GLYCAEMIC CONTROL AND PREVALENCE OF MICROALBUMINURIA AMONG CHILDREN WITH TYPE 1 DIABETES MELLITUS ATTENDING MULAGO HOSPITAL CLINICS

BY

DR OBURU OFUMBI GEOFFREY MB,Ch.B (MUK)

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH

May 2009
DECLARATION

I Oburu Ofumbi Geoffrey, hereby declare that the work presented in this dissertation has not been presented for any other degree in any University.

Signed………………………………………...………………………………………

DR. OBURU OFUMBI GEOFFREY Date

This dissertation has been submitted for examination with the approval of the following supervisors;

…………………………………………………………………………………………...

DR EDISON MWOROZI Date

MB.Ch.B, M.Med (MUK), Dip.CEH

Senior Consultant Paediatrician, School of Health Science, Makerere University

…………………………………………………………………………………………...

DR ISRAEL KALYESUBULA Date

MB.Ch.B, M.Med (MUK) DTCH (Liv)

Consultant Paediatrician, School of Health Science,

Makerere University

…………………………………………………………………………………………...

DR AMOS ODIIT Date

MB.Ch.B, M.Med.Paed

Consultant Paediatrician, and honorary lecturer,

School of Health Science, Makerere University
DEDICATION

To the memory of my late mother Mrs Damalie Abbo who passed away just before I started School.

To the memory of my grandmother Faith Norah Ajuang who passed away only months after I had started the hectic journey of a Masters programme in paediatrics and child health.

To my father Dr Alex Ofumbi for his love and value for education, to my sister Betty Ofumbi, to the lady of my life Dr Rebecca Esther for her endurance and support and finally to the paediatric diabetic patients in the country.
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<td>Angiotensin Converting Enzyme - Inhibitor</td>
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<td>ACR</td>
<td>Albumin creatinine ratio</td>
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<td>AER</td>
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<td>Microalbuminuria</td>
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<td>Interquartile range</td>
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<td>Research Assistant</td>
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<td>MAP</td>
<td>Mean Arterial pressure</td>
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<td>MHPDC</td>
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<td>PI</td>
<td>Principal Investigator</td>
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<td>T1DM</td>
<td>Type 1 diabetes mellitus</td>
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OPERATIONAL DEFINITIONS

Glycosylated haemoglobin (HbA1C): A component of haemoglobin A1 that has undergone glycosylation, it is measured as a proxy for glycaemic control.

Sub-optimal glycaemic control: A level of glycosylated haemoglobin above the ideal for age: less than 2 years of age >9.5%, 2-5 years of age > 9.0%, 6-16 years of age >8.5%, and over 16 years of age >7.5%.

Severe hypoglycaemia: Hypoglycaemia resulting in coma or convulsion or requiring the assistance of another person for treatment.

For younger children below seven years, the definition will include those events with obvious neuroglycopenia manifesting as confusion or drowsiness and requiring immediate treatment.

Diabetic ketoacidosis is defined as a combination of:

✓ Heavy glycosuria above (4+) or 55 mmol/l
✓ Ketonuria (3+) using colour ranging from buff-pink for a negative to maroon for positive.
✓ Hyperglycaemia [blood glucose level above (198mg/dl) or > 11 mmol/l] and
✓ Dehydration loss of greater than 5% of body weight, which requires admission.

Microalbuminuria: Albumin/creatinine ratio (ACR) in spot urine of 2.5–25 mg/mmol (males) or 3.5–25 mg/mmol (females).

No albuminuria: Albumin/creatinine ratio in spot urine of < 2.5 mg/mmol (male) and < 3.5mg/mmol (female).

Overt albuminuria: Albumin/creatinine ratio in spot urine of > 25 mg/mmol regardless of sex.
Weight and height percentiles: The age and sex specific cut off points, for sexes from 2 years to 18 years.

Hypertension: Systolic blood pressure above the 95th percentile value for age, sex, and height for those with no history of diabetes mellitus or hypertension in first degree relatives.

Insulin accessibility: Is the daily availability of insulin to children three months prior to enrolment into the study.

Insulin insecurity: Is none availability of insulin to children in doses and frequencies prescribed, three months prior to enrolment into the study.
ABSTRACT

Background: Uganda has an estimated 900 children under the age of 14 years with T1DM. Currently, there is limited information on burden and complications of diabetes in the country, as it is in sub-Saharan Africa where diagnosis is often missed, monitoring is erratic and availability of insulin is poor.

Glycosylated haemoglobin is a reliable indicator of glycaemic control needed to provide protection of body organs. Acute complications of T1DM include DKA, infection, hypoglycaemia, and electrolyte imbalance. Chronic complications of T1DM include neuropathy, nephropathy, retinopathy and neuropsychiatric.

Microalbuminuria is a good indicator of early renal damage when treatment with angiotensin converting enzyme inhibitors may reverse the disease.

Objective: This study assessed glycaemic control and microalbuminuria in children with type 1 diabetes attending Mulago hospital clinic.

Methods: A cross sectional study was conducted at the diabetic clinic in Mulago hospital, after informed consent and assent (when applicable) was obtained. All children were on insulin, either soluble-lente combination or mixtard. Data was collected on socio-demographic, patient’s characteristics, insulin usage, duration of disease and factors affecting glycaemic control. It was then exported into EpiData v 3.1. The prevalence of glycaemic control and microalbuminuria was performed using Stata v 10.0 software package. Odds ratio was used to measure factors of association with sub optimal glycaemic control. Statistical significance was considered when P-value was ≤ 0.05.
**Results:** Of the 83 children studied, female to male ratio was 1.2:1, mean ± SD age was 14.2 ± 3.5 years, duration of diabetes was 3.24 ± 2.77. The prevalence of children with sub-optimal glycaemic control was 48 (57.8%) whilst 35 (42.2%) had optimal glycaemic control. Microalbuminuria was present in 52 (62.7%) children, 30 (36.1%) had overt albuminuria and 1.2% had no albuminuria. Among the factors investigated, insulin insecurity through self rationing was the only significant factor associated with sub-optimal glycaemic control.

