 2 to 5 years and 10 to 14 years at 18.3%, 7% and 4.9% respectively. This correlates with other studies done including the Nigerian one by Oyenusi et al[76] that noted similar gender difference and commonest age

at diagnosis of congenital hypothyroidism was 1.6 years. For children who may have congenital hypothyroidism, diagnosis beyond the first few weeks of life has been shown to pose a high risk of mental and growth retardation amongst many other complications hence the need for neonatal screening[84]. Nevertheless, hyperthyroidism had more females at 60% correlating with Oyenusi et al[76] that found that all affected children and adolescents were female as well as other peer reviewed articles [85,87]. These children and adolescents with hyperthyroidism commonly, 60% presented between 6-14 years, within which 6 to 9 year and 10 to 14 year age group constituted 30% frequency each comparable to various other studies that found a close to similar age group results [76,86,87]. The female gender preponderance and onset around puberty is thought to be attributed to the positive modulatory effect of pubertal sex steroids, more so, estrogen hormone on autoimmune diseases[86,87] as well as the effect of the X chromosome on autoimmune diseases[87]. X chromosome stains many immune related/regulatory genes hence double dose in females [87].

Half of the patients diagnosed with hypothyroidism got lost to follow up while 6% were discharged from the clinic. Nevertheless, only one patient diagnosed to have hyperthyroidism was lost to follow up. These findings greatly differ with the Indian study that found only 14.8% loss to follow up. Factors contributing to this may be several and a more comprehensive study is required to check on the outcomes as well.

Mean duration between symptom onset and actual presentation to the hospital was 79 days and a median of 30 days in hypothyroid patients and an average of 156 days with a median of 98 days in hyperthyroid patients. The findings signify the need for greater awareness of the conditions among the primary health care workers and general population, increased need for neonatal screening and need to improve the referral system.

Growth disorders

There was a sharp reducing trend of growth disorders up to the year 2020 with a slight gradual rise thereafter. This reducing trend was similar to rickets, perhaps signifying a connecting relationship between these two disorders. Majority of the growth disorders presented with short stature and failure to thrive was the most common. This finding closely correlates with studies done by Belloto et al[13] and Thomsett et al[14] that found that short stature was the commonest endocrine diagnosis. These study findings are in keeping with several that record failure to thrive as leading causes of short stature and

in fact causes of failure to thrive must always be ruled out first during evaluation of a patient with short stature[88,89]. Failure to thrive presents with both height and weight retardation and has varied causes ranging from poor nutrition, inadequate caloric absorption, social, psychological and environmental factors, chronic illnesses, cardiac defects and chromosomal abnormalities[88,90]. Nasir et al[19] however recorded that familial short stature was the most frequent cause of growth disorder in his study correlating with other studies[89] but contrasting with ours where no single case of familial short stature was recorded. This may have been either underdiagnosed, misdiagnosed or perhaps there was reduced awareness of the condition. Secondary causes of short stature were considerable at 4.4% and were as a result of adrenal tumors, hypothyroidism and pituitary tumors with the treatment sequelae. There were only five confirmed cases of primary short stature in this study, comprising 1.4% of the total short stature cases. This finding doesn't correlate with an Indian population study that found the prevalence to be 6.8%[91.] Primary short stature has causes intrinsic to the growth plate and may be dueto growth hormone deficiency, skeletal dysplasias or syndromic cases[92]. All cases of tall stature were secondary to conditions relating to precocious puberty. This differs with reports in literature that records familial tall stature as the most common cause[93].

Majority of patients with short stature presented with delayed milestones, malnutrition and convulsions at 40%, 31% and 28% respectively indicating possible underlying pathological causes in keeping with failure to thrive. Tall stature on the other hand commonly presented with penile enlargement followed by acne and early pubic hair development in keeping with precocious puberty. Most, 90%, of the patients with short stature were initially admitted in the wards probably to manage accompanying comorbid conditions associated with malnutrition, convulsions and delay in milestones. Only one patient, however, with tall stature got admitted. Nairobi county recorded the greatest number of patients with growth disorders at 65.6% possibly due to proximity to the tertiary institution but also correlates with the trend in rickets, perhaps due to slum congestion and poor socioeconomic status[g]. Kiambu, Murang'a, Kajiado and Nyeri counties followed at a far distance at 7.9%, 4.7%, 2.8% and 2.8% also perhaps due to proximity to Kenyatta national hospital.

Majority of the children and adolescents who were diagnosed with short stature were male at 60.7% and had the diagnosis frequently, 87.4%, made below 2 years of age. This is because majority who had failure to thrive presented with various other underlying conditions like malnutrition, delayed

milestones and convulsions hence early diagnosis. These findings are in keeping with Kahlil et al[95] that found a male preponderance and majority frequently presented within the first 2 years of life.

All patients who were diagnosed with tall stature on the other hand were male and mainly presented within 6 to 9 years of age as a result of precocious puberty. A great percentage of patients with growth disorders, 50.6%, more so those with short stature were discharged since majority of their underlying conditions are treatable just like nutritional rickets. 29.6% of the ones with short stature got lost to follow up but only one patient with tall stature was lost to follow up. This difference could be explained by several factors which can only be elucidated in a different study.

The mean duration between onset of symptoms to presentation at Kenyatta national hospital was 121 days with a median of 26 days for patients diagnosed to have short stature. However, this had a wide variation between 7 days and 4500 days. This wide variation may be due to the nature of presenting complaints and perhaps late diagnosis. Patients who were diagnosed to have tall stature on the other hand had a mean duration of 583 days and a median of 450 days with an interval of between 400 and 900 days. Since majority of patients who had tall stature first presented with penile enlargement and pubic hair, it is possible these were not easily picked out by the care givers owing to the age of diagnosis as well. Overall, there is a delay to presentation to the tertiary institutions and efforts should be mad towards increasing awareness in the general population, continued education to primary health care workers on anthropometry and improve referral systems.

