BETWEEN TOO LITTLE AND TOO MUCH: UNRAVELING THE MYSTERY AND MISERY OF ENDOCRINE DISORDERS IN CHILDREN

An Inaugural Lecture Delivered at Oduduwa Hall, Obafemi Awolowo University, Ile-Ife, Nigeria
On Tuesday 24th September, 2019

By

Jerome Boluwaji Elutayo ELUSIYAN
Professor of Paediatrics and Child Health

Inaugural Lecture Series 345
BETWEEN TOO LITTLE AND TOO MUCH: UNRAVELING THE MYSTERY AND MISERY OF ENDOCRINE DISORDERS IN CHILDREN

INTRODUCTION
Mr. Vice Chancellor Sir, I am highly delighted to stand before you and this distinguished audience today to deliver the 345th inaugural lecture of the Obafemi Awolowo University, Ile-Ife, Nigeria. Standing at this podium to present this lecture today is an accomplished vision that no one in my lineage would ever have dreamed of nor imagined, but for the grace and benevolence of the Omnipotent, Omniscient Being- God Almighty. Today’s inaugural is the fourth from the Department of Paediatrics and Child Health of this great University. My professorship was announced in September 2018, just a year ago though backdated to 2016, the question in many people’s mouth is why the hurry to deliver the inaugural lecture. The sunshine bookseller describes an inaugural lecture as an occasion of significance in an academic staff member’s career at the University. Inaugural lectures provide newly appointed professors with the opportunity to inform colleagues, the campus community and the general public of their work to date, including current research and future plans. Professors are usually required to give their inaugural lectures within 12 months of their appointment. I thus feel very much fulfilled to present this inaugural today the 24th day of September, 2019.

I will thus start this short discourse with your permission, Mr. Vice Chancellor, by returning all the glory and honour to Him who is worthy of all praises and adoration. The king of glory, the Lord of Lords, the I am that I am, the one that was, that is and that is to come. The One that makes a way when men say there is no way, the One who says there is lifting when others are talking about casting down, the One that lifts from the miry clay and set on the mountain top to sit with the kings and nobles. The lifter up of my head and my helper. The triune one, the God the father, the God the son, and the God the Holy Spirit. Without Him, I surely could not have made it at all not to talk of making it this far. My Lord Jesus, the whole of eternity cannot be enough to thank you.
On 14th June 1994 as a part 5 medical student, I attended my first inaugural lecture in this hall, it was the 148th Inaugural lecture series delivered by my Uncle Prof Akinsolape Olowu of the Department of Psychology (now retired). The inaugural lecture was titled Explorations into the Person, you could imagine my feeling standing on the same podium today 25 years later to present my inaugural. I also count myself lucky to stand on the same podium that many erudite scholars had stood to present their inaugurals.

**Early Education and career in Medicine**

I am the 11th of the 15 children of Late Chief Gabriel Eludire Elusiyan, the late Parakoyi Onisowo of Okeigbo Kingdom. My schooling was highly challenging and tough. I hardly could afford books and other necessity but somehow, in a way that I could not explain, I saw myself making progress in my academics. I had to break schooling at the age of 16 years to work for two years to be able to further my studies. But at many stages, God made helpers to be located at every junction of my career. If time permits, I will mention few of these destiny helpers later.

After my University education and the National Youth Service, I, was confronted with the challenge of a career choice and I got a job with a private Hospital at Ondo in 1998. But I experienced a life-transforming encounter with the Lord, and this encounter changed my whole life story. My decision to follow Him made it possible for me to stand before you today. He is true to His world that **whoever comes to Him will have rest** (Paraphrased Mathew 11:28 KJV). By that encounter, the direction of my life was firmly established and I started my Residency training in Paediatrics and was led by providence to choose Endocrinology as a sub specialty. Apart from my training in Nigeria under Prof Abiola Oduwole at the Lagos University Teaching Hospital, Idi Araba, Lagos, I did a 15 month training at the World Diabetes Foundation sponsored Paediatric Endocrinology Training Centre for Africa based at Nairobi, Kenya. Subsequently I had trainings at the Washington University of St Louis, United States of America, Poznan University of Medical Sciences, Poznan, Poland and Cincinnati Children’s’ Hospital, Cincinnati, Ohio, United States of America Professor Zeev Hochberg from (Haifa Israel), Professor Lorenzo Iughetti (Italy).
Professor Marek Ndiezla (Poland), Dr Nancy Crimmins (USA) and Dr Adekunle Dawodu (Nigeria and USA) and a host of others were of tremendous assistance as they offered themselves (and their houses) and their facilities to me during the training stages. I remain ever grateful.

**WHAT IS ENDOCRINOLOGY AND WHY ENDOCRINOLOGY?**

Endocrinology is the branch of medicine that is concerned with the study of the production and functions of the endocrine systems of the body. Endocrine system deals with the production of hormones from the endocrine glands of the body like the Thyroid glands, Adrenals, Pancreas, Gonads (Testes and Ovaries), Pituitary and Hypothalamus. (Figure 1)

The hormones are produced in small quantities, and they are usually transferred in the blood to their site of actions. They could be **autocrine** when they function on the cells that produced them, **paracrine** when they act on surrounding tissues or **endocrine** when they are transported to distant tissues for their activities.

As simple and un-noticeable as these functions seem problems often arise when these hormones are not produced at all or when they are produced in excessive quantities, or they are produced too soon or too late. Hence the topic of this inaugural is **Between Too Little and Too Much: Unraveling The Mystery and Misery of Endocrine Disorders in Children.**
Figure 1: The Endocrine Systems of the body

I will illustrate with typical examples of the Ovary and the Pancreas. The ovaries are the female gonads and produce oestrogen. Oestrogen is the hormone (chemical) that is responsible for the development of secondary sexual characteristics in the female. In cases of an early production of the oestrogen, this will lead to precocious puberty in which a girl develops secondary sexual characteristics before the age of 8 years. In a situation where oestrogen is produced too late, it causes delayed puberty in which there are no secondary sexual characteristics after the age of 15 years. If the pancreas produces too much of the Insulin hormone, hyperinsulinism ensues and this development leads to severe and persistent hypoglycaemia, whereas in the absence or failure of
production of Insulin, it leads to Diabetes Mellitus. I will talk more about these conditions later. The endocrinologist thus works to navigate between these extremes of too little or not at all and too much or too soon.

I remember at my interview for the post of Lecturer 1 at the University in 2005, the then Dean of the Faculty of Clinical Sciences, Prof Joshua Aderinsola Owa asked me why I was interested in Endocrinology more so the conditions were not as common in our practice. I could not vividly remember what my answer were then, but I think my response could have been something like I have read about many of the conditions though as at that time I have seen very few of such cases. But I believe that even if they were few, they also deserve to be well catered for so that they could also optimise their potential. Many years down the lane, I have not a single regret that I chose this path.

Mr, Vice Chancellor sir, Let me thank the University for giving me the opportunity and platform to develop myself and make a modest contribution to the subject of Endocrinology. The University permitted me to use the many travel grants and scholarships to attend the various trainings and Fellowships. I have played a pioneering role in the field of paediatric endocrinology, not only in this University, but in Nigeria as a whole and also in the continent of Africa. As at the time I started, I was the third practising Paediatric Endocrinologist in Nigeria, but there are now about 40 as at the last count. I will then go ahead to describe some of the conditions encountered in paediatric endocrinology and thereafter expatiate on my contributions to this field.