**Conclusion:** The prevalence of sub-optimal glycaemic control and that of microalbuminuria was high, indicating a very high incidence of poor glycaemic control, and early renal disease among study children.

**Recommendations:**

- Regular monitoring of glycaemic control and screening for microalbuminuria in Ugandan children with T1DM should start as soon as the diagnosis is made.

- There is need for adequate stocks of insulin to improve glycaemic control.

- A longitudinal study should be carried out to monitor and screen for complications that may arise in early adulthood.
CHAPTER ONE

1.0 Background Information

There are about 400,000 children with diabetes with additional 70,000 annually world wide\textsuperscript{1} and the incidence is on the increase at about 3\% per year\textsuperscript{2}.

Uganda has an estimated 900 children under the age of 14 years with diabetes\textsuperscript{1}. Limited information on burden and complications is available in sub-Saharan Africa where diagnosis is often missed, monitoring is erratic and availability of insulin is not predictable\textsuperscript{3}.

Acute complications of T1DM include DKA, infection, hypoglycaemia, and electrolyte imbalance while chronic ones are neuropathy, nephropathy, retinopathy and neuropsychiatric.

Renal microvascular damage leads to progressive renal disease starting with reversible \textsuperscript{4-11} stages 1-3 to irreversible \textsuperscript{12-17} stages 4-5. MA is a good indicator of early renal damage when treatment with angiotensin converting enzyme inhibitors (ACE-I) may reverse the disease\textsuperscript{18,19}.

Glycosylated heamoglobin (HbA\textsubscript{1C}) at different age dependent cut-offs is a reliable indicator of glycaemic control\textsuperscript{20,21}. Positive predictive factors for the development of microalbuminuria include increasing age\textsuperscript{22-25}, poor metabolic control within the first 5 years, dyslipidemia\textsuperscript{23-26}, smoking\textsuperscript{27}, and familial and genetic factors\textsuperscript{28,29}.

1.1 Literature review

In the developed world, enormous efforts are made to reduce chronic complications of diabetes, yet in many developing countries, the incidence of these complications in children is not known, making their management even more difficult. Information on chronic complications of diabetes
in sub-Saharan Africa is scarce; however, the occurrence of new cases of paediatric T1DM has gone hand in hand with the growing disease prevalence, demonstrating the importance of assessing for these complications\textsuperscript{30-32}.

Microalbuminuria denotes increases in albumin excretion rate (AER) outside the normal range but too low to register on the conventional clinic testing. It is an early sign of diabetic nephropathy at a stage when nephropathy may be reversible with careful glycaemic and blood pressure control\textsuperscript{19}, and by use of angiotensin converting enzyme inhibitors\textsuperscript{18}. Depending on the method of screening the prevalence of MA in children and young adults with T1DM varies world wide between 5\% and 22\%\textsuperscript{33,34}. In those with T1DM onset under 20 years of age, diabetic nephropathy is a described complication associated with generalized microvascular\textsuperscript{35} and macrovascular\textsuperscript{36} damage, and increases all-cause mortality in this age category\textsuperscript{37-39}. Therefore, it is important to carefully monitor all children with T1DM to ensure diabetes control is optimized and to look for evidence of early renal disease, because the occurrence of persistent microalbuminuria (PMA) predicts later development of renal failure in T1DM patients\textsuperscript{40-42}. This involves regular screening for microalbuminuria. Urinary albumin excretion is the best marker and the most practical method for detecting diabetic nephropathy. The gold standard for the assessment of MA and overt albuminuria in children is the quantitative analysis of a 24 hour urine collection\textsuperscript{43,44}. However, the American diabetes association considers on-spot urine collections for albumin creatinine to be an acceptable screening strategy in children, with more intensive investigation required for those who screen positive\textsuperscript{45,46}.

1.2 Global situation of type 1 diabetes mellitus

There has been an upturn in the incidence of T1DM, a trend that is now observed in countries around the world\textsuperscript{2}. The incidence is increasing in children and youth by about 3\% \textit{(range about...}
2–5%) per annum, with the greatest rate of rise in under 4-yr-old age group\textsuperscript{2}. However, there are a large number of adolescents who present in early puberty. In 2006, the number of children globally aged 0–14 yr with T1DM was estimated to be 440 000, with 70 000 newly diagnosed cases each year\textsuperscript{1}. More than one quarter of these newly diagnosed cases came from South East Asia and more than one fifth from Europe. This increase in incidence has been observed in countries with both high and low prevalence, with an indication of a steeper increase in some of the low-prevalence countries\textsuperscript{47,48}.

The outlook of children with type 1 diabetes in the developing world, its natural history, including its complications, are largely unknown\textsuperscript{49}. With few data available on sub-Saharan African children, the incidence in Tanzania was estimated to be 1.5/100,000\textsuperscript{50}. An Increase in incidence in Sudan from 9.5/100,000 in 1991 to 10.3/100,000 in 1995 has been reported\textsuperscript{51,52}. Complications of diabetes mellitus are grouped into acute and chronic complications. Acute complications include hypoglycaemia, DKA, recurrent infection, dehydration, and electrolyte imbalance. Chronic complications include microalbuminuria, neuropathy, retinopathy, short stature, and neuropsychiatry complications.