Disorders of the testes and male reproductive system

Disorders of the testes and male reproductive system comprised 11.6%, 252 cases, of the total endocrine cases. Notably, majority were seen and treated between the years 2013 to 2016, a time when free urology camps were prevalent at Kenyatta national hospital, surgical unit. There is ongoing discussion on when and how to conduct hormonal profile on first contact with children presenting with these disorders [24, 25, 26]. Population studies have shown that undescended testes occur in 1% of boys by 1 year of age, 3% in full term neonates and 33% in preterm babies[96]. In our study, maldescended testes and disorders of the penis were the most common cases at 64.6% and 28% respectively. Maldescended testes were either unilateral or bilateral. Descent of testes is usually depended on 2 stages, the intraabdominal and inguinoscrotal stage and both of these levels depend on the thickening of the gubernaculum, effect of testosterone, Anti-mullerian hormone and to some extend members of the

HOX gene family[97]. There is recorded increasing prevalence due to endocrine disrupting chemicals in the environment or breastmilk hence interfering with the action of factors that control testicular descent[97]. Disorders of the penis were majorly hypospadias with or without chordee. Its exact etiology is still under study but it has been shown to be a factor of genetics, environmental and endocrine factors[98]. It has been demonstrated that males presenting with hypospadias may have reduced androgens or with receptors that lower androgen sensitivity. In utero exposure to estrogens in pesticides and plastic linings may reduce androgen effect[99]. Majority of patients with hypospadias, 85.9%, presented with isolated malformation while the rest had hypospadias with either ambiguous genitalia and or undescended testes and this is in line with the study conducted by Rodrigues et al[98]. A half of the patients with maldescended testes had unilateral cryptorchidism while 43% had bilateral undescended tests. The rest presented with either inguinal hernia with or hypospadias. Almost all the penile disorders were hypospadias and epispadias of varying degrees with or without chordee. Some patients comprising 3.2% presented with both maldescended testes and hypospadias. These patients could have likely had disorders of sexual differentiation owing to the varied degrees of hypospadias, presence of chordee and accompanying bilateral descended testes. It is generally recommended that patients presenting with bilateral cryptorchidism or those with undescended testes with additional malformations undergo endocrine and genetic evaluation to determine karyotype and 17-hydroxyprogesterone levels as well as level of androgen and Anti-mullerian hormone level[96,101]. Most, of the patients with maldescended testes and hypospadias were admitted at 94.7% and 98% respectively mainly in paediatric surgical units for surgery and majority did not pass through the paediatric endocrinology clinic for preliminary evaluation first. It is possible that a number of these patients could have had endocrine conditions that could affect fertility or reproductive function at a later stage in life and a number may have associated malformations like renal malformations, aniridia, Wilm's tumor, CHARGE syndrome among others[98]. Most of the cases of maldescended testes and penile disorders came from Nairobi County followed by Kiambu, Murang'a and Machakos perhaps due to proximity to the national referral hospital. There were a few patients who presented with ambiguous genitalia but a greater percentage were phenotypically male. Notably, majority, 36.5%, of patients with maldescended testes presented in the first 2 years of life followed by 2-5 years, 6 to 9 years, 10 to 14 years and more than 15 years of age at 28.4%, 18.6%, 11% and 5.2% respectively. However, only 6.9% were picked out early within the first month of life indicating missed opportunities in early identification. On the other hand, majority, 54.1%, of patients with hypospadias presented in

the first 2 years of life followed by 2-5 years, 6 to 9 years, 10 to 14 years and over 15 years of age at 18%, 6.9%, 11.1% and 9.3% respectively. There is a slight similarity of these findings to Chenabwei et al[100] that found that 16.8% of children with hypospadias presented at 18 months of age and this delayed surgical management whereby most underwent corrective surgery beyond 18 months of age as opposed to the recommended 6 to 18 months [101,102]. This late presentation has been shown to have a negative impact on the functionality of the testes hence impaired fertility[101], increased risk of testicular cancer and general low quality of life due to poor urinary stream as a result of delayed correction of hypospadias [102]. More studies are definitely needed to inquire on the reasons of late presentation to the hospital. We found that 90% and 77.7% of patients with maldescended testes and hypospadias were discharged respectively, 19.4% and 7.5% with hypospadias and cryptorchidism were lost to follow up respectively while the rest, 2.3% and 1.3% of cryptorchidism and hypospadias are still on follow up respectively. Owing to the risks anticipated with late presentation of these conditions and underlying causes like androgen insensitivity, it is recommended that patients with bilateral undescended testes and or hypospadias get followed up till puberty to ascertain reproductive functionality [102]. There was a long duration between symptom onset and presentation to the hospital with a mean of 629 days and interval of 7 to 7000 days and a median of 280 days for maldescended testes and a mean of 1244 days and interval of 14 to 8000 days with a median of 363 days for disorders of the penis. This significantly differs with a study by Wenzler et al [103] that showed most patients presented within 6 months of life and were referred to pediatric surgical specialist immediately a diagnosis was made. Diagnosis of these disorders is mainly made by physical examination and this should be done early to facilitate timely correction. Early treatment can reduce but not eliminate risk of reduced fertility and testicular malignancy hence the need to follow up [104].

Sex development and gender disorders

Sex development and gender disorders constituted 2.67%, 67 cases, of the total endocrine cases seen at Kenyatta national hospital and all of these cases comprised disorders of sexual development. These cases peaked between the year 2013 to 2016, possibly because this was a period in which Kenyatta hospital ran various urology camps. There was no single case reported in 2020, a year in which Covid-19 affected patient visits to hospitals. This finding poses the question on how and where urgent cases like CAH were managed from. Ambiguous genitalia were the most frequent presenting complaint at 84.8% followed by hypospadias and undescended testis with or without micropenis at 15 %. This

finding is closely in tandem with the studies done by Amolo et al[105] and Kihiko et al[106] both done at Kenyatta National hospital that found a frequency of 93% and 87% respectively. Disorders of sexual differentiation may present with overt genital ambiguity, apparent female phenotype with clitoral enlargement, apparent male phenotype with hypospadias, undescended testes or micropenis or discordance between the phenotype and prenatal karyotype findings[107]. Majority, 74.6% of these patients were admitted at some point during follow up for work up or surgery. Most cases, 67%, were referred directly from various counties while 31.3% got referred from other Kenyatta national hospital clinics. Nairobi county formed the bulk of referrals at approximately 50% followed by Kiambu and Makueni county at 9% and 6% respectively. Murang'a, Kajiado and Machakos counties constituted 4.5% each. This referral pattern could be because of proximal distance to the referral hospital. However, the fairly considerable cases from Makueni county may warrant a follow up study to determine the cause. Majority, 84.8%, of these patients had undefined gender at presentation while those who had been gender assigned as male or female were 13.6% and 1.5% respectively. Most, 68.6%, children with DSD were diagnosed within the first 2 years of life within which only 35.8% got identified in the first month of life. This was followed by 2 to 5 years, 6 to 9 years and 10 to 25 years at 14.9%, 4.4% and 8.7% respectively. The median age at diagnosis was 5 months in tandem with Amolo et al[105] who found the mean age at diagnosis to be 2.7 years with a median of 3 months. Similarly, it correlates with one done by Kihiko et al [106] that recorded patients from 1 to 19 years with a median of 5 months. Most of these conditions could easily be picked out right from birth by either the parent or the midwife since majority present with ambiguous genitalia. These findings mean most cases are either missed or there are uncertainties in decision making hence the need for further studies to determine the actual reason. From literature, late diagnosis could be due to previously unrecognized genital ambiguity, inguinal hernia in a girl (for example complete androgen insensitivity), delayed or incomplete puberty, primary amenorrhea or virilization in a girl, breast development in a boy, and gross or cyclic hematuria in a boy[107]. Majority of these cases, 78.7%, got lost to follow up while only 1.5% were discharged from the clinic. This massive percentage loss to follow up is concerning and follow up study is needed to decipher the reasons. It is generally recommended that management of these cases require a well-structured multidisciplinary team, including psychologists and socialworkers to follow up these patients[106]. Long-term follow up to transition to adulthood is of paramount importance because some of these patients are likely to require hormonal replacement especially in cases of androgen insensitivity while others need to have evaluation of long-term risk for gonadal