**DIABETES MELLITUS**
This condition commonly referred to in Yoruba language as *ítò súgà*” or “*ítò àtògbẹ*” is a chronic metabolic condition of carbohydrate metabolism that is due to absolute or relative insulin deficiency. The insulin deficiency made it impossible for glucose to enter the cells of the body for metabolism. The resulting hyperglycaemia leads to the myriads of problems and complications seen in patients with Diabetes Mellitus (DM). Diabetes Mellitus is classified as type 1 in which the deficiency of Insulin is absolute and
type 2 that is due to relative Insulin deficiency. Type 1 is the form that is typically seen in children, while type 2 occurs more in adults, and it is associated with obesity. Although in the western world, type 2 is now seen often in children due to the increased burden of obesity. Many in this audience will be surprised that children, too, suffers from Diabetes Mellitus. Although there is now a better understanding of the pathophysiology of type 1 DM, there are as yet some lacunas yet to be filled. The pathophysiology is hinged on a tripod of interaction of environmental trigger factor in genetically predisposed individuals, this then in the face of autoimmunity leads to the destruction of the pancreatic Islet cells. (Figure 2)

![Aetiology of Type 1 Diabetes Mellitus](image)

Figure 2: Aetiopathogenesis of Type 1 Diabetes Mellitus

Unfortunately, the Islet cell loss is a silent loss to the extent that at diagnosis the islet cell mass is almost completely gone and sadly too the cell loss is irreversible (even if detected early). Several haplotypes have been identified to be associated with Type 1 DM, but HLA-DR3 DQB1 and HLA-DR4 DQB1 loci are said to occur in close to 90-95% of newly diagnosed diabetes. However, some HLA haplotypes are protective. Some of the environmental trigger factors include exposure to Nitrates, enteroviruses like Coxsackie B virus,
Rotavirus and early exposure to cow milk. Although there may be a single trigger of beta-cell autoimmunity in a given individual, it is highly unlikely that there is one exogenous determinant of type 1 diabetes. Rather, we have a complicated interaction between environmental factors and genetic disease predisposition resulting in progression to clinical type 1 diabetes in those genetically susceptible individuals who experience an unfortunate timing and/or clustering of a diabetogenic exogeneous culprit and/or a lack of protective environmental modifiers. This variability in the haplotypes and environmental factors may account to a large extent the changing epidemiology across countries and regions. Some of the lacunas in the aetiology include what is the haplotype of African with DM and what are the environmental trigger factors. The question that has bugged Endocrinologists for many years is why type 1 DM is not common in the West African population as in the Eastern and Northern African people. My gut feelings are two. First is the early exposure of our children to many kinds of allergens as they grow up in the dirty environment, eating all sorts that may stimulate their immunity early and protect them against autoimmunity. Second is the possibility of our children dying from several of the plaguing communicable and infectious diseases and thereby not making them survive to develop Diabetes. Why I feel so strongly about this is the fact that Scandinavian countries like Finland and Norway, with the lowest mortality rate among their infants and under-fives are the countries with the highest prevalence of Type 1 DM. In the years to come, our research shall focus on resolving these issues. Additionally, the practice of early and sustained breast-feeding in our region may also be protective against the development of Diabetes Mellitus.

The Clinical presentation
The hyperglycaemia (Fasting blood glucose more than 7 mmol/l or 156mg/dl OR random blood glucose of more than 11.1mmol/l or 200mg/dl) leads to glycosuria once the renal threshold for glucose is exceeded. Glucose being osmotically active draws water along with resultant polyuria and polydipsia in a bid to tackle the dehydration that ultimately develops. The absence of Insulin makes the movement of glucose into the cells impossible, and this sets up
adaptive mechanisms to ensure glucose gets into the tissue for metabolism. These mechanisms lead to the breakdown of tissues by ketolysis, glycogenolysis and proteolysis all these then lead to the weight loss that is seen in patients with Diabetes Mellitus. If this process continues un-checked, there is then production of acids which use up the buffers in the body and worsening of the symptoms with fatigue, severe dehydration, altered sensorium (and at times frank coma), fast and laboured breathing and ultimately an acute complicated state of Diabetes Ketoacidosis (DKA). DKA is the commonest and usual way of presentation of Diabetes in children, particularly in the absence of a family history of Diabetes Mellitus. DKA is reported in the literature to account for 13-70% in newly diagnosed DM patients in the Western world. But we find it to account for 86.7% of all the patients’ presentation in our unit (Elusiyan & Kareem in press). Oyenusi and Odewole recorded a prevalence of 55% in Lagos. DKA is often the major cause of death in newly diagnosed DM children and these deaths often result from cerebral oedema and injudicious use of intravenous fluid and sodium bicarbonate. Contrary to this reported poor outcome from DKA we have recorded a good outcome of DKA management in our unit as we have never lost any of our admitted patients to DKA. The three of our patients that died occurred at home, though we assumed it was probably due to DKA. (Elusiyan & Kareem in press). This we have achieved in our Unit by following a slow intravenous fluid replacement, thorough and careful insulin administration and scrupulous monitoring and documentation.

**Epidemiology of T1DM**
Diabetes Mellitus is the most common metabolic disease in childhood. About 1 in every 400-600 children and adolescent has type 1 DM. A 2011 report from the US Centres for Disease Control and Prevention (CDC) estimated that approximately 1 million Americans have T1DM. The CDC estimated that each year from 2002 to 2005, type 1 DM was newly diagnosed in 15,600 young people. Incidence is reported to be increasing at a rate of 2-5% per year, and approximately 200 children are diagnosed with new-onset type 1 diabetes every day. However, the prevalence of diabetes in
Africa is still very low compared with what obtains in the Western worlds.  

**Treatment of T1DM**

Treatment of Type 1 Diabetes Mellitus revolves around the administration of Insulin to reverse the metabolic derangement. Insulin was discovered in the 1920s by Frederick Banting and Charles Best. And the discovery of Insulin revolutionised the outcome of Diabetes in children. Before then, children with DM are placed on starvation therapy (near-complete elimination of carbohydrate in the diet) in a bid to prevent elevation of blood glucose. And at that, it only takes a matter of a few weeks to months before the affected children will die. The first patient to be given Insulin was 14 years old Leonard Thompson in 1922, and he made such a dramatic improvement and lived for 13 more years after that. (Figure 3)

And Banting was given Nobel prize for Medicine in the year 1923. However, for optimal outcome, a lot more than Insulin administration is required. Education, dietary management, and exercise are equally of paramount importance.

In my experience, the most significant challenges to the management of Type 1 DM are three, non-availability of Insulin, dietary management and Needle phobia. The cost of a vial of Insulin ranges between 3,500 -5000 Naira, and this can only last maximum of 3 weeks in children of adolescent age. Only one of my patients can comfortably afford regular Insulin (and that goes with a lot of sacrifices), but to the Glory of God, the Unit has been able to source and supply FREE Insulin to all our patients. The dietary management has been very daunting; a Diabetes child is expected to take a diet consisting of 50-60% of carbohydrate, 30% fats and 20% protein. (Figure 4)
But most staple food in Nigeria is carbohydrate, and an average family can hardly afford these regimens. Making the children adapt to dietary prescription has been the major source of conflict between the child and their parents and this has a negative effect on compliance with management. The fear of needles (needle phobia) for injection of Insulin and for blood glucose monitoring has also in no small way prevented optimising care of children with DM in our practice. The question in their mind and mouth is always “when will I stop taking these injections”. This has prevented the use of multiple daily doses and restricted us to the twice-daily regimen (which many of them don’t even comply with).
Mr, Vice Chancellor sir, when I took up the appointment and established the Diabetes Clinic at the OAUTHC, there was not a single patient with Diabetes, but today we have 20 registered patients out of which we have lost 3. These three died because the parents did not believe the explanation of the aetiology but held on to superstition of some supernatural forces behind their children’s affliction and failed to comply with our prescription. The first registered patient in our clinic was diagnosed at the age of 8 years and has been managed for 11 years, and he is doing well. Three of my patients are currently undergraduates, while one has graduated. One of them is a student of the College of Health Sciences of this
great University, and one of them also recently delivered a bouncing baby boy. I am sure many of these patients and their parents are in this hall tonight. Also for the first time in the history of our clinic, we are presently transferring them to the Adult Endocrinologist after attaining the age of 18 years (3 years more than the mandatory cut off for the age of children in the Teaching Hospital). But expectedly, they have all refused to leave our clinic to the adult endocrinologists. This excellent outcome is contrary to the widely held belief that a diagnosis of childhood diabetes is a death warrant to the child. I have often told my patients and their parents that the diagnosis of Diabetes is just like any other childhood diseases, which once it is diagnosed, requires adequate and proper management and follow up. I have also encouraged them that having Diabetes should not stop them from attaining their life goals (Figure 5)

![Figure 5: A diabetes lady that won a beauty pageant in the USA](image)

We had advocated continuous education and provision of free Insulin to affected children either by the government or non-governmental organisations (NGO) or through strengthening the National Health Insurance Scheme. The only one of these suggested options that have helped these children is the NGOs. We signed an MOU for free supply of Insulin with the International Diabetes Foundation (IDF), and, this agency is ready to supply free
Insulin (as they have done in many African countries like Ghana, Kenya, Tanzania and South Africa). We however, failed to secure waiver from the Custom/ Government for a long time despite all entreaty to them but for the immediate past Minister of Health, Professor Isaac Adewole that assisted our Association. This need is one of the reasons that informed the establishment of the Elusiyan Memorial Foundation (EMF) in 2015. I shall talk more about this later.