In Uganda, estimates show that there should be about 900 children under the age of 14 years with T1DM\textsuperscript{2}. Whilst MA is generally considered to be rare in children, these data are derived primarily from North America and European populations. In sub-Saharan Africa a few studies evaluating complications in both adult and children reported a 7.5% prevalence of nephropathy\textsuperscript{3}. In Tanzania\textsuperscript{53}, a study in children reported prevalence of MA of 29.3%. In Uganda, studies in adult patients reported an overall prevalence of MA of 69% with levels of glycaemic control of 11% and above. In the Ugandan study\textsuperscript{54}, 94% of all the patients with MA also had raised HbA\textsubscript{1c}, whilst the majority 68% of the patients with hypertension also had MA.
1.3 Type 1 diabetes mellitus and nephropathy

Natural history, early pathohistological changes, and pathogenesis

Chronic hyperglycaemia is an important factor in the pathogenesis of diabetic nephropathy\(^{55-57}\). Long standing hyperglycaemia up regulates the expression of a fibrogenic growth factor, transforming growth factor-\(\beta\), which is involved in both early and later stages DN\(^{58}\). Following vascular injury, a cytokine cascade is activated which increases capillary permeability to plasma protein. Within the renal vasculature the effect of increased endothelial permeability to proteins is the occurrence of MA\(^{57,59}\).

The natural history of renal involvement in patients with T1DM is classified into five stages according to the degree of changes in renal function and morphology\(^{60,61}\).

Stage I

With the onset of diabetes, the only changes—which are encountered in 25–50% of patients are increased renal size and increased GFR by 20–40%, called hyper-filtration. Microalbuminuria may be present but is readily reversible with insulin treatment. The increases in renal size and GFR may normalize or may persist in some patients. Hyper-filtration is thought to predispose these patients to the development of diabetic kidney disease\(^{4,6,7}\), but other findings support the view that renal hypertrophy is the primary dysfunction, and it precedes hyper-filtration during the development of MA\(^{11}\). Blood pressure typically is normal during this period. There is no evidence of histological lesion in glomeruli or vascular structures.
Stage II

Two to 5 years following onset of T1DM glomerular basement membrane (GBM) thickening and mesangial matrix expansion occurs in all individuals. In most studies, MA was only present during periods of poor metabolic control and with exercise. Many patients continue in this stage for many years or throughout their lives. Toward the end of this silent period, urinary albumin excretion (UAE) will begin to rise within the normal range in a set of patients that will ultimately develop MA.

Stage III

The third stage of DN develops 7–10 years after onset of T1DM. Usually, it is found in about a third of the patients, and is characterized by the appearance of MA. Microalbuminuria is widely accepted as the first clinical sign of DN. In adolescents with MA detected in the first decade of diabetes, progression is much less predictable than in adults\(^6,8,10,23,25\). Glomerular filtration rate (GFR) is normal or still elevated. Incipient increase in BP (about 3 mmHg/year), albeit still within the conventional age-corrected normal range, may be found in this stage. In adolescents, an increase in nocturnal systolic BP precedes the development of MA\(^9\). Some long-standing normoalbuminuric (NA) patients may have reduced GFR associated with more advanced glomerular lesions and, probably, an increased risk of progression\(^5\). Pathology shows a progression of the glomerular lesions.

Stage IV

The onset of the fourth stage, found in 15–20% of patients or less after 15–25 years of diabetes\(^12,15-17\), is heralded by overt (clinical) proteinuria (>0.5 g/24 h) that is commonly associated with the presence of other microvascular complications, particularly retinopathy.
Increasing albumin excretion rate (AER) is generally accompanied by a steady rise in BP (by about 3 mmHg/year) and declining GFR in most patients (by about 10 ml/min per year). Decline of GFR has been slowed by administration of angiotensin converting enzyme inhibitors (ACE-I) but not necessarily stopped\textsuperscript{18}. Proteinuria is an ominous finding, as studies report a 40-fold increase in mortality in this group.

**Stage V**

The final stage occurs with the progression to end-stage renal disease (ESRD), usually 5–10 years after the appearance of overt proteinuria. However, there are few reports of young children or teenagers with T1DM of short duration (4–11 years) with accelerated development of clinical DN and associated glomerular lesions typical of this stage of the disease\textsuperscript{13,14}.

**1.4 Risk factors**

A number of risk factors have been identified that influence the onset and/or progression of DN: glycaemic control, duration of diabetes, puberty, age at onset, higher BP, smoking, hyperlipidemia, and family history of diabetic complications, and genetic factors. Some of these factors, such as disease duration or family history, are clearly not modifiable, whereas others, including the degree of metabolic control achieved or the presence of hypertension may be amenable to highly effective interventions.

**1.5 Microalbuminuria**

**1.5.0 Definitions and methods of screening**

Clinically detectable DN begins with the development of MA or incipient DN. The term microalbuminuria denotes increases in albumin excretion rate outside the normal range but too
low to register on a conventional clinic testing. Microalbuminuria is an early sign of DN at a stage when nephropathy may be reversible with careful glycaemic and BP control\(^\text{19}\).

Microalbuminuria is defined by the American diabetes association as any of the following \(^\text{19,62-64}\):

- Albumin/creatinine ratio (ACR) in spot urine of 2.5–25 mg/mmol (males) or 3.5–25 mg/mmol (females).
- Albumin excretion rate (AER) of between 20 and 200 mcg/min in timed overnight urine collection or AER 30–300 mg in 24-h urine collections \(^\text{43,44}\).