malignancy [107,108]. Duration from onset of symptoms to presentation to the hospital varied from 1 day of life to 6500 days with a mean of 724 days and a median of 90 days. The long duration of presentation has negative implications including challenges in societal integration after gender re-assignment, re-naming, cognitive and social functioning as well as endocrine effects on phenotypic development[109].

Syndromes with endocrine features

Syndromes with endocrine features comprised 4.7% of the total pediatric endocrine cases seen at Kenyatta national hospital. Out of this, presumed numerical chromosomal abnormalities constituted 78% while dysmorphic syndromes were 23%. Out of the numerical chromosomal abnormalities, Down syndrome was the most frequent at 97% while Turner's syndrome had only one case. The frequency of Down syndrome is in keeping with various other studies that have a found a high prevalence in numerical abnormalities[110]. Dysmorphic syndromes commonly presented with difficulty in breathing followed by convulsions at 60.8% and 39.1% respectively. Numerical chromosomal abnormalities on the other hand had features of congestive cardiac failure, poor growth and pneumonia as the most common presenting complaints at frequencies of 45%, 32% and 23% respectively. This correlates with studies found in Down syndrome patients that reported similar findings of increased incidence of cardiac defects amongst children with Down syndrome[111,112] hence the recommendation to have all children with Down syndrome undergo neonatal echo evaluation[113]. Poor growth may be associated with the presence of cardiac defects, gastrointestinal abnormalities, thyroid disorders, musculoskeletal abnormalities among others[113]. Most patients, 88.3%, of patients with numerical chromosomal abnormalities were admitted with an almost similar frequency, 86.9%, among those with dysmorphic syndromes. This correlates with the study by Esperanza et al and may be due to other accompanying co-morbid conditions affecting various body systems like cardiac, central nervous system or gastrointestinal system[114]. Majority, 76.4% of dysmorphic syndrome conditions were referred from the counties while the rest came from other Kenyatta national hospital clinics. Similarly, majority, 63.8%, of patients diagnosed with numerical chromosomal abnormalities were referred from various counties but a substantial percentage, 27.7% were sent from other Kenyatta national hospital clinics, mainly cardiac clinic. Nairobi county recorded bulk of referrals in both dysmorphic and numerical chromosomal abnormalities at 76.4% and 57% respectively followed by Kiambu and Murang'a counties due to nearness to KNH. There was a male preponderance in both dysmorphic and numerical

chromosomal abnormalities at a ratio of 2:1 and 1.16:1 respectively. This tallies with the findings in other studies[115] that found a slight male preponderance in large studies. Most the children with numerical chromosomal abnormalities presented at the age of 6-9 years followed by 2-5 years, less than 2 years and 10 to 18 years at 49.3%, 35%, 11% and 5.2% correspondingly while dysmorphic syndromes mainly presented below 2 years at 41% followed by 2-5 years and 6-9 years at 20.8% and 8.3% respectively. This discrepancy at age of presentation in these two conditions may be due to reduced awareness of features of Down syndrome by the general population hence delayed referrals. This differs with population studies carried out in some developed countries that found majority, 76%, had earlier hospital referrals by the age of 1 year[116]. Earlier diagnosis and identification of complications accompanying these conditions is vital in improving growth and treating cardiac abnormalities hence preventing grave prognosis [114]. Most of the patients, 57.6%, with numerical chromosomal abnormalities were lost to follow up while 11% got discharged. In view of the potential complications in these patients, it is recommended that long term follow up is done to evaluate various co-morbidities like thyroid disorders, hematological disorders among others[111,112]. Dysmorphic features on the other hand had 39.1% loss to follow up while a significant number, 34.7% were discharged. Duration between symptom onset and presentation to the hospital had a mean of 229 days, median of 28 days and an interval of 7 to 3000 days for dysmorphic syndromes and a mean of 84 days, median of 45 days and interval of 8 to 1200 days amongst cases of numerical chromosomal abnormalities. These correlate with presenting complaints like poor growth and congestive cardiac failure that pointed towards late presentation to the hospital. It is necessary to mention however that most of these syndromic conditions were diagnosed clinically without genetic confirmation owing to the high cost and unaffordability by majority of patients who attend public hospitals.

7. CONCLUSION AND RECOMMENDATIONS

Rickets, failure to thrive, type 1 diabetes, disorders of the testes and penis, Down syndrome and thyroid disorders top the list of pediatric endocrine disorders seen at KNH. There is a decreasing annualincidence trend in rickets and failure to thrive cases with an opposite, increasing trend in type 1 diabetesand thyroid disorders.

The study findings show a delay in diagnosis in most endocrine conditions and most children presented with symptoms suggesting longstanding effects of the disease. Majority of patients with disorders of the testes and male reproductive system got discharged. Similarly, a considerable numberof patients were lost to follow up. The recommendations from this study therefore are as follows:

1. Special training to primary care physicians and nurses on early identification of disorders like hypothyroidism, type 1 diabetes, DSD, maldescended testes and hypospadias.
2. Elaborate population education program to recognize early symptoms of type 1 diabetes.
3. There is need to allocate more resources towards management of increasing cases of T1DM.
4. There is need to synchronize management of disorders of maldescended testes and hypospadias with the pediatric surgery unit to allow endocrine investigations and follow up prior to surgery.
5. Build laboratory capacity to aid in genetic confirmation of endocrine disorders more so syndromes with endocrine conditions.
6. There is need to commence fortification of foods with vitamin D and standardize infant supplementation.
7. Neonatal screening of congenital hypothyroidism is encouraged.
8. Further studies are required to help understand factors associated with delay in diagnosis and loss to follow up in pediatric patients with endocrine disorders.
9. Kenyatta National Hospital should consider active patient tracking mechanisms to reduce loss to follow up.