Neonatal Diabetes is said to occur when Diabetes is diagnosed before 6 months of age. Neonatal Diabetes is described as monogenic because they result from mutation of single genes and some of them may respond to oral hypoglycaemic agents. It is a rare condition with an incidence of 1 in 100,000-500,000. The only patient with such a diagnosis under my care was diagnosed at 4 months of age in our hospital, and he is the 2nd reported case to have been managed in Nigeria. He was managed with oral hypoglycaemic agents out of necessity, and he is now 5 years old and doing very well on follow up. Genetic study carried out on him with colleagues from the United States of America revealed he had ABCC8 (p.Asp212Glu) mutation, which made him responsive to the oral hypoglycaemic agent. His T1D genetic risk score was noted to be extremely low in the <5th percentile category. However, for some of these patients with Neonatal Diabetes, they may develop Diabetes Mellitus later in life hence the need for long term follow up.

**Hypoglycaemia**

Hypoglycaemia is the occurrence of low glucose in the blood. The causes of hypoglycaemia in children are myriad and a timely identification of same could be lifesaving. Glucose is the major metabolic fuel in the body. There are two major pathophysiologic bases of hypoglycaemia—inadequate substrate or excessive insulin. In many stressful conditions in children either because of ill health or the accompanying anorexia and the relatively poor reserve, children often present with hypoglycaemia when they took ill. For several years in paediatric practice, the assumption of the presence of hypoglycaemia has *dictated* the administration of glucose to every child admitted for severe illness into children emergency. Many of such children often make dramatic response upon the
administration of glucose and many others fail to respond, this should have raised our curiosity to find out why, but we did not. As at then too, blood glucose monitoring devices were not readily available and sending samples to the laboratories did not meet these urgent needs for various reasons.

Mr, Vice Chancellor sir, I am happy to report to you today and this August gathering that through my research efforts, I have played a pioneering role in the unraveling of the problem of hypoglycaemia in children in Nigeria. My dissertation titled Hypoglycaemia In Emergency Paediatric Admissions At The Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife submitted to the West African College of Physician for the award of the Fellowship of the college in 2004 was the first documented effort in Nigeria to holistically research into the problem of blood glucose abnormalities in ill children. I found that hypoglycaemia is a common problem in children and is present in 6.4% of children admitted into the emergency ward. We equally documented that it is common in children with diagnoses of Malaria, Septicaemia, Pneumonia and Protein Energy Malnutrition. I found out too that it is common when the child has not eaten for about 12hours. The presence of hypoglycaemia was also found to be associated with high mortality as 28.6 % of the children with hypoglycaemia died compared to 4.2 % of those without hypoglycaemia. The finding of this study was similar to what has been documented in other countries-(both developed and developing). In Mozambique a prevalence of 7% was documented, and in Kenya 7.3% was documented, and in USA an incidence of 6.54% was obtained

This study on hypoglycaemia has encouraged several interests and many studies on the subject across the length and breadth of Nigeria. Jaja in Port Harcourt, Oyenusi in Lagos and Salma in Kano. All these studies corroborated our finding that hypoglycaemia is a common problem in ill children world-wide.

Up until that time, determination of blood glucose in patient required sending the blood sample to the laboratories and many times, this delays the diagnosis of hypoglycaemia for several reasons of---lack of equipment, lack of trained personnel, power
outage and unavailability of reagents. I then set out to investigate the reliability of bed side glucometers for the diagnosis of hypoglycaemia in children. We recruited 392 children and simultaneously tested their blood glucose with a glucometer and also in the laboratory, the result showed that the reading of the glucometer has a 96.00 % sensitivity 96.19 % specificity, 63.2 % positive predictive index and 99.72% negative predicted index.\textsuperscript{18} We thus recommended that glucometer could be reliably used for blood glucose determination in emergency wards.

Mr, Vice Chancellor sir, based on this our recommendations, glucometers are now widely used in emergency wards all over the country to the extent that it is almost becoming like a crime not to have one in any emergency ward and such hospital could be denied accreditation by the various accreditation bodies.

Incidentally, during our study on hypoglycaemia, we discovered that contrary to our expectations and widely held opinion then, that some of the children present with high blood glucose (hyperglycaemia) when they are ill. We documented a prevalence rate of hyperglycaemia of 3.3% in our study\textsuperscript{19}. We also found out that the presence of hyperglycaemia is also associated with high mortality, and this may explain why some children that were given glucose empirically did not respond to the glucose. These hyperglycaemias were, however, transient, and all reverted to normal glucose levels following the management of the primary pathology. This finding of hyperglycaemia reinforced our recommendation for the use of glucometer in children in emergency wards, and that glucose should only be given to children with documented hypoglycaemia.\textsuperscript{19}

\textbf{DISORDERS OF THE THYROID GLAND}

The thyroid gland is a bi-lobed structure in the front of the neck and overlies the second to the fourth cervical vertebrae, and it is connected by an isthmus. (Figure 6)
Its major function is to produce the hormone Thyroxine. Thyroxine is a primary metabolic hormone that is needed for the general well-being and functioning of all body organs and systems. It is particularly important for brain development. Its absence has a permanent detrimental effect on the brain and is a leading cause of mental retardation in children. Abnormality of the Thyroid gland is the second commonest endocrine condition in children world-wide. Like we have discussed for the pancreas and glucose abnormalities, the malfunctioning of the thyroid gland could result into hyperthyroidism (excessive levels of Thyroxine hormone) or hypothyroidism (low or reduced concentration of the Thyroxine hormone). The thyroid disorders could also be congenital when it is present at or shortly after birth or acquired when it develops in an healthy child later in life. Many times, thyroid gland disorders may present with hyperplasia and or hypertrophy. This is referred to as goitre, and this can be seen in cases of hyperthyroidism, hypothyroidism and even in euthyroid states. Other presenting clinical features and results of investigations will help to characterise which one. (Figure 7)
Hyperthyroidism.
This is a condition of hyper-functioning of the thyroid gland in which the level of circulating serum level of Thyroxine exceeds the normal physiologic level. (The normal serum level of Thyroxine in children is- FT4 7-14.8 pg/ml and FT3 1.7-3.7 pg/ml.) This is also accompanied by suppression of the thyroid stimulating hormone (TSH) as a result of the negative feedback mechanism between the pituitary gland and the thyroid gland. Thyrotoxicosis on the other hand is the clinical and biochemical condition characterised by a high level of thyroid hormone. Common causes of thyrotoxicosis include Grave’s disease, autonomous thyroid hyper-function, TSH-dependent hyper-function, thyroiditis or from exogenous sources.