Persistent/permanent MA (PMA) is defined as AER of 20–200 mcg/min (30–300 mg/24 h) in a minimum of two out of three urine samples collected consecutively, preferably within a 3- to 6-month period\(^\text{19,62-64}\). This definition is exactly the same as that adopted by general consensus in adults. The belief is that it represents the best available marker for progression to advanced stages of DN\(^\text{42,65}\). The arbitrary value for MA of 20 mcg/min is far above 7.2–7.6 mcg/min, the 95\(^{\text{th}}\) centile of AER in healthy children and adolescents\(^\text{66,67}\), but high day-to-day variability in AER validates its use\(^\text{45,62,64}\). Other studies, however, found higher 95\(^{\text{th}}\) percentiles, 15.1 or 20 mcg/min, for healthy children and adolescents\(^\text{24,68}\).

For practical reasons, ACR in early morning (first void) urine sample can be used. Values of \(\geq 2.5\) mg/mmol predict an overnight AER > 20 mcg/min, with both sensitivity and specificity in the ranges of 82–100\(^{\%}\)\(^\text{69,70}\). The positive predictive value of ACR in early morning urine sample is 66\(^{\%}\) for MA using established definitions based on timed collections\(^\text{71}\). However, screening should be postponed in circumstances known to acutely or transiently increase the AER, such as extreme exercise within 24 h, fever, and urinary tract or other infections, menstrual bleeding and haematuria\(^\text{42,63,64}\). Many researchers prefer overnight timed urine collection or ACR in first-void
morning urine, because it reduces the influence of confounding factors\textsuperscript{45,72}. ACR in random urine sample, although easier to obtain, may be influenced by orthostatic or post-exercise proteinuria\textsuperscript{70}. Regardless of the procedure used, at least two of three samples over a 3 to 6-month period should confirm MA, because AER has an intra-individual coefficient of variation of approximately 40%\textsuperscript{19,62-64}. Some researchers have recommended that at least 1 month should elapse between urine sampling\textsuperscript{45}.

**Methods used in this study**

This was an index cross-sectional study in our setting. We needed to establish basis for feature studies so we used on spot urine collection for albumin creatinine ratio recommended by the American diabetes association as a screening strategy in children, with more intensive investigation required for those who screen positive\textsuperscript{45,46}. It also eliminates the possibility of orthostatic proteinuria.

**1.5.1 Screening and monitoring**

It is recommended that screening for MA be started depending on the age of T1DM onset\textsuperscript{19,62,63}. In patients with prepubertal onset, screening should start from 11 years with 2 years of diabetes duration and from 9 years with 5 years of duration. In patients with pubertal onset of DM, annual screening should start 2 years after diagnosis\textsuperscript{73}; more frequent testing is indicated if the AER values are increasing.

In case of no albuminuria (NA), testing is performed annually. In patients with MA, repeated testing should be done over the next 3– 6 months for confirming or excluding PMA. Patients with intermittent MA should be checked monthly over 3 months because they may be at risk for
progression\textsuperscript{74}. When PMA is confirmed, non-T1DM-related causes of renal disease should be excluded, with further evaluation determined by disease history and clinical examination. It is recommended that each urinary albumin test be accompanied by BP measurements at least annually; comparing values obtained with centile charts appropriate for sex, age, and height. Confirmation about hypertension may be assisted by 24-h ambulatory blood pressure monitoring\textsuperscript{62,75}. Particular attention should be paid to BP readings in those with intermittent or persistent MA and in those with positive family history of hypertension, stroke, or kidney or cardiovascular disease. Annual screening for retinopathy, neuropathy, and lipid abnormalities is also recommended, and GFR is also determined annually when PMA has been confirmed.

1.5.2 Prevention and intervention

Interventions can be divided into those that prevent the onset of complications (primary prevention) and those that slow or halt their progress (secondary intervention). The goal of a prevention strategy involves changing potentially modifiable risk factors: optimizing blood glucose control, discouraging smoking, encouraging healthy diet, controlling BP, and encouraging healthy exercise\textsuperscript{19,64,72}.

In patients with proven MA, non-pharmacological and/or pharmacological measures should be initiated with repeated (at 6 months) testing of AER. The treatment principles are almost the same as those adopted for the prevention of DN, although in this case, more aggressive strategies must be used\textsuperscript{63}. The goal of treatment is to prevent progression of MA to overt proteinuria and to mitigate the decline in renal function. Measures in adolescents with PMA include improving metabolic control ($HbA1c < 8.0–8.5\%$), maintaining normal BP, smoking cessation, maintaining normal plasma lipid profile, and encouraging exercise.
Longitudinal studies with a large number of T1DM youngsters are lacking, where normal protein intake is recommended\textsuperscript{18,72}.

There is no general consensus among paediatrician’s on who should receive treatment with renoprotective drugs, when and for how long, and various treatment policies are in use in different centres\textsuperscript{75}. In an attempt to establish some rules for renoprotective drugs use, Chiarelli et al\textsuperscript{18,72} proposed some recommendations based on the present knowledge on risk factors for initiation or progression of DN.

Treatment with ACE inhibitors titrated to normalize albumin excretion rate was recommended for all children with MA because of their renoprotective effect \textsuperscript{19,63}. 
CHAPTER TWO

2.0 Problem statement

There are about 400,000 children with diabetes with additional 70,000 annually world wide\(^1\) and the incidence is on the increase at about 3% per year\(^2\). Uganda has an estimated 900 children under the age of 14 years with diabetes\(^1\).

Depending on the method of screening the prevalence of MA in children and young adults with T1DM varies world wide between 5% and 22\(^{33,34}\). Many studies\(^3\) in Africa report prevalence of microalbuminuria of about 7.5% in both adults and children with Tanzania\(^53\) reporting microalbuminuria in children at 29.3% studies in Ugandan\(^54\) adults reported the prevalence at 69%.

In the developed\(^34\) world enormous efforts are made to reduce chronic complications of diabetes by control of the glycaemic level. However, in Uganda there are no studies about glycaemic control among children with T1DM, and their frequently affected organ damage (in particular the kidneys), making planning and management of diabetes difficult.