8. STUDY LIMITATION

1. There was missing data in the medical records. This mainly comprised of age and marital status of parents. In such cases it was indicated as “unstated”.

2 Files from 2008 to 2014 could not be retrieved because the records department had not acquired a software for entering the ICD 10 codes. Owing to limited space in the records department a number of files in subsequent years were getting weeded out as well as the study went on. As a result, the deceased files and other files could not be retrieved.

3. Selection bias: Data was hospital based and from a single center

REFERENCES

1. Savage et al; Global Inequalities in Pediatric Endocrine Practice: Statement of Minimal Acceptable Care Statement from the International Societies for Pediatric Endocrinology. Horm Res. 2006;65(3):111-3. doi: 10.1159/000091278. Epub 2006 Feb 2.
2. Odundo et al; The Impact and Successes of a Paediatric Endocrinology Fellowship Program in Africa; Int J Endocrinol. 2016; 2016: 1560248. doi: 10.1155/2016/1560248.
3. knh.or.ke: "About Kenyatta National Hospital". Nairobi: Kenyatta National Hospital (KNH). KNH (23 October 2016).
4. Merab et al; "KNH plans to end outpatient services in two years in bid to reduce congestion". Daily Nation, Nairobi. Retrieved 23 October 2016.
5. Zacharin et al; Promoting excellence in the care of Paediatric endocrine diseases in the developing world. Paediatrics. 2013;131: 573-578.
6. Tamunopriye et al; Causes, diagnosis and treatment of central precocious puberty; Lancet Diabetes Endocrinol. AJPR, 2(2): 1-7, 2019; Article no.AJPR.47781 7. 2016;4:265-274.
7. Wit et al; ESPE classification of paediatric endocrine diagnosis. Syndromes with endocrine features. Horm Res 2007;68(suppl 2):101–106
8. Toppr: Introduction to Endocrine System (Basic).
9. Nasir et al; Spectrum of endocrine disorders at the Pediatric Endocrine Clinic, King Khalid University hospital, Riyadh, Kingdom of Saudi Arabia Journal of Taibah University Medical Sciences Volume 7, Issue 2, December 2012, Pages 99-103.
10. Jaja et al; Pattern of Pediatric Endocrine Disorders According to ICD-10 Classification in a Tertiary Centre in Southern Nigeria; Asian Journal of Pediatric Research, Page 1-7 DOI: 10.9734/ajpr/2019/v2i230103.
11. Ayotunde et al; Spectrum of Endocrine Disorders as Seen in a Tertiary Health Facility in Sagamu, Southwest Nigeria Niger Med J. 2019 Sep-Oct; 60(5): 252–256. Published online 2019 Nov 26. doi: 10.4103/nmj.NMJ_41_19.
12. Osei et al; Spectrum of Endocrine Disorders in Central Ghana; Int J Endocrinol 2017;2017:5470731. doi: 10.1155/2017/5470731. Epub 2017 Feb 23.

13. Bellotto1 et al; Pattern and Features of Pediatric Endocrinology Referrals: A Retrospective Study in a Single Tertiary Center in Italy Front. Pediatr. 02 October 2020 | https://doi.org/10.3389/fped.2020.580588.

14. Thomsett.et al; The spectrum of clinical pediatric endocrinology: 28 years of referrals to an individual consultant. J Paediatr Child Health. 2010 Jun; 46(6):304-9. doi: 10.1111/j.1440-1754.2010.01713.x. Epub 2010 Mar 29. PMID: 20367763.

15. Sherita et al; Clinical review: Prevalence and incidence of endocrine and metabolic disorder in the United States: A comprehensive review. J Clin Endocrinol Metab. 2009;94:1853-1878.

16. Jeesuk et al; Endocrine disorders and the neurologic manifestations Pediatr Endocrinol Metab 2014;19:184-190.

17. Fenichel; Clinical pediatric neurology: a signs and symptoms approach. 4th ed. Philadelphia: W.B. Saunders, 2001.

18. Sharma et al; Myopathies of endocrine disorders: a prospective clinical and biochemical study. Ann Indian Acad Neurol 2014;17:298-302.

19. Tonner et al; Neurologic complications of thyroid and parathyroid disease. Med Clin North Am 1993;77:251-63

20. Jarrett et al; Paediatric endocrine disorders at the University college hospital, Ibadan: 2002 – 2009; Ann Ib Postgrad Med. 2013 Dec; 11(2): 96–101.

21. Pettifor et al; Primer on the metabolic bone diseases and disorders of mineral metabolism. 6th ed. Washington, DC: American Society for Bone and Mineral Research; 2006. Nutritional and drug-induced rickets and osteomalacia; pp. 399–407. [Google Scholar]

22. Thacher et al; Vitamin D and rickets. Basel: Karger; 2003. Calcium-deficiency rickets; pp. 105–25. [Google Scholar]

23. Thacher et al; Nutritional rickets around the world: causes and future directions. Ann Trop Paediatr. 2006;26:1–16. [PubMed] [Google Scholar]

24. Ashwin; Prevalence of rickets: a clinical study, 2020; 10.18203/2349-3291.ijcp20200684 JO - International Journal of Contemporary Pediatrics.

25. Mohanna et al; East African Medical Journal Vol. 92 No. 12 December 2015 Prevalence of nutritional rickets among symptomatic children and associated risk factors in Specialised Paediatric Centre Yemen

26. Thierry et al; An Overview and Future Directions, with Special Reference to Bangladesh A Summary of the Rickets Convergence Group Meeting, Dhaka, 26–27 January 2006.

27. Kelsey et al; Vitamin D deficiency causes rickets in an urban informal settlement in Kenya and is associated with malnutrition.

28. Rajakumar et al; Vitamin D, cod-liver oil, sunlight, and rickets: a historical perspective. Pediatrics. 2003;112(2):e132-5.

29. Karuri et al; Clinical Information Network authors. Using data from a multi-hospital clinical network to explore prevalence of pediatric rickets in Kenya. Wellcome Open Res. 2017 Nov 1;2:64. doi: 10.12688/wellcomeopenres.12038.2. PMID: 29062911; PMCID:

30. Muhammad et al ; The Emerging Burden of Rickets: Impact of High Rise Buildings in Karachi VL - 3 The Punjab medical journal.

31. Van et al; Immunoregulation by 1,25-dihydroxyvitamin D3: basic concepts. J Steroid Biochem Mol Biol. 2005;97:93–101. doi: 10.1016/j.jsbmb.2005.06.002. [PubMed] [CrossRef] [Google Scholar].