Grave’s Disease
This is the commonest form of thyrotoxicosis, and accounts for 95% of cases of thyrotoxicosis. Its incidence in pediatric age is put at 1-5% and incidence increases with age in each sex. It affects females more than males by as much as 3-5 times. There is often a history of relatives affected by autoimmune thyroid diseases (30-60%) and it has a high association with other autoimmune diseases (like Type 1 Diabetes Mellitus, Coeliac Disease, Addison, Vitiligo, Lupus and Rheumatoid Arthritis). Although the exact pathologic mechanism for the development of Grave’s disease remains unclear, it is caused by the production of IgG autoantibodies directed against the thyrotropin receptor. These antibodies bind to and activate the receptor, causing the autonomous production of thyroid hormones. The common symptoms of Grave’s disease include goitre,
tachycardia, irritability, hypertension, exophthalmos, tremors, loss of weight despite increased appetite, hyperactivity, excessive sweating, poor school performance, sleep disturbances and diarrhoea.\(^{20}\) The exophthalmos in them is due to the effect of the autoimmune antibodies binding to the muscles and soft tissues surrounding the eyes. (Figure 8)

In the series from our clinic, we have recorded nine cases affecting three males and six females. We equally reported a case of neonatal Graves, which was diagnosed at the age of 3 days in the newborn of a mother with Graves disease in pregnancy. Early detection saved the baby from the untoward effect which could include, heart failure, neonatal jaundice, failure to thrive and even death. There are three widely used modalities of treatment viz: Chemotherapy, Surgery and Radiotherapy. The first-line treatment is to use drugs. The Thionamides- they function by inhibiting the release of thyroid hormones from the gland, some also inhibit the peripheral conversion of the prodrug. Other adjunct medications include the β blockers and corticosteroids. Surgery involves the removal of the thyroid glands either completely (total thyroidectomy) or leaving a remnant of the glands behind (sub-total thyroidectomy). Radiotherapy involves the use of radiolabelled iodide, which when trapped in the thyroid gland disrupts the normal functioning of the gland. One of the side effects of the latter two modalities of treatment is that it could tilt the child to hypothyroidism that may warrant treatment. Out of all the endocrine conditions I have encountered in my practice, treating hyperthyroidism has been most rewarding. The response to cure is often dramatic and very rewarding. All the cases that we managed did quite well with almost 100% cure with only one that may end up requiring surgery because the medical therapy has failed to achieve complete remission and in the face of a persistent goitre in a 12 year old girl. The drug is also very cheap and readily available.
Hypothyroidism
This condition is due to insufficient or absent thyroid hormone in a child. The causes of hypothyroidism include thyroid agenesis, ectopic thyroid gland and inborn errors of thyroxine metabolism, among others. (Table I)

Table I: Aetiology of Hypothyroidism

A. Congenital
   1. Thyroid dysgenesis (partial or complete athyreosis
   2. Ectopic thyroid gland
3. Inborn errors of synthesis
4. Hypothalamic – pituitary- thyroid axis abnormality
   (Thyrotropin Releasing Hormone (TRH) deficiency, Thyroid Stimulating Hormone (TSH) deficiency, Thyroid gland unresponsiveness)
5. Iodine deficiency (endemic cretinism)
6. Transplacental passage of anti thyroid drugs, chemicals, agents
7. Peripheral resistance to thyroid hormone

**B. Acquired**
1. TRH/TSH deficiency
2. Post thyroidectomy
3. Post 133I therapy
4. Goitrogenic induced (Propylthiouracil, methimazole, iodide excess, cobalt)
5. Post suppurative or non suppurative thyroiditis
6. chronic lymphocytic thyroiditis
7. Infiltrative disease of the thyroid (cystinosis, histiocytosis X)
8. Post – craniospinal irradiation therapy

The most frequent cause, however, is the thyroid agenesis. The clinical presentation of this condition depends on when the situation began. The most feared condition is the congenital hypothyroidism because of the deleterious effect on the brain if diagnosis and or treatment are delayed. Clinical features of congenital hypothyroidism are not specific and take some times before the full pictures become obvious at which time it is too late for optimum outcome. (Figure 9) In the Western world, congenital hypothyroidism (and several other congenital endocrine and metabolic conditions) is diagnosed during Newborn screening. The newborn screening started well over 50 years in the western world, but sadly it is not available routinely in any Sub Saharan Africa. Sufferers of these conditions are thus left undiagnosed or diagnosed when it is very late for optimal effects.
I will illustrate with two pathetic cases among the many children with congenital hypothyroidism under my care. One presented at age 13 months to the clinic with a referral from India for continuation of treatment. She was delivered in Nigeria and after several consultations with many Doctors, she was referred to India for corrective heart surgery. But as part of routine work up for surgery they discovered that she actually has congenital hypothyroidism and was just started on chemotherapy and sent back to Nigeria. The trauma and the consequences of this scenario (tragedy) to the child and the parents are better imagined. The second case was also a girl that was referred to our clinic at the age of nine years. She had presented to several hospitals and when they could not make a diagnosis she was labelled ‘abnormal child’ and sent to live with grandparents in the village somewhere in Cross Rivers State until an uncle who graduated from our college saw her and referred to us only to discover after a simple laboratory diagnosis that she has congenital hypothyroidism. She has made a significant improvement in her physical growth, but has remained permanently mentally retarded. We presently have about 10 patients on treatment for congenital hypothyroidism diagnosed at varying
ages. Sadly two of them are siblings from the same parent. For excellent and optimum outcome of congenital hypothyroidism, adequate treatment MUST be started before 3 weeks. When diagnosis and or treatment is delayed beyond this period, various degrees of mental retardation results.

Let me at this juncture Mr, Vice Chancellor sir, speak on behalf of the teeming unborn Nigeria children that the Nigerian government should as a matter of urgency and necessity put in place mechanism to begin compulsory nationwide newborn screening for endocrine and metabolic conditions in Nigeria. With the birth rate of 36.9 births /1000 population in Nigeria, it is estimated that 7 Million babies are born in Nigeria yearly and given the incidence of congenital hypothyroidism of 1 in 1,500 live births, one will expect about 47 children with Congenital Hypothyroidism annually. And because we shall be screening for more than one condition at the same setting, the cost per condition will be reduced, and we can even incorporate it into the National Health Insurance scheme. Doing a newborn screening is not rocket science and it does not require so much fund that the country cannot afford, it only calls for getting our health priorities right. We can start by establishing regional centres for sample collation and analysis as is done in other nations.

One point that I will also like to emphasise at this point is the possibility of overtreatment of the conditions enumerated above. Overtreatment of the too low state with replacement hormone can lead to too much condition and overtreatment of a too much situation in a child can equally inadvertently lead to a too low condition. For example, in a child with Diabetes Mellitus in which the level of insulin is too low with resultant hyperglycaemia, treatment with Insulin, if not well monitored can lead to hypoglycaemia with untoward adverse effect. Similarly, the treatment of hyperthyroidism with all the drugs mentioned above or by surgery can over-suppress the Thyroid gland leading to hypothyroidism. The job of the Endocrinologist is thus, not only to identify and treat these conditions of too little or too much, but it is also to maintain a delicate balance and prevent iatrogenic opposite too much or too little. (Figure 10)
The Paediatric Endocrinologist thus cannot afford to take the eye off the child and the parent once treatment is started. The child must, therefore, be under follow up care to ensure this. This will also involve the services of other professionals in the management of these conditions. Of paramount importance here is the Chemical Pathologist whose job it is to assay and interpret the hormonal levels in these patients.

**DISORDERS OF THE ADRENAL GLANDS**

The Adrenal glands (also known as suprarenal glands) are endocrine glands that produce a variety of hormones including adrenaline and the steroids aldosterone and cortisol. They are found above the kidneys. Each gland has an outer cortex which produces steroid hormone and an inner medulla. The abnormalities of the Adrenal gland could result from either or both of the two layers of cells—the Adrenal Cortex or the Adrenal Medulla. The abnormalities of the adrenal glands in children are very rare in the literature and that may also explain why I have not personally managed quite many cases. The only one condition of the adrenal gland that is seen commonly in our practice is congenital adrenal hyperplasia (CAH) manifesting...
as disorders of sexual differentiation (DSD) called ambiguous genitalia or intersex disorders in the past. These are by far the most challenging and tasking paediatric endocrine conditions to be managed by an endocrinologist. I will illustrate these challenges shortly. But like my Bulgarian tutor Professor Violeta Iotova used to say then in Nairobi that the commonest of the rarest conditions is still less common than the rarest of the common conditions. This scenario aptly applies more with endocrine conditions more so Adrenal gland diseases in sub-Saharan African where we are still inundated with infectious and communicable conditions.