With erratic availability of insulin at Mulago hospital together with the lack of urine and blood sugar monitoring devices at home, control is bound to be poor and risk of organ damage high. To make matters worse, the lack of cold storage for insulin, travel expenses to hospitals and drug purchase costs being unaffordable for most Ugandans. It is possible that the majority of children with diabetes in Uganda die without ever being diagnosed or adequately treated.
2.1 Justification

Although microalbuminuria is generally considered to be rare in children this data is derived primarily from North American and European populations\(^8\) where diabetes management is better. The prevalence of MA among Ugandan diabetic children is not known. The high rates of microvascular\(^{35}\) and macrovascular\(^{36}\) disease reported in adult studies and progression to early renal disease, might have its origin in childhood, for those with T1DM.

This study was designed to assess the control of diabetes, describe factors associated with poor control of diabetes and prevalence of microalbuminuria.

Results of this study are to form a background for better planning and management of children with T1DM. However, screening for microalbuminuria and monitoring glycaemic control in the country will be recommended if the prevalence of MA is found to be significant.

2.2 Research questions

**Primary questions**

1. What is the prevalence of sub-optimal glycaemic control in children with T1DM attending Mulago hospital diabetic clinic?

2. What is the prevalence of microalbuminuria among children with T1DM attending Mulago hospital diabetic clinic?

**Secondary question**

1. What are the factors associated with sub-optimal glycaemic control among children with T1DM attending Mulago hospital diabetes clinic?
2.3 Objectives

General objective

This study assessed the prevalence of glycaemic control and microalbuminuria in children with type 1 diabetes attending Mulago hospital clinic.

2.3.1 Specific objectives

Primary objective:

✔ To determine the level of glycosylated HbA$_{1C}$ in children with type 1 diabetes attending Mulago hospital diabetic clinic.

✔ To determine the prevalence of microalbuminuria among children with T1DM attending the Mulago hospital clinic.

Secondary objective:

✔ To identify factors associated with sub-optimal glycaemic control among children with TIDM attending the Mulago hospital clinic.
Figure 1: Conceptual framework

- Insulin insecurity
- Lack of glucose monitoring device
- Lack of education on signs and symptoms of DM
- Age of T1DM onset
- Puberty
- Sex
- Duration of T1DM

- Number of clinic visits in the last 3-months
- Level of education of caretakers and or patient
- Socioeconomic factors
- Smoking
- Alcohol
- High blood pressure
- Diet

Sub-optimal glycaemic control

Organ damage

Microvascular
- Kidneys
- Increasing BP

Macrovascular
- Optic atrophy
- Neuropathy
- Muscular atrophy
CHAPTER THREE

3.0 Methods

Study design

Descriptive cross-sectional study

3.1 Sample size estimation

Using a sample size formula by Kish Leslie for cross-sectional studies:

\[ N = \frac{Z_\alpha^2 \cdot P \cdot (1-P)}{\delta^2} \]

Where \( N \) = sample size estimate of children with type 1 diabetes mellitus.

\( P \) = assumed true population prevalence of microalbuminuria, results of a study in Tanzanian children with T1DM \(^53\), so \( P = 29.3\% \).

\( 1-P \) = the probability of not having microalbuminuria, so \( 1-P = 70.7\% \)

\( Z_\alpha \) = Standard normal deviate at 95% confidence interval corresponding to 1.96

\( \delta \) = Absolute error between the estimated and true population prevalence of MA of 5%.

The calculated sample size \( N = \frac{1.96 \times 1.96 \times (0.293 \times 0.707)}{0.05^2} = 318 \) Children

However, using the modified Kish Leslie formula for available sample size:

\[ N = \frac{N}{1 + (N-1)/K} \]

\( K \) = available number of children with T1DM registered at the clinic in Mulago hospital.
Hence $K = \frac{318}{[1 + (318 - 1)/83]} = 65.985$ children

After adjusting for a 20% failure to turn up for the interviews we got a sample size of 78 children. However we studied a total of 83 children.

**Study duration**

The study was carried out from August 2008 to March 2009.

**Target population**

These were children aged 6-months to 18 years with a diagnosis of T1DM, attending Mulago hospital clinic.

**Eligible population:** Were children aged six months to 18 years with known diagnosis of Type 1 Diabetes Mellitus attending Mulago diabetes clinic.

**3.2 Selection of patients**

**Inclusion criteria**

✓ Age six months to 18 years

✓ Diagnosis of type 1 diabetes mellitus.

✓ Children whose caretakers had consented,

✓ Children assent for those aged more than 7 years.
Delayed inclusion criteria for HbA₁C and MA in children thought to have:

✓ Fever (> 38 °C)
✓ Haematuria (*Bayer Multiple Reagent Strip*)
✓ Urinary tract infection (*leucocyturia with consecutive subsequent positive culture result*)
✓ Alkaline urine (*pH* > 8), which would explain false positive result in Bayer multiple reagent strip.
✓ Menstruation

Exclusion criteria

✓ Congenital heart disease
✓ Children with known diagnosis of nephrotic/ nephritic syndrome
✓ Children with sickle cell disease/anaemia

Sampling procedure

Children were enrolled consecutively on a regular outpatient visit until the required sample was obtained.

3.3 Study setting

The study was carried out at the Peadiatric Diabetes Clinic located on 4th floor medical out patient department of New Mulago hospital. The hospital serves as Uganda’s national referral unit and teaching hospital for Makerere University Medical School. Approximately eighty three children attend to the clinic which runs every Wednesday from 9:00 AM to 2:00PM. On an average clinic day fourteen children are seen by the diabetic team. The team consists of a medical officer, two paediatric nurses with a special training in diabetes, a nutritionist and a
The Principal Investigator is also part of the team. The Mulago hospital pharmacy dispenses free insulin to patients with a prescription, but the pharmacy is chronically in short supply for insulin. The clinic is served by a side laboratory that performs urinalysis, random blood sugar and blood slide for malaria parasites on each clinic day. More complex tests like renal and liver functional tests are performed in the hospital main biochemistry laboratory located on 3rd floor.