32. Lemire et al; Immunosuppressive actions of 1,25-dihydroxyvitamin D3: prefential inhibitions of Th1 functions. J Nutr. 1995;125:1704–8. [PubMed] [Google Scholar].

33. Underwood et al; Defensin-barbed innate immunity: clinical associations in the pediatric population. Pediatrics. 2010;125:1237–47. doi: 10.1542/peds.2009-3289. [PubMed] [CrossRef] [Google Scholar].

34. Holter et al; Vitamin D status and long-term mortality in community-acquired pneumonia: Secondary data analysis from a prospective cohort. PLoS One, 11(7), e0158536 10.1371/journal.pone.0158536. 2016. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

35. Yilmaz et al; Dilated cardiomyopathy secondary to rickets-related hypocalcaemia: Eight case reports and a review of the literature. Cardiology in the Young, 25(2), 261-266. doi:10.1017/S1047951113002023

36. Ganmaa et al; Vitamin D supplementation and growth in urban Mongol school children: Results from two randomized clinical trials. PLoS One, 12(5), e0175237 10.1371/journal.pone.0175237. 2017; [PMC free article] [PubMed] [CrossRef] [Google Scholar]

37. Munns et al; Global consensus recommendations on prevention and management of nutritional rickets. Hormone Research in Pædiatrics, 85(2), 83–106. 10.1159/000443136. 2016. [PubMed] [CrossRef] [Google Scholar]

38. Thacher et al; Increasing incidence of nutritional rickets: a population-based study in Olmsted County, Minnesota. Mayo Clin Proc. 2013 Feb;88(2):176-83. doi: 10.1016/j.mayocp.2012.10.018. PMID: 23374621; PMCID: PMC3612965.

39. Robinson et al; The re-emerging burden of rickets: a decade of experience from Sydney. Arch Dis Child. 2006 Jul;91(7):564-8. doi: 10.1136/adc.2004.069575. Epub 2005 Jun 14. PMID: 15956045; PMCID: PMC2082843.

40. Zaki et al; Effect of vitamin D deficiency in developed countries, British Medical Bulletin, Volume 122, Issue 1, June 2017, Pages 79–89, https://doi.org/10.1093/bmb/ldx005

41. Lin et al; Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Scientific reports. 2020;10(1):14790. Epub 2020/09/10. pmid:32901098 PubMed/NCBIGoogle Scholar.

42. Karvonen et al; Incidence of childhood type 1 diabetes worldwide. Diabetes Mondiale (DiaMond) Project Group. Diabetes care. 2000;23(10):1516–26. Epub 2000/10/07. pmid:11023146 PubMed/NCBIGoogle Scholar.

43. Patterson et al; Diabetes in the young—a global view and worldwide estimates of numbers of children with type 1 diabetes. Diabetes research and clinical practice. 2014;103(2):161–75. Epub 2013/12/18. pmid:24331235.

44. Ludvigsson et al; Environmental risk factors for type 1 diabetes. Lancet (London, England). 2016;387(10035):2340–8. Epub 2016/06/16. pmid:27302273 PubMed/NCBIGoogle Scholar

45. Lukacs et al; Environmental factors and epidemiology of childhood type 1 diabetes. Orv Hetil. 2021;162(1):13–22. Epub 2021/01/04. pmid:33388734 PubMed/NCBIGoogle Scholar

46. Forlenza et al; The epidemic of type 1 diabetes: what is it telling us? Current opinion in endocrinology, diabetes, and obesity. 2011;18(4):248–51. Epub 2011/08/17. pmid:21844707 PubMed/NCBI Google Scholar.

47. Peng et al; Environmental factors in the development of Type 1 diabetes. Rev Endocr Metab Disord. 2006;7(3):149–62. Epub 2007/01/05. pmid:17203405 PubMed/NCBIGoogle Scholar.

48. Ferreira et al. A type I interferon transcriptional signature precedes autoimmunity in children genetically at risk for type 1 diabetes. Diabetes. 2014;63(7):2538–50. Epub 2014/02/25. pmid:24561305 PubMed/NCBIGoogle Scholar.

49. Lerner et al; The World Incidence and Prevalence of Autoimmune Diseases is Increasing International Journal of Celiac Disease,. 2015;3(4):151–5. Google Scholar.

50. Wändell et al; Time trends and gender differences in incidence and prevalence of type 1 diabetes in Sweden. Curr Diabetes Rev. 2013 Jul;9(4):342-9. doi: 10.2174/15733998113099990064. PMID: 23721159.

51. Patrizio et al; Gender Difference in Type 1 Diabetes: An Underevaluated Dimension of the Disease † Istituto I.N.I.–Via S. Anna SNC, Grottaferrata, 00046 Roma, Italy, 2022.

52. Dabelea et al; et al. Incidence of diabetes in youth in the United States. JAMA. 2007;297:2716–2724. [PubMed] [Google Scholar].

53. Incidence and trends of childhood Type 1 diabetes worldwide 1990–1999. Diabet Med. 2006; 23:857–866. [PubMed] [Google Scholar].

54. Variation and trends in incidence of childhood diabetes in Europe. EURODIAB ACE Study Group. Lancet. 2000;355:873–876. [PubMed] [Google Scholar].

55. Patterson et al; Incidence trends for childhood type 1 diabetes in Europe during 1989–2003 and predicted new cases 2005–20: a multicentre prospective registration study. Lancet. 2009;373:2027–2033. [PubMed] [Google Scholar].

56. Maahs et al; Epidemiology of type 1 diabetes. Endocrinol Metab Clin North Am. 2010 Sep;39(3):481-97. doi: 10.1016/j.ecl.2010.05.011. PMID: 20723815; PMCID: PMC2925303.

57. Limenis et al; Is the frequency of ketoacidosis at onset of type 1 diabetes a child health indicator that is related to income inequality? Diabetes Care. 2012;35(2).

58. Hekkala et al; Ketoacidosis at diagnosis of type 1 diabetes in children in northern Finland: temporal changes over 20 years. Diabetes Care. 2007;30(4):861-866.

59. Rewers et al; Incidence of Diabetic Ketoacidosis at Diagnosis of Type 1 Diabetes in Colorado Youth, 1998-2012. JAMA. 2015;313(15):1570–1572. doi:10.1001/jama.2015.1414.

60. Usher-Smith et al; Variation between countries in the frequency of diabetic ketoacidosis at first presentation of type 1 diabetes in children: a systematic review. Diabetologia. 2012;55(11):2878-2894.