**Congenital Adrenal Hyperplasia**

As mentioned earlier, this condition is a common condition reported in the literature. In Great Britain, an incidence of one affected child in every 18000 live born was documented. Although no epidemiological data exists in the country about the prevalence of this condition in Nigeria, but anecdotal evidence suggests that it is a relatively common condition. It is one condition whose incidence is almost equal to its prevalence because they all tend to die soon after diagnosis is made. The conditions are the most difficult to manage and clinical practice varies substantially throughout the world. Even though the management in the Western world has dramatically improved over the years owing to the availability of better diagnostic armamentarium, it is still fraught with several challenges in our practice.

To understand the problem of disorders of sexual differentiation, it is pertinent that I do a brief review of the embryology of sexual differentiation. The internal and external genital structures in both male and female foetus develop from a single origin, the undifferentiated primitive mesonephric kidney and the genital tubercle and genital swelling respectively. But under the influence of the hormones and several factors leads to development into definitive male or female structures. (Figure 11)
In congenital adrenal hyperplasia (CAH), the basic problem is the absence or reduction of activities of several of the enzymes that is involved in the steroidogenesis pathway leading to the absence or reduced production of any one or more of the three lines of Aldosterone, Cortisol or the Androgens (Figure 12).

This absence or reduced production thus sends a negative feedback to the anterior Pituitary leading it to produce more Adrenocorticotropic hormone (ACTH). This ACTH continues to drive the adrenal gland to produce more of the intended end product (which it cannot produce because of the enzymatic blockage in its pathway) and thereby causing the adrenal gland to become hyperplastic hence the name congenital adrenal hyperplasia. It should also be explained that the blockage in the production of one pathway leads to excessive production of the product in the other pathway. For example, in the presence of deficiency of the 21 B hydroxylase enzyme (21βOH), there is a failure of production of Aldosterone and Cortisol, this leads to excessive production of the androgen, testosterone leading to the masculinization of the female external genitalia. Conversely, in the face of deficiency of any of the enzymes required in the androgen pathway, there is reduced production of testosterone, and this leads to under masculinisation of the male external genitalia. (Figure 13)
Figure 12: Steroidogenesis pathway
The clinical presentation is also dependent on the severity of the enzyme deficiency. In complete absence of some of the enzyme, like the 21βOH deficiency, it could lead to very devastating consequences in the new born period leading to severe salt wasting with an attendant hypovolaemic shock which can lead to death in the new born period if not recognised and promptly managed.

We have not been lucky in the management of children with these conditions in the unit. We have seen about a dozen cases, but they are almost always lost to follow up.

Perhaps due to our feet dragging at making a diagnosis or at giving appropriate management. The first challenge we faced in managing them is what sex do we assign them, particularly in our setting where a lot of emphasis is placed on the sex of the baby. What we have resulted to do is to advice the parents to give a unisex name, and we have several here. Another challenge we face is in making a
definitive diagnosis, yes we are able to do karyotyping (OAUTHC is the only public Institution where this is done in Nigeria), but we are not able to measure the hormones that will help to make a definitive diagnosis- most patients are lost to follow up when we send them to private laboratories to do the test. Definitive management will be to replace the deficient hormone. For the cortisol deficiency, we give hydrocortisone to replace and when not available we give prednisolone (as it is the case with our patients), for the aldosterone deficiency, we replace with Fludrocortisone to help conserve sodium loss from the kidney. This drug is also not readily available or accessible in Nigeria but what we did was to instruct the mother to give extra salt in the diet. We also do regular monitoring of the serum electrolyte to be sure we are giving enough. Apart from the medical treatment to prevent further virilisation, there is also the need for the repair of the ambiguous genitalia. There is still a lot of controversy about the timing and the necessity of this as well. Why some think that it should be left untreated, others advocate for surgery before the age of 12 months, while yet others are of the opinion that the child should be left until about 12 years to decide for himself or herself. The only two patients that we managed to a significant extent had surgery done after a lot of “modifications” but one died immediately after surgery due to Addison crisis (insufficient steroid replacement post surgery) the other did not even attend a single follow up after discharge.

The male disorder of sexual differentiations is the most difficult to manage, while the female DSD with masculinised genitalia could easily be corrected not so with the under masculinised male. Sex assignment is also very difficult and takes time. Experts have set guidelines for sex assignment (Table II)

Table II: Guidelines for sex assignment in Disorders of Sexual Differentiation

- (1) Minimising physical risk to child.
- (2) Minimising psycho-social risk to child.
- (3) Preserving potential for fertility.
- (4) Preserving or promoting capacity to have satisfying sexual relations.
- (5) Leaving options open for the future.
- (6) Respecting the parents’ wishes and beliefs.
Even at that, they are not very easy cases to manage. I once have such a case of a child that was referred by the Paediatric surgeon at age 12 years. The complaints were that the parents had noticed ambiguous external genitalia since birth but have not developed breast. She has been raised as a girl and attends a girls-only school. The surgeons worked her up and investigated and found out she has a 46 XY karyotype, and abdominal ultrasound did not show any uterus (womb). She was thus actually genetically and phenotypically a male child but has been reared as a female. We had several counselling sessions with the parents and the child including the reproductive consequences, but they insisted on raising her as a girl. We have thus commenced her on oestrogen, and she is developing breast as we speak.

GROWTH AND PUBERTY DISORDERS
Endocrinologists also deal with children with growth and puberty disorders. The clinical conditions encountered here could be diverse, ranging from abnormalities of stature and weight and that of puberty.

Overweight and Obesity
Overweight and obesity are conditions of excessive adiposity. The prevalence of obesity has been documented to be increasing worldwide and even in developing countries like ours where one would think it should not be a problem. The documented prevalence of obesity among Nigerian children and Adolescents varies from 0.0% - 5.8% over the last 3 decades,\(^{26-28}\) two main contributory factors are excess intake and reduced physical activity. Obesity has been shown to be more with more affluent family or population and the debate as to whether obesity is a function of Nurture or Nature has raged for ages. I think it is both but think the way the child is nurtured is significant for its expression. Paediatricians and Endocrinologists are bothered about Overweight and Obesity because childhood obesity too often track to adulthood and because of its numerous social and medical complications like poor self-esteem, bullying and name-calling, Diabetes Mellitus, Hypertension, Obstructive Sleep Apnoea to mention a few. The treatment of obesity is also not easy. Prevention by eating only what an individual requires and ample exercise are the only way out. But
the way our environment is structured and our practices may lead to an implosion of Obesity like it is already the case in many developed countries. We send our children to school at very tender ages, they are given empty calorie foods and snacks, little or no time for play at school (that is if the facility is available), they are carried in cars everywhere and they now have more screen time (Television, video games, hand set games etc). The prevalence of obesity among children in the USA is currently put at 18.5% and affects about 13.7 Million children\textsuperscript{29} with equally high complications in the affected children and adolescent.