**Study instruments**

A semi-structured questionnaire was used to collect data. The questionnaire was administered by the principal investigator with the help of trained research assistants. A Salter weighing scale was used to during the study.

### 3.4 Study procedure

Both new and old children registered and attending to the diabetic clinic at Mulago hospital were involved in the study. A verbal consent from caretakers and assent from older children was obtained by the study nurse before children were sent to the principal investigator (PI) or trained research assistant (RA). The PI or RA explained more about the study, obtained a written consent from caretakers and an assent from children above 7 years, took the history, and did a physical examination.

Two millilitres of blood was drawn using a sterile disposable syringe and needle after cleaning the anterior cubital fossa or dorsum of hand *(Venipuncture site)* with a swab soaked in 70% alcohol. A drop of blood was placed on a glucometer to determine random/fasting blood glucose. The rest of the blood sample was kept in a fluoride bottle for measurement of HbA1C. A single sample for HbA1C was required for the study.
Two millilitres of fresh urine samples were collected on the spot in a clean general container, with no advance instructions concerning fluid intake or urination. All urine samples were first tested using Bayer multi-reagent strips to determine the presence of proteins, Ketones, nitrites, leukocytes and sugar. Urine samples that tested 1+ or greater reading \( (albumin \geq 30 \text{ mg/dl}) \) were considered overtly albuminuric and were not examined further. Urine samples that tested negative on the strip were then tested quantitatively for albuminuria and creatinine by calorimetric and alkaline Picrate methods respectively.

Both new and old children were enrolled consecutively into the study, all data including laboratory results were recorded in a pre-coded and pre-tested questionnaire for completeness. Recruitment of patients ended at 2:00pm on a regular outpatient visit to allow specimen handling in the laboratory before 5:00pm.

**Feedback to the patients’ and further care**

Results of each patient’s test were communicated or explained to the caretaker and the patient at their next visit by the principal investigator. However, if laboratory results indicated poor glycaemic control and/or albuminuria, immediate evaluation of the patient was performed by the PI and a paediatric nephrologist was consulted.

### 3.5 Study measurements

**Measurement variables**

- Albumin in the on-spot urine samples measured in mg/dl.
- Creatinine in the on spot urine samples measured in mmol/l.
✓ Glycosylated haemoglobin (HbA1C) was determined quantitatively by the Diamat high performance chromatography expressed as a percentage.

✓ A systolic blood pressure above the 95th centile value for age, sex, and height was measured by Omron blood pressure machine.

✓ Weight and height centiles for age and sex from 2 to 18 years were considered.

3.6 Data collection procedure

Data was collected using a semi-structured pre-coded and pre-tested questionnaire. Children with delayed inclusion criteria were treated and re-evaluated for inclusion into the study. Sociodemographic data were entered into the questionnaire as the PI took the history, while data from physical examination and laboratory investigations were entered as soon as they were generated.

3.7 Laboratory methods

3.7.1 Glycosylated haemoglobin (HbA1C)

Haemoglobin A1C was measured electrophoretically according to the Diamat high-performance liquid chromatographic method (Bio-Rad Laboratories, Hercules, Cali)\(^{77}\); and the latter assay was calibrated to match the reference system used by the central haemoglobin A1C laboratory of the Diabetes Control and Complication Trial (DCCT). The correlation between the two sets of results was obtained, and linear regression analysis was used to determine a conversion formula that would yield haemoglobin A1C values that corresponds approximately to the haemoglobin A1 values obtained in our laboratory.

\[
\text{Haemoglobin A1c} = \frac{[\text{haemoglobin A1} - 0.14]}{1.23}
\]
3.7.2 Urine investigations

Bayer multiple reagent strip is a semiquantitative strip test for proteinuria, ketonuria and glycosuria based on a purely chemical principle. Multiple Reagent test strip is based on dye binding using a high-affinity sulfonephthalein dye. At a constant pH, the development of any blue colour is due to the presence of albumin. In the spot urine portion the multiple strips was used to screen for proteinuria following the manufacturer’s instructions. Semiquantitative results of 10, 30, 80, and 150 mg albumin/l was read reflectometrically by comparing the colour scale on the bottle following dipping the strip in fresh urine sample for 60 seconds. The semiquantitative determination of creatinine (Bayer strip) is based on the peroxidase-like activity of a copper creatinine complex that catalyses the reaction of diisopropyl- benzene dihydroperoxide and 3, 3', 5, 5'-tetramethylbenzidine. The resulting colour ranges from orange to green to blue, corresponding to a reflectometrically read creatinine concentration of 0.9, 4.4, 8.8, 17.7, and 26.5 mmol/l.

Each urine sample was analyzed for MA and creatinine concentrations. MA was measured from the clinical chemistry laboratory of Mulago hospital by calorimetric method that is based on the Biurets reaction principle using alkaline copper solution while the urine creatinine was measured using the alkaline Picrate method.

The urine albumin/creatinine ratio was calculated using the formula below:

\[
\text{Urine albumin/creatinine} = \frac{\text{Urine albumin (mg/dl)}}{\text{Urine creatinine (mmol/l)}} \times 1000
\]
3.8 Data management and analysis

All values are expressed as means ± SD the overall prevalence of common complications was calculated using frequency distributions and the Fisher’s exact test. The participants were divided into three age-groups (i.e., < 11, 11.5- 15, and 15.5–18 years) according to the age of onset of T1DM. Given the non-normal distribution of the variables, differences between the age groups was tested using the Kruskal-Wallis test. Statistical analysis was performed using Stata v 10.0 software. The statistical significance level was P < 0.05.