61. Elizabeth et al; Increase in Prevalence of Diabetic Ketoacidosis at Diagnosis Among Youth With Type 1 Diabetes: The SEARCH for Diabetes in Youth Study. Diabetes Care 1 July 2021; 44 (7): 1573–1578. https://doi.org/10.2337/dc20-0389.

62. Desai et al; Health care utilization and burden of diabetic ketoacidosis in the U.S. over the past decade: a nationwide analysis. Diabetes Care. 2018;41(8):1631-1638. doi:10.2337/DC17-1379.

63. Duca et al. Diabetic ketoacidosis at diagnosis of type 1 diabetes and glycemic control over time: the SEARCH for diabetes in youth study. Pediatr Diabetes. 2019;20(2):172-179. doi:10.1111/PEDI.12809.

64. Aye et al. Impact of early diabetic ketoacidosis on the developing brain. Diabetes Care. 2019;42(3):443-449. doi:10.2337/DC18-1405.

65. Saydah et al; Medical costs among youth younger than 20 years of age with and without diabetic ketoacidosis at the time of diabetes diagnosis. Diabetes Care. 2019;42(12):2256-2261. doi:10.2337/DC19-1041.

66. Chiavaroli et al; Partial remission in type 1 diabetes and associated factors: analysis based on the insulin dose-adjusted hemoglobin A1c in children and adolescents from a regional diabetes center, Auckland, New Zealand. Pediatr Diabetes. 2019;20(7):892-900. doi:10.1111/PEDI.12881.

67. Musoma et al; Outcomes of Children and Adolescents Admitted with Diabetic Ketoacidosis at Kenyatta National Hospital (KNH), Kenya. J Diabetes Res. 2020 Oct 20;2020:8987403. doi: 10.1155/2020/8987403. PMID: 33134396; PMCID: PMC7593731.

68. Grobe et al; Incidence of Diabetic Ketoacidosis of New-Onset Type 1 Diabetes in Children and Adolescents in Different Countries Correlates with Human Development Index (HDI): An Updated Systematic Review, Meta-Analysis, and Meta-Regression. Horm Metab Res. 2018 Mar;50(3):209-222.

doi: 10.1055/s-0044-102090. Epub 2018 Mar 9. Erratum in: Horm Metab Res. 2018 Mar;50(3):e2. PMID: 29523007.

69. Niels et al; Sreekumaran Nair; Diabetes and Protein Metabolism. Diabetes 1 January 2008; 57 (1): 3–4. https://doi.org/10.2337/db07-1581.

70. Fournier et al; Diagnosing diabetes. A practitioner's plea: keep it simple. J Gen Intern Med. 2000 Aug;15(8):603-4. doi: 10.1046/j.1525-1497.2000.00535.x. PMID: 10940154; PMCID: PMC1495577.

71. Tino et al; Predictors of loss to follow up among patients with type 2 diabetes mellitus attending a private not for profit urban diabetes clinic in Uganda - a descriptive retrospective study. BMC Health Serv Res. 2019 Aug 23;19(1):598. doi: 10.1186/s12913-019-4415-4. PMID: 31443649; PMCID: PMC6708238.

72. Al Rashed et al; Pattern of presentation in type 1 diabetic patients at the diabetes center of a university hospital. Ann Saudi Med. 2011 May-Jun;31(3):243-9. doi: 10.4103/0256-4947.81529. PMID: 21623052; PMCID: PMC3119963.

73. Głowińska-Olszewska et al; Increasing Co-occurrence of Additional Autoimmune Disorders at Diabetes Type 1 Onset Among Children and Adolescents Diagnosed in Years 2010-2018-Single-Center Study. Front Endocrinol (Lausanne). 2020 Aug 6;11:476. doi: 10.3389/fendo.2020.00476. PMID: 32849272; PMCID: PMC7424019.

74. Singh et al; Prevalence of Thyroid Disorders in Children at a Tertiary Care Hospital in Western India. J Clin Diagn Res. 2016 Feb;10(2):SC01-4. doi: 10.7860/JCDR/2016/16315.7189. Epub 2016 Feb 1. PMID: 27042544; PMCID: PMC4800610.

75. Al Aaraj et al; Prevalence of thyroid dysfunctions in infants and children with Down Syndrome (DS) and the effect of thyroxine treatment on linear growth and weight gain in treated subjects versus DS subjects with normal thyroid function: a controlled study. Acta Biomed. 2019 Sep 23;90(8-S):36-42. doi: 10.23750/abm.v90i8-S.8503. PMID: 31544805; PMCID: PMC7233681.

76. Oyenusi et al; 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 May-Jun;58(3):101-106. doi: 10.4103/nmj.NMJ_156_16. PMID: 29962651; PMCID: PMC6009143.

77. Fatourechi et al; Subclinical hypothyroidism: an update for primary care physicians. Mayo Clin Proc. 2009;84(1):65-71. doi: 10.1016/S0025-6196(11)60809-4. PMID: 19121255; PMCID: PMC2664572.

78. Mahadevan et al; Subclinical Hypothyroidism in Children 10.1007/s13312-14-0522-9 Indian pediatrics.

79. Prabhakara et al Prevalence of subclinical hypothyroidism in children and adolescents of northern Andhra radesh population and its association with hyperlipidemia DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20175078.

80. Mathew et al; Hyperthyroidism. [Updated 2022 Jul 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537053/.

81. Udovcic et al; Hypothyroidism and the Heart. Methodist Debakey Cardiovasc J. 2017 Apr-Jun;13(2):55-59. doi: 10.14797/mdcj-13-2-55. PMID: 28740582; PMCID: PMC5512679.

82. Williams et al; Thyroid diseases and bone health. J Endocrinol Invest. 2018 Jan;41(1):99-109. doi: 10.1007/s40618-017-0753-4. Epub 2017 Aug 29. PMID: 28853052; PMCID: PMC5754375.

83. Annunziata et al; Metabolic Effects of the Intracellular Regulation of Thyroid Hormone: Old Players, New Concepts. Thyroid Endocrinology https://doi.org/10.3389/fendo.2018.00474.

84. Büyükgebiz et al; Newborn screening for congenital hypothyroidism. J Clin Res Pediatr Endocrinol. 2013;5 Suppl 1(Suppl 1):8-12. doi: 10.4274/jcrpe.845. Epub 2012 Nov 15. PMID: 23154158; PMCID: PMC3608007.

85. Tunbridge et al; The spectrum of thyroid disease in a community: the Whickham survey. Clin Endocrinol (Oxf). 1977 Dec;7(6):481-93.