**Abnormality of stature**
It appears from our experience that the Nigerian population is hardly bothered with abnormalities of stature. The Yorubas for example even venerates short people and describe them with such appellations as “kurumbete”, “akuruyejo” meaning the short ones are fit for dancing. Same also goes for tall stature except in a few cases where the parents consider it out of proportion with siblings and or neighbours. One such case was a six-year old girl that was brought to our clinic with a history of poor growth since about 2 years. She was evaluated and confirmed to have growth hormone deficiency. For over 2 years after confirming the diagnosis, we could not treat, but eventually, we secured a one-year dosage of free growth hormone from a pharmaceutical company in USA. The drug performed a ‘miracle’ as the girl grew 7cm in one year as opposed to 2 cm growth annually. Unfortunately, since we exhausted the free drug the parent could not purchase the drug, and for about 3 years now we waited and hope they will be able to buy the medicine. (Figure 14)

But just about two months ago luck smiled on the girl and she had a donation of an amount of money which enabled her buy more drugs. A new patient just presented with short stature at 6 years, and we are currently investigating him for the possible aetiology so that we can commence appropriate treatment (Figure 15)

**Disorders of Puberty**
Earlier on, I mentioned the condition of precocious puberty in which a girl develops secondary sexual characteristics before the age of
eight years and in a boy before the age of 9.6 years. It is more often seen in females. The aetiologies are myriad and such cases will need a thorough evaluation to elucidate the causes. One of the major reasons to investigate is to exclude intracranial or intra-abdominal tumours, which may present with precocious puberty. It is also important to investigate so as to know which one to treat. But more often than not, when it presents before 5 years, there is usually the need to treat to prevent progression and the attendant complications like sexual abuse, early fusion of ossification centres and ultimate development into short stature. Among the cases, I have managed two of them stood out. One was 11 months, and the other was 9 months old. (Figure 16)

The former we suspected to be due to intracranial tumour but was lost to follow up when the parent could not afford investigations while the latter developed precocious puberty following the usage of a herbal remedy by mother as a form of contraceptives. The concoction apparently contained oestrogen. The puberty development ceased on discontinuation of the offending mixture by the mother. For those that will require treatment, this is done with the use of gonadotropin releasing hormone analogue which is given monthly or every three months until the child is 12 years old when she can then be allowed to progress to normal puberty.
Figure 14: Growth chart of a patient with Growth Hormone Deficiency
I have also managed a case of delayed puberty in a 15-year old boy. He presented with a small-sized penis that has not increased in size so much since birth. There was associated inability to smell, and our investigation and treatment confirm a condition called Kallmann Syndrome, also called Olfactogenital Dysplasia to emphasise the association between the agenesis of the olfactory bulbs and
hypogonadism. This syndrome is said to occur when the hypothalamic neurons that are responsible for releasing gonadotropic releasing hormone failed to migrate into the hypothalamus during embryonic development. The patient made tremendous improvement following treatment with Testosterone-induced virilisation and development of secondary sex characteristics and improved quality of life, as he now feels manly and could also smell. However, his future fertility will require attention.\textsuperscript{30} His genitalia and investigation results before and after treatment are shown in Figure 17 and Table III.

Figure 16: A-11 Month old with precocious puberty

Figure 17: The patient at presentation and after 8 months of testosterone treatment

Table III: Results of investigations
<table>
<thead>
<tr>
<th>Test</th>
<th>Normal Value</th>
<th>Initial result</th>
<th>8 months of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH</td>
<td>0-25 iu/ml</td>
<td>1.3 iu/ml</td>
<td>4 iu/ml</td>
</tr>
<tr>
<td>LH</td>
<td>0-20 iu/ml</td>
<td>&lt;1 iu/ml</td>
<td>5 iu/ml</td>
</tr>
<tr>
<td>Testosterone</td>
<td>3-10 iu/ml</td>
<td>1.1 iu/ml</td>
<td>47 iu/ml</td>
</tr>
<tr>
<td>Karyotype</td>
<td></td>
<td>46 XY</td>
<td></td>
</tr>
</tbody>
</table>

FSH: Follicle Stimulating Hormone
LH: Leuteinizing Hormone

THE MYSTERY AND MISERY OF ENDOCRINE CONDITIONS IN CHILDREN

I have titled this inaugural lecture **Between too little and too much: Unraveling the mystery and misery of endocrine disorders in children.** Endocrine conditions in children appear to be a mystery, unlike infectious and communicable conditions where you can easily lay your hands on the causative organisms. Once the causative organisms or mechanism of causation of infectious disease is identified, treatment is usually a done deal. But in endocrine conditions, its aetiologies are usually not definite and often multifactorial, and this additionally makes the treatment not as easy too. Even though there is a better understanding of the pathogenesis of many endocrine conditions today unlike in the yesteryears, there is still a lot of gaps in the understanding of the actual pathogenesis and why some children are affected, and others are not is also not very clear. One question I have always avoided from my patients’ parents and wished is not asked is “why is my child affected with this condition”, on many occasions I have always started with “actually I don’t know” before going on to explain the textbook pathogenesis. I will then quickly shift gear to explain what we need to do to manage the condition and raise their hopes that with time, there will be a better understanding of the aetiopathogenesis and treatment. On many such occasions, I know I am often not too convincing. For example, as mentioned earlier for Diabetes Mellitus, we know there is interplay of environmental and auto immunity in genetically susceptible individuals, what made the individual susceptible genetically and to the auto immunity or to the environmental situation is largely yet unknown. Science and all of us that work in the field are making tremendous efforts to unravel
this mystery, and according to T. Huxley, 1887 “The known is finite, the unknown infinite, intellectually we stand on an islet in the midst of limitless ocean beyond comprehension. Our business in every generation is to reclaim a little more land.”

Endocrine conditions in our clime is also a misery in that affected children, and their parents are left alone to bear the burden of the disease and provide for their care, unlike what obtains in developed worlds. Majority of our patients could hardly afford the cost of comprehensive investigation and treatment of endocrine conditions. They always inform us that they could not afford the cost of several investigations and this has made us not to be able to optimise their care to our satisfaction. For example, out of the nine cases with thyroid disorders that I have managed, we could only assay for antibodies in just two of them, worst hit are children with Disorders of Sex Differentiation, (ambiguous external genitalia) the several hormonal assays, and dynamic tests that we need to do to cone down on the specific defects are not affordable for most of the patients. Why these conditions affect people of low socio economic status is another mystery, and this contributes to the misery of endocrine conditions in our environment. Despite what one may call a “double jeopardy” we have tried several means to overcome these appalling situations to get the modest results that we have. In the following section, I will enumerate my contributions to unraveling the mystery and dealing with the misery.

CONTRIBUTION TO KNOWLEDGE AND TRAINING IN THE FIELD OF ENDOCRINOLOGY AND PAEDIATRICS

Mr, Vice Chancellor sir, having tried to educate this audience on the spectrum of paediatric endocrine disorders, I will then briefly enumerate my modest contributions to the field of paediatrics in general and endocrinology in particular. Like I mentioned earlier in the course of this lecture, I have played a pioneering role in the field of paediatric endocrinology in Nigeria and Africa. I was a member of the pioneer set to be trained in Africa at the World Diabetes Foundation (WDF) Paediatric Endocrinology Training Centre for Africa (PETCA) based in Nairobi, Kenya. (Figure 18)
Figure 18: At graduation from the Paediatric Endocrinology Training Centre for Africa

I am the first to be appointed a consultant paediatric endocrinologist in the Obafemi Awolowo University and the Obafemi Awolowo University Teaching Hospital, Ile-Ife and by the help and grace of the almighty God rose to the position of Professor. As at the time I was appointed I was the third practising paediatric endocrinologist in the country and can boldly say that we now have over 40 paediatric endocrinologists across Nigeria. I have been involved with the training and building up of this critical mass of specialists. I am a foundation member of the Africa Society for Paediatric and Adolescent Endocrinology (ASPAE), and I have been the chair of training and education of the Society of Paediatric and Adolescent Endocrinology of Nigeria (SPAEN) since inception. (Figure 19)
Figure 19: Participants at the 2019 African Society for Paediatric and Adolescent Endocrinology Annual Conference held in Lagos, Nigeria.

I have been a tutor and supervisor at the Paediatric Endocrinology Training Centre for West Africa, Lagos. A world Diabetes Foundation-sponsored training centre for West Africa which was modelled after the Kenya school.