Primary objective based on analytical component

✓ Patients found to have HbA1C values within the normal range for age (Appendix 7) were categorized as optimal and those above as sub-optimal. The proportion of children with sub-optimal glycaemic control was determined by dividing the number of children with HbA1C above normal range by the total number of children in the study.

✓ The prevalence of microalbuminuria was computed as the number of patients with MA being the numerator and the total number of patients studied as a denominator.

Secondary Objective based on analytical component

✓ A bivariate Analysis was used to establish the association between individual predictors and outcome (glycaemic control). Odds ratio was used as a measure of association and a statistical significance was determined using a p-value of 0.05 and a 95% confidence interval.

Quality control

The questionnaires were pre-tested, translated into Luganda, the most widely spoken local language in the study setting so as to ensure that the patients understood the questions that were
being asked. Research assistants were recruited from among the health workers in the paediatric diabetic clinic; they were briefed about the study and then trained on data collection. Questionnaires were cross checked every day for completeness. Laboratory instruments were calibrated using the manufacturer’s instructions to avoid errors in the data management. A Salter weighing scale was calibrated according to the Uganda bureau of standard.

3.9 Ethical considerations

Approval to carry out the study was sought and obtained from the department of Paediatrics and Child Health, Makerere University; Makerere University School of Medicine Ethics and Research committee, and from Mulago hospital Ethics and Research committee. Informed consent was obtained from all respondents and confidentiality was ensured. Access to data was limited to those directly involved in the study, and the attending diabetes team to assist in the management of the patients. The consent/assent form was translated into the local language so that participants understood very well what they were signing. The study carried no potential risks to the participants who were free to pull out at anytime of the study.

3.10. Dissemination of study findings

The results of the study will be availed to the department of Paediatrics and Child Health, Makerere University Medical School, Makerere University School of Post graduate studies, Sir Albert Cook Medical School Library. Results will be availed to the Deputy Director of Mulago hospital and Ministry of Health. The work will be availed to the Uganda national council of science and technology and will be submitted to local and international peer reviewed journals for publication.
CHAPTER FOUR

4.0 Results

4.1 Description of study participants

Figure 2: Study profile of participants
As shown in figure 2, a total of 83 children were studied during the months of November 2008 to March 2009.

4.2 Baseline clinical characteristics

Subject clinical characteristics and anthropometric measurements are reported in Table 1. Children were categorized into three groups: below 11 years, 11.5 – 15 years, and 15.5 – 18 years, according to age at diagnosis of T1DM. Female to male ratio was 1.2:1, mean ± SD age was 14.2 ± 3.5 years, duration of diabetes was 3.24 ± 2.77.

The overall prevalence of acute complications: history of hypoglycaemia was 14 (16.9%); diabetic ketoacidosis was 1 (1.2%).

Among children with daily insulin accessibility, 19.3% children did have self rationing of insulin doses to ensure longer period of treatment. Conventional insulin (soluble–Lente) and mixtard (Humulin 30/70 = Humulin R and Humulin NPH) regimens were used, doses ranged from 0.37 to 3.9IU/Kg/day. Fifty two (62.7%) children were treated on soluble-lente, 31 (37.5%) children were treated on Mixtard.

Forty one (49.4%) children had glucometer at home but lacked glucostrips. The rest of the children had neither glucometers nor glucostrips.
# Table 1: Base line characteristics

<table>
<thead>
<tr>
<th>Factors</th>
<th>All</th>
<th>3 - 11 years</th>
<th>11.5 – 15 years</th>
<th>15.5 – 18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N= 83</td>
<td>n= 16</td>
<td>n= 30</td>
<td>n= 37</td>
</tr>
<tr>
<td>Age in years ± SD</td>
<td>14.17 ± 3.50</td>
<td>8.37 ± 2.75</td>
<td>13.8 ± 1.13</td>
<td>16.97 ± 0.76</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>43.02 ± 13.42</td>
<td>26.13 ± 6.74</td>
<td>39.66 ± 9.55</td>
<td>53.06 ± 8.85</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>131.47 ± 12.97</td>
<td>114.12 ± 12.90</td>
<td>131.30 ± 7.94</td>
<td>139.11 ± 8.34</td>
</tr>
<tr>
<td>Height z-score</td>
<td>-3.79 ± 1.63</td>
<td>-2.40 ± 1.78</td>
<td>-3.84 ± 1.43</td>
<td>-4.34 ± 1.37</td>
</tr>
<tr>
<td>Weight z-score</td>
<td>-1.07 ± 2.04</td>
<td>-0.33 ± 1.09</td>
<td>-1.72 ± 2.60</td>
<td>-0.86 ± 1.70</td>
</tr>
<tr>
<td>BMI z-score</td>
<td>0.95 ± 1.61</td>
<td>1.11 ± 1.12</td>
<td>0.47 ± 2.32</td>
<td>1.27 ± 0.84</td>
</tr>
<tr>
<td>Systolic BP ( mmHg)</td>
<td>113.5 ± 12.6</td>
<td>104.5 ± 11.3</td>
<td>112.8 ± 11.6</td>
<td>117.9 ± 12.1</td>
</tr>
<tr>
<td>Sex : Male</td>
<td>38 (45.8)</td>
<td>8 (50.0)</td>
<td>16 (53.3)</td>
<td>14 (37.8)</td>
</tr>
<tr>
<td>Female</td>
<td>45 (54.2)</td>
<td>8 (50.0)</td>
<td>14 (46.7)</td>
<td>23 (63.2)</td>
</tr>
<tr>
<td>Daily accessibility of insulin</td>
<td>Yes</td>
<td>62 (74.7)</td>
<td>13 (81.3)</td>
<td>22 (73.3)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>21 (25.3)</td>
<td>3 (18.8)</td>
<td>8 (26.7)</td>
</tr>
<tr>
<td>Insulin dosages</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 0.8units/Kg</td>
<td>12 (14.4)</td>
<td>2 (12.5)</td>
<td>3 (10.0)</td>
<td>7 (18.9)</td>
</tr>
<tr>
<td>0.81-2units/Kg</td>
<td>33 (39.8)</td>
<td>4 (25.0)</td>
<td>13 (43.3)</td>
<td>16 (43.2)</td>
</tr>
<tr>
<td>&gt; 1.2units/Kg</td>
<td>38 (45.8)</td>
<td>10 (62.5)</td>
<td>14 (46.7)</td>
<td>14 (37.8)</td>
</tr>
<tr>
<td>Duration of diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1 year</td>
<td>17 (20.5)</td>
<td>4 (25.0)</td>
<td>6 (20.0)</td>
<td>7 (18.9)</td>
</tr>
<tr>
<td>1-5 years</td>
<td>52 (62.6)</td>
<td>11 (68.8)</td>
<td>19 (63.3)</td>
<td>22 (59.5)</td>
</tr>
<tr>
<td>Above 5 years</td>
<td>14 (16.9)</td>
<td>1 (6.3)</td>
<td>5 (16.7)</td>
<td>8 (21.6)</td>
</tr>
<tr>
<td>Clinic visits in last 3mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2 visits</td>
<td>28 (33.7)</td>
<td>4 (25.0)</td>
<td>14 (46.7)</td>
<td>10 (27.0)</td>
</tr>
<tr>
<td>3-9 visits</td>
<td>55 (66.3)</td>
<td>12 (75.0)</td>
<td>16 (53.3)</td>
<td>27 (73.0)</td>
</tr>
</tbody>
</table>