86. Madhukar et al; Grave's Disease in Childhood Published: December 1st, 2021 DOI: 10.5772/intechopen.97569.

87. Angum et al; The Prevalence of Autoimmune Disorders in Women: A Narrative Review. Cureus. 2020 May 13;12(5):8094. doi: 10.7759/cureus.8094. PMID: 32542149; PMCID: PMC7292717.

88. Grissom et al; Disorders of childhood growth and development: failure to thrive versus short stature. FP Essent. 2013 Jul;410:11-9. PMID: 23869390.

89. Barstow et al; Evaluation of Short and Tall Stature in Children. Am Fam Physician. 2015 Jul 1;92(1):43-50. PMID: 26132126.

90. Venkateshwar et al; FAILURE TO THRIVE. Med J Armed Forces India. 2000 Jul;56(3):219-224. doi: 10.1016/S0377-1237(17)30171-5. Epub 2017 Jun 10. PMID: 28790712; PMCID: PMC5532051.

91. Velayutham et al; Prevalence and Etiological Profile of Short Stature among School Children in a South Indian Population. Indian J Endocrinol Metab. 2017 Nov-Dec;21(6):820-822. doi: 10.4103/ijem.IJEM_149_17. PMID: 29285442; PMCID: PMC5729667.

92. Image et al; https://doi.org/10.3389/fendo.2017.00374 Short Stature Diagnosis and Referral Front. Endocrinol., 11 January 2018.

93. Urakami et al; Tall stature in children and adolescents. Minerva Pediatr. 2020 Dec;72(6):472-483. doi: 10.23736/S0026-4946.20.05971-X. Epub 2020 Aug 4. PMID: 32748612.

94. Antonina et al. Prevalence and overlap of known undernutrition risk factors in children in Nairobi Kenya 06 August 2021 https://doi.org/10.1111/mcn.13261.

95. Hassan et al Failure To Thrive In Children Under Two Years Of Age And Associated Factors, A Hospital- Based Study December 2019 DOI:10.26505/DJM.17024770703 Diyala Journal of Medicine.

96. Mouriquand et al; Undescended testes in children: the paediatric urologist's point of view, European Journal of Endocrinology, 159(suppl_1), S83-S86.(2008). Retrieved Oct 10, 2022, from https://eje.bioscientifica.com/view/journals/eje/159/suppl_1/S83.xml.

97. Hughes et al; Factors controlling testis descent, European Journal of Endocrinology, 159(suppl_1), S75-S82. (2008) Retrieved Oct 10, 2022, from https://eje.bioscientifica.com/view/journals/eje/159/suppl_1/S75.xml.

98. Rodríguez et al; Accurate Diagnosis of Severe Hypospadias Using 2D and 3D Ultrasounds. Case Rep Obstet Gynecol. 2016;2016:2450341.

99. Haraux et al; Maternal Exposure to Domestic Hair Cosmetics and Occupational Endocrine Disruptors Is Associated with a Higher Risk of Hypospadias in the Offspring. Int J Environ Res Public Health. 2016 Dec 29;14(1).

100. Yu-Fen et al Factors associated with delayed pediatric hypospadias surgery in Taiwan: A population-based, nationwide analysis https://doi.org/10.1016/j.jfma.2012.02.014.

101. Mengel et al; Studies on cryptorchidism: a comparison of histological findings in the germinative epithelium before and after the second year of life. Journal of Pediatric Surgery. 1974;9:445–450.

102. Kolon et al. Evaluation and treatment of cryptorchidism: AUA guideline. J Urol. 2014 Aug;192(2):337–45.

103. Wenzler et al; What is the rate of spontaneous testicular descent in infants with cryptorchidism? J Urol. 2004 Feb;171(2 Pt 1):849–51.

104. Kurz et al; Current Management of Undescended Testes. Curr Treat Options Pediatr. 2016 Mar;2(1):43-51. doi: 10.1007/s40746-016-0039-7. Epub 2016 Jan 25. PMID: 27158583; PMCID: PMC4856300.

105. Amolo et al; "Etiology and Clinical Presentation of Disorders of Sex Development in Kenyan Children and Adolescents", International Journal of Endocrinology, vol. 2019, Article ID 2985347, 9 pages, 2019. https://doi.org/10.1155/2019/2985347.

106. Kihiko et al; East African Medical Journal Vol. 93 No. 1 January 2016 Disorders of sexual differentiation as seen at Kenyatta National hospital.

107. Lee et al; International Consensus Conference on Intersex organized by the Lawson Wilkins Pediatric Endocrine Society and the European Society for Paediatric Endocrinology. Consensus

statement on management of intersex disorders. International Consensus Conference on Intersex. Pediatrics. 2006;118:e488–e500.

108. Sarma et al; A review of the essential concepts in diagnosis, therapy, and gender assignment in disorders of sexual development. Ann Pediatr Surg 18, 13 (2022). https://doi.org/10.1186/s43159-021-00149-w.

109. Annastasia et al; Quality of Life in Late-Treated Patients With Disorders of Sex Development: Insights for Patient-Centered Care Front. Pediatr., 30 January 2019 Sec. Pediatric Urology https://doi.org/10.3389/fped.2018.00434.

110. Ingrid et al; Birth Defects: Causes and Statistics Nature Education) © 2008 Nature Education.

111. Asim et al; "Down syndrome: an insight of the disease". J Biomed Sci. 2015 Jun 11;22:41.

112. Wiseman et al; Down syndrome--recent progress and future prospects. Hum Mol Genet. 2009 Apr 15;18(R1):R75-83.

113. Akhtar et al; Down Syndrome. [Updated 2021 Dec 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK526016/.

114. Esperanza et al; Hurt Hospital admissions in infants with Down syndrome: a record-linked population-based cohort study in Wales First published: 03 December 2021 https://doi.org/10.1111/jir.12903.

115. Verma et al; Sex ratio of children with trisomy 21 or Down syndrome. Cytobios. 1987;51(206-207):145-8. PMID: 2960497.

116. Fitzgerald et al; Hospital admissions in children with Down syndrome: experience of a population-based cohort followed from birth. PLoS ONE 8, e70401.

117. Muenzer et al; Ten years of the Hunter Outcome Survey (HOS): insights, achievements, and lessons learned from a global patient registry. Orphanet J Rare Dis 12, 82 (2017). https://doi.org/10.1186/s13023-017-0635-z.

APPENDICES

1) Data collection tool

SPECTRUM OF PEDIATRIC AND ADOLESCENT ENDOCRINE DISORDERS AS SEEN IN KENYATTA NATIONAL HOSPITAL. A 14-year retrospective study.