In the five years of its existence, we trained and certified 33 paediatric endocrinologists. This is in collaboration with volunteer tutors from the European Society for Paediatric Endocrinology ESPE and the International Society for Paediatric and Adolescent Diabetes ISPAD. I have also taught medical students and Resident Doctors paediatric endocrinology since my appointment in 2005. (Figure 20)
I have been a resource person at the yearly update and revision course of the West African College of Physicians for almost a decade. I have supervised Eleven Part 2 dissertation project out of which eight have been successfully defended at either the National Postgraduate Medical College of Nigeria or the West African College of Physician. All the graduates are now Consultants in various Hospitals across the country. My research focus has been in the area of Diabetes Mellitus, Hypoglycaemia and thyroid disorders. My publication titled Hypoglycaemia in Emergency Paediatric Admissions published in the Journal of Tropical Pediatrics in 2005 was one of the most widely read articles for over 6 months. The singular work has propelled many researchers in Nigeria to study the problem of hypoglycaemia and hyperglycaemia in Nigerian children. Through my publications on hypoglycaemia and its method of determination, it has become the practice now at every emergency room to have a glucometer and determine blood glucose on all admitted patients not only to determine the presence of hypoglycaemia but to equally exclude hyperglycaemia and to
monitor treatment with glucose. My focus on several of the endocrine conditions was aimed at raising awareness and documenting the challenges encountered in managing the patients.\textsuperscript{8,31,32} We identified low income family support and lack of funds for adequate management of patients with Diabetes and other endocrine conditions. Illiteracy and superstitious beliefs are also rampant. Lack of support from sources other than the family has also been identified as part of the challenges. All these challenges have contributed in no small way to the grim outcome of the patients with this condition. A typical example is the 11 months old girl, (mentioned earlier) that presented with rapid breast development, which started at about 8 months. Our plan of management was to do a neuroimaging and blood hormonal assays, but because the parent could not understand the gravity of the problem that it could be due to an intracranial malignancy and poverty, she did not come back for follow-up for treatment and would most likely have died. We have also proffered several solutions which include government and non-governmental organisation support, the scale-up of the national health insurance scheme to cover the people in the non-formal sectors. It is not even too much for the government to make the treatment of children with chronic diseases like Diabetes Mellitus and others mentioned to enjoy free and qualitative health services at all levels of healthcare delivery in Nigeria. Because of this poor management outcome, we have also documented the early onset of complications in these children. We have documented early onset of bilateral cataract in an adolescent after just about 5 years of development of Diabetes Mellitus (Elusiyan and Onakpoya not yet published). With other colleagues in Radiology and Chemical Pathology, we documented prevalent early onset renal function impairment and ultrasonic evidence of ongoing atherosclerosis consequent on the poor glycaemic control\textsuperscript{33,34} We also documented the problems of delayed and missed diagnosis of congenital hypothyroidism in Nigeria Children. I have 10 such patients under my care. The delayed diagnosis has led to varying degree of mental retardation as evidenced by measured intelligence quotient (IQ) ranging between 30 and 90 (Elusiyan and Oke unpublished) this means that these children due to no fault of theirs other than being born in Nigeria will never attain their maximum potential and will remain a burden on their parents, the community and the nation for
life. With other colleagues, I have also tried to establish normative data for parameters for Nigerian children. Growth is influenced by several factors, including the gene and the environment this has led to development of country-specific growth charts and normative values. With colleagues from the three main tribes of Hausa, Ibo and Yoruba, we made an attempt to produce growth charts to be used for Nigerian children. We sampled 4350 school-aged children between 4-16 years, and with collaboration with a colleague from London, we found out that height of school-age Nigeria children was similar to international references at the start of school and then started to decline. The decline appeared to peak at 15 years for boys and 13 years for girls. At all age, sex, ethnicity and affluence, school age Nigeria children were lighter than international standard.\(^{35}\) (Figure 21) The chart was launched at the Paediatric Association of Nigeria Annual Conference (PANCONF) at Abakaliki in 2015. However, it was suggested we include more subjects to make it more robust. We are in the process of doing that and hopefully, very soon we will have a widely acceptable chart for Nigerian Children.(Figures 22 & 23)

Figure 21: Charts of Nigerian children compared to CDC 2000 references
Figure 22: The Nigerian Growth Chart for girls

Figure 23: The Nigerian Growth Chart for boys
We also measured the normal penile length of Nigerian children. The first study was conducted among children in Port Harcourt\textsuperscript{36} and another one at Ile-Ife (Kareem, Elusiyan and Owa in press). We got a mean ± SD of 3.17 ± 0.5 cm and 3.4 ±06cm respectively, both studies agreed that any stretched penile length in Nigerian newborn that is less than 2.3cm should be regarded as micropenis. This was similar to the recommendation of other workers in Nigeria\textsuperscript{37,38} We also documented the normal anogenital distance (AGD) of Nigerian newborn, this is a measure of adequacy or deficiency of exposure to androgen in utero.(Figure 24)

Figure 24: Diagram of Anogenital Distance in Males and Females

We documented a measurement of 28.3 ± 3.9 mm in males and 15.2 ± 2.4 mm in females.\textsuperscript{39} This is important and may be a pointer to disorders of sexual differentiation. In another study, we found a very good correlation between the measured AGD and serum testosterone level and thus proposed that the measurement of the AGD may be a surrogate measurement for testosterone determination. (Kareem AJ, Owa JA and Elusiyan JBE In press). In preparation for when new born screening for Congenital Hypothyroidism will start in the Country, with other colleagues in the SPAEN we determined the normative thyroid stimulating hormone values for healthy Nigerian newborns and found the mean cord TSH value to be 1.86µIU/ml.\textsuperscript{40} We used cord blood because of the envisaged difficulty in getting babies to come to hospital between day 3-5 when screening for hypothyroidism is usually carried out. We also determined the normal position of the umbilicus in Nigerian newborns and found that the umbilicus is located at point 66% of the distance between the xyphoid process and the pubic
symphysis or point 79% of the distance between the suprasternal notch and the pubic symphysis. This will help the surgeon when there is a need for surgical repair and reconstruction of congenital anomalies around the umbilicus.

**SERVICE TO THE COMMUNITY**
The three pivots on which an Academician stands on are Teaching, Research and Community service, I have tried to give an account of the former two. Mr. Vice Chancellor sir, as I gradually bring this lecture to a close, permit me to mention some of the services I have rendered to the community over the years. I have been a resource person to various media houses to educate the populace on topical health issues and giving medical advice to improve the health of Nigerian children. I have been a member and then chairperson of the OAUTHC Baby Friendly Hospital Initiative and for over a decade we organise world breast feeding week activities in Ife-Ijesa zones to reinforce and educate the people on the importance of baby friendly practices, this was widely accepted and has led to improvement of the health of the children of the zone. I have also through the Christian Medical and Dental Association of Nigeria (of which I served as Chairman between 2007-2011) and the Chapel of Grace, OAUTHC participated in several free medical mission outreaches to several communities like-Iperindo, Yekemi, Aba-Oyibo, Ilesa, Osu, Abata Egba, Garage Olode, Ifetedo, Ora Igbomina to mention a few.

At these outreaches, we freely gave of our expertise to the community through health talks, medical examinations, treatment and surgeries and distributions of eye glasses free of charge. We also preached the gospel of the Lord Jesus Christ to them. I have also served the University at various capacities: I served as Part 5 M.B.Ch.B programme coordinator for the Faculty between 2007-2010, I was a member of the management team of the Glory Land Medical Students Hostel between 2012 to 2016. I was appointed acting Head of the Department of Paediatrics and Child Health between August 1 2017 and July 31st 2018. I have also served in various committees of the Department of Paediatrics and Child Health, Faculty of Clinical Sciences and the College of Health Sciences and the University. I was appointed the Deputy Chairman
Medical Advisory Committee (DCMAC) at the OAUTHC between June 2014 and April 2018 when I was appointed the substantive Chairman Medical Advisory Committee (CMAC). I was elected the National Secretary of the Paediatric Association of Nigeria, where I served under the Presidency of Professor Adebiyi Olowu for three years from 2013 to 2016. I am also a member of the Okeigbo Light bearers, Okeigbo Economic Development Initiative (OEDI) and the Okeigbo New Era (ONE). I have been a member of the Chapel of Grace OAUTHC and the Full Gospel Business Men’s Fellowship International (FGBMFI) where I have served in various capacities. In all of these positions of responsibilities, I deployed my God-given abilities and His Grace in the way and manner that left indelible footprints. I have always believed what the Holy Bible says that whatever anyone has, have only been given to him and like Apostle Paul said “But by Grace of God I am what I am: and His grace which was bestowed upon me was not in vain” (1 Corinthians 15: 10a, KJV). I am grateful to God for the various opportunities to serve and to all those that worked with me and that I worked with to achieve whatever modest achievement we recorded. I was opportuned to do a one-year Sabbatical as Research Advisor with the Community Health Department of Shell Petroleum Development Company (SPDC) in 2015 and I facilitated the upgrading of paediatric services and established the Neonatal unit at the Obio Cottage Hospital, Rumobiakhani, Port Harcourt.

Because of the challenges I have personally encountered while growing up and going through school and seeing several of my patients dying or suffering severe morbidities due to lack of funds, I together with my wife established the GABRIEL ELUDIRE AND VICTORIA BOLATITO ELUSIYAN MEMORIAL FOUNDATION in honour of my late parents to provide succour for indigents patients and students. This was officially launched in July 2018 although our activities started much earlier. They through their lives taught us to give even when we feel we do not have. Through this Foundation, we have given support to several students in Secondary and Tertiary Education and to many needy patients to buy drugs, pay for admission or settle Hospital discharge fees. I equally give God the glory for this opportunity.
More than anything else that has happened to me or that I have become, I give glory to God for this opportunity and hope to leave this as a legacy to be remembered for. We are at www.elusiyanmemorialfoundation.org

CONCLUSION AND RECOMMENDATIONS
Mr, Vice Chancellor sir, distinguished audience, playing a pioneering role in paediatric endocrinology has not been a smooth sail because of the many obstacles; I have through my research and observation enumerated the many challenges and ways we have tried to overcome them to provide the little succour we have been able to provide. The Government should be alive to its responsibility to cater for its citizens. The children of today are the leaders of tomorrow even though many have been left to wonder whether tomorrow will ever come for them. The Government should make health care accessible and affordable to all. I will want to appeal to the Government to make treatment of children with chronic diseases free and if not entirely free at least subsidised. We have through the Paediatric Association of Nigeria, advocated for the provision of free health care to children in Nigeria. We suggested funding for such could be sourced through GSM tax of few kobos on every minute call and pooled together to fund free health care delivery. Scaling up of the National Health Insurance Scheme to reach the informal sectors is also suggested as a means of improving access to care. Such that patients will not have to pay out of pocket to access care. The Government should as a matter of urgency set up COMPULSORY NATIONWIDE new born screening for Congenital Hypothyroidism and other common congenital metabolic and endocrine conditions, so that affected children could be picked early and treated before complications and or death sets in. There is a need for more research in the field of paediatric endocrinology to understand the natural histories and characteristics of these conditions and bring out their peculiarities in the sub-region. A team approach to the management of endocrine conditions should also be encouraged for optimal outcome in children with endocrine conditions.

APPRECIATION
Mr, Vice Chancellor sir, I started this lecture by thanking God for this rare privilege given to me to stand before this august gathering to present my inaugural. It has been God, and to him again I am returning all the praises. Nobody would have ever thought that the little boy that roamed the streets of Okeigbo hawking pepper and tomatoes in the 70s and cutting weekend jobs with bricklayers will in this short time be standing here to present this lecture. But God through a divine hand and providence brought me this far. The whole of eternity will not be enough to thank God.

“Osuba re re o Oluwa,
Osuba re re o Oluwa,
Oba ta o ri, ta a ri ise owo re,
Osuba re re o.”

If anyone here is still doubting that there is a God that makes a way when humans say there is no way you need not go far as you have seen such a man who God helped. And I will challenge you to come to Him and experience His help.

Several people too numerous to mention allowed themselves to be used to lift me up. Many others had the opportunity to help but did not. I thank them both. My late parents deserved mention here again, Baami Gabriel Eludire and Moomi Bolatito Aweke,

I find it difficult to say you are late because every day I still see you, hear you, think of you and talk about you. They set my feet on this path and so painful none of you is here to witness today. And my hope is that one day I will see you at the resurrection to part no more. My brother Mr Kayode Elusiyan (aka Baba koko), you have stood not only as a brother but as a father, and mother to all of us your siblings. I am very grateful for your love and support over the years. You gave when you had little to give, but those little giving were timely and helpful. I will ever remain grateful. To all my other siblings Aunti Theresa, Aunti Olawunmi, Osedayo, Moromoke, Eluyemi, Olapeju and their spouses and children, thank you all for been there all the time, when you had to sacrifice that I could finish Medical School. To my half-brothers, and sisters, uncles and aunts, I appreciate your love. I have mentioned some of my Overseas mentors earlier, I have also been fortunate to have many ‘local’
mentors in Ife: Professors AA Akinsola, JA Owa, CT Akanbi, OO Adeodu, OA Oyelami, WA Olowu, Ebun Adejuyigbe, Adesegun Fatusi (My Pastor, Mentor and Role Model), BA Kolawole, Kayode Olabanji, Victor Adetiloye (My oga at the top) and Dr MO Onigbinde. I cherish you all and I appreciate your tutelage. Prof Oluwagbenga Mokuolu of the University of Ilorin and Teaching Hospital motivated and stimulated me to choose Paediatrics and looking back I have no regret. Thank you sir, for the encouragements and being a role model. Prof Tolu Odugbemi, former Vice Chancellor, University of Lagos and Baba Ijo St Lukes Church, Okeigbo, has also been a source of encouragement and role model; he gave me a letter to University of Ilorin Teaching Hospital in 1995 for my housemanship. I appreciate you sir. I will not fail to mention the encouragement and motivation I received from His Royal Majesty, Oba Lawrence Olu Babajide, Bamgbala 1, the Olouke of Okeigbo Kingdom, since my medical students days and up until the present. You saw this day many years before now, and I thank God that has spared your life to witness this day. I also immensely appreciate my Spiritual parents and friends Pastor (Dr) MA Oyelami, Pastor (Dr) Odun Orioke, Bro (Prof) Sunday Isehunwa, Bro Steve Ogundipe, Bro Nnamdi Madueke, Daddy Ademola and Mummy Folake Adepetu. I also appreciate the other Pastors and entire members of the Chapel of Grace, OAUTHC and the National Directors and entire members of the Full Gospel Business Men’s Fellowship International, Ile-Ife Zone, I love you all. Special mention must also be made of the supports from some of my friends Professor Akinyemi Akanni, Mr and Dr (Mrs) Sina & Debola Akinjokun, Drs Akin Adepiti, Toyin Adetan, Lanre Oyegbade, Akinwumi Fajola (SPDC Port Harcourt), Messrs Anthony Adeniyi, Dayo Odugbemi and Charles Adedeji. I equally appreciate my in-laws; Mr and Mrs Bankole Bello and Adelusis. I will also like to thank all the staff of the Department of Paediatrics and Child Health, OAU and OAUTHC for your support and cooperation and contributions to my progress. I sincerely appreciate and thank all my co-Researchers within the Department, Faculty, College and those outside the University and the Country, especially my Colleagues in the Society of Paediatric and Adolescent Endocrinology of Nigeria (SPAEN) and the African Society for Paediatric and Adolescent Endocrinology (ASPAE). I thank the Director of Administrations
Mrs Bola Alejo and all the staff of OAUTHC for the support I have enjoyed working with you all.

I thank the inaugural lecture planning committee for your contributions to the success of this inaugural lecture with special mention and appreciation to my mentees Drs Funke Odunlade, Elizabeth Oyenusi, Henry Anyabolu, Tosin Olorunmoteni and Abiodun Kareem.

Finally, I will like to appreciate my wife, Christianah Abimbola for the support and encouragement all these 18 years of our marriage. Thank you Oyami.

To our wonderful boys Boluwatife David, Toluwanimi John and Oluwadamilola Joshua (Jerome Jnr, carbon copy). I thank God for the gift that you all are to me. I cherish every moment I have spent with you and the many more years we will still spend together. I publicly declare my unconditional love to you all.

I thank you all for your presence and attention. May God in His infinite mercies bless you all.

REFERENCES

15. Jaja T. Hypoglycaemia in emergency admissions at the University of Port Harcourt Teaching Hospital Dissertation submitted to the National Postgraduate Medical College of Nigeria (FMCPaed) Nov 2008
16. Oyenusi E.E. Hypoglycaemia in children aged one month to 10 years admitted to the children’s emergency centre of the Lagos