PATIENT'S BIODATA:

Patients' Age	Age at diagnosis	Gender	Weight	Height	BMI	BP	Referral source(county, KNH, Self)	Presenting complaints (top 3)

Parameter	Time in days
Time between symptom onset and presentation to Endocrine clinic	

PARENTS' BIODATA

	Age	Residence
Father		
Mother		

DIAGNOSIS

1. Growth disorders:

   A. Short stature (-2SDS)

	FTT	Primary	Secondary	Syndromic	FSS	CDGP	Lost to follow up (yes/no)
Diagnosis							

   B. Tall stature:(+2SDS)

	Primary	Secondary	Familial	Syndromic	Lost to follow up (yes/no)
Diagnosis					

2. PUBERTY DISORDERS

	Precocious puberty	Delayed puberty	Contrasexual development of sexual characteristics	Non pathological sexual variations(PT/PA)	Others	Lost to follow up (yes/no)
Diagnosis						

3. SEX DEVELOPMENT AND GENDER DISORDERS

	DSD	Variations of gender development	Others	Lost to follow up (yes/no)
Diagnosis				

4. Obesity

	Genetic	Polygenic	Iatrogenic	Nutritional	CNS	Lost to follow up (yes/no)
Diagnosis						

5. Thyroid disorders

	Hyperthyroidism	Hypothyroidism(subclinical, primary, central)	Goitre	Thyroid tumor	Lost to follow up (yes/no)
Diagnosis					

6. Pituitary, Hypothalamus, CNS disorders

	Deficiency of pituitary hormones	Overproduction of pituitary hormones	Hypothalamus disorders	Vasopressin def	Congenital CNS malformations	Acquired pituitary disorders	Lost to follow up (yes/no)
Diagnosis							

7. Disorders of the adrenal glands

	Primary adrenal insufficiency	Secondary adrenal insufficiency	Primary adrenal hormone excess	Secondary adrenal hormone excess	Adrenal medulla disorders	Lost to follow up (yes/no)
Diagnosis						

8. Testes and male reproductive tract conditions

	Hypergonadotropic hypogonadism (HH)	Maldescended testes	Tumors of testes	Disorders of penis	Disorders of scrotum	Acquired testicular without HH	Lost to follow up (yes/no)
Diagnosis							

9. Endocrine disorders of the ovaries and female reproductive tract

	Ovarian disorders	Menstrual disorders	Anatomical defects	Disorders of breasts and nipples	Others	Lost to follow up (yes/no)
Diagnosis						

10. Glucose and lipid metabolism disorders:

	Type 1 DM	Type 2 DM	Hypoglycemia	Lipoprotein metabolism	Lost to follow up (yes/no)
Diagnosis					

11. Calcium and phosphate metabolism disorders

	transient neonatal hypocalcemia	permanent hypocalcemia	rickets	soft tissue calcification	hypercalcemia.	altered bone mass	Lost to follow up (yes/no)
Diagnosis							

12. Salt and water regulation conditions

	Hypernatremia	Hyponatremia	Diabetes Inspidus	Lost to follow up (yes/no)
Diagnosis				

13. Syndromes with endocrine features

	Numerical chromosomal abnormalities	Dysmorphic syndromes	Non-dysmorphic syndromes	MENS	Lost to follow up (yes/no)
Diagnosis					

14. Inborn errors of metabolism

	Hunter's dse	Gaucher's dse	Unspecified (unconfirmed)	Lost to follow up(yes/no)
Diagnosis				

Annual Paediatric endocrine visits (NEW).

DX/YEAR	'08	'09	'10	'11	'12	'13	'14	'15	'16	'17	'18	'19	'20	'21
Growth disorders														
Puberty disorders														
Sex dvp/gender dx														
Obesity														
Thyroid														
CNS/pit/hypoth														
Adrenal glands														
Testes/male R.Tract														

Ovaries/female R.Tract														
Glucose/lipid DX: TIDM HYPOGLYCEMIA T2DM LIPID DX														
CA/P MET: Rickets:														
Salt/H2O reg. dx														
Syndromes with endocrine abn.														
Inborn errors of metabolism														

NOTES

1. Growth disorders: Primary: Growth plate; Secondary: Endocrine, chronic illness; psychological, nutritional, associated with syndromes like Turner/Klinfeleter.
2. Puberty disorders: Precocious (<8yrs in girls; <9yrs in boys); Delayed Puberty (>13 yrs in girls; > 14 yrs in boys); Premature Thelarche (isolated breast devp in girls) Premature Adrenarche (early isolated pubarche). Contrasexual development of sexual characteristics: e.g facial hair/hirsuitism/voice deepening in girls; gynecomastia in boys.
3. Specific disease cause is for instance CAH as a result of 21 hydroxylase def causing 46 XX DSD.
4. Loss to follow up means 6 months of not attending clinic from last appointment
5. Criteria used for diagnosis where tests weren't done to confirm

2) Study timeline

The following was the study timeline

Research Activity	Year	2021		2022											
	Mon	N	D	J	F	M	A	M	J	J	A	S	O	N	D
Proposal presentation		X													
Approval by Ethics committee			X	X	X	X									
Data collection						X	X	X	X	X					
Data analysis											X	X	X	X	
Presentation of results															X

3) Study Budget

The following was the study budget.

ITEM	UNIT	QUANTITY	UNIT PRICE (KSH)	TOTAL COST (KSH)
STATIONERY	-			
Biro pen	1	10	25	250
Pencil	1	10	25	250
Pencil sharpener	1	5	40	200
White-out pen	1	3	300	900
Spring file	1	10	150	1500
Stapler	1	1	1200	1200
Paper punch	1	1	3000	3000
Staple remover	1	1	2000	2000
Notebook	1	10	200	2000
Flash disk (8GB)	1	1	2500	2500
SUBTOTAL				**14,200**
SERVICES				
Proposal printing	35 Pages	1 copy	10	350
Proposal printing (corrections from Ethics Committee)	35 Pages	1 copy	10	350
Photocopying	35 pages Book-let	11 copies	5	1,925
Proposal binding	Book-let	8	300	2400
Final dissertation booklet		8	1000	8000
Data collection tools	10 Pages	1000	5	5,000
SUBTOTAL				**18,025**
Institution's research fees	-	1	22,000	22,000

SUBTOTAL				**22,000**
PERSONNEL Statistician's pay (data entry and analysis)	1 person	40 days	2,000 per day	80,000
Research assistants (file retrieval, data mining)	2 people	30 days	1,500 per day	45,000
SUBTOTAL				**125,000**
TOTAL				**179,225**
MISCELLANEOUS EXPENSES	10% TOTAL			17,922
GRAND TOTAL				**197,147**

4) KNH-UoN ERC Approval