Data are mean ± SD or n (%), SDS, SD score.
4.3 Prevalence of sub-optimal glycaemic control and albuminuria

Among 83 children studied, forty eight (57.8%) children had sub-optimal glycaemic control whilst 35 (42.2%) had optimal glycaemic control (figure2).

Of all studied children, the prevalence of albuminuria was; 1.2% children had no albumin, 62.7% children had microalbuminuria, 36.1% children had overt albuminuria.

4.4 Glycaemic control and percentage of albuminuria among study children

The distribution of albuminuria among glycaemic level was; 56.2% microalbuminuria [OR (95% CI) = 1.96 (0.8 – 5), P = 1.16], 41.6% overt albuminuria [OR (95% CI) = 0.6 (0.2 – 1.4), P = 0.2], whilst 2.2% no albumin for Sub– optimal glycaemic control.

Optimal glycaemic control; 28.6% overt albuminuria [OR (95%CI) = 1.8 (0.7 – 4.5, P = 0.2], 71.4% microalbuminuria [OR (95%CI) = 0.51 (0.2 – 1.3), P = 0.16].
The figure 3; Percentages of albuminuria and glycaemic control among study children

The figure above compares percentage of albuminuria and glycaemic control. No significant difference was noted in the percentage of albuminuria and the level of glycaemic control among study children.
Table 2: Bivariate analysis of factors associated with sub optimal HbA1C levels

<table>
<thead>
<tr>
<th>Factors</th>
<th>Sub- optimal HbA1C (n=48)</th>
<th>Optimal HbA1C(n=35)</th>
<th>OR (95% CI)</th>
<th>P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 11 years</td>
<td>8 (50.0)</td>
<td>8 (50.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.5-15 years</td>
<td>15 (50.0)</td>
<td>15 (50.0)</td>
<td>1 (0.30 - 3.36)</td>
<td>1.00</td>
</tr>
<tr>
<td>15 – 18 years</td>
<td>25 (67.6)</td>
<td>12 (32.4)</td>
<td>2.1 (0.63 - 6.90)</td>
<td>0.23</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male / Female</td>
<td>23 (60.5)/25 (55.6)</td>
<td>15 (39.5)/20 (44.5)</td>
<td>0.8 (0.34 - 1.96)</td>
<td>0.65</td>
</tr>
<tr>
<td>Height z-score</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Scores &gt; - 2</td>
<td>8 (80.0)</td>
<td>2 (20.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score &lt; - 2</td>
<td>40 (54.8)</td>
<td>33 (45.2)</td>
<td>0.3 (0.06 - 1.53)</td>
<td>0.15</td>
</tr>
<tr>
<td>Weight z-score</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>z - score &gt; - 2</td>
<td>12 (48.0)</td>
<td>13 (52.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>z - score &lt; - 2</td>
<td>36 (62.1)</td>
<td>22 (37.9)</td>
<td>1.8 (0.69 - 4.57)</td>
<td>0.24</td>
</tr>
<tr>
<td>BMI z-score</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Scores &gt;</td>
<td>40 (57.1)</td>
<td>30 (42.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score &lt; 0</td>
<td>8 (61.5)</td>
<td>5 (38.5)</td>
<td>1.2 (0.36 - 4.04)</td>
<td>0.77</td>
</tr>
<tr>
<td>Duration of T1DM.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1 year</td>
<td>10 (58.8)</td>
<td>7 (41.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 - 5 years</td>
<td>32 (61.5)</td>
<td>20 (38.5)</td>
<td>1.1 (0.37 - 3.42)</td>
<td>0.84</td>
</tr>
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<td>Above 5 years</td>
<td>6 (42.9)</td>
<td>8 (57.1)</td>
<td>0.5 (0.13 - 2.20)</td>
<td>0.38</td>
</tr>
<tr>
<td>Clinic visits in last 3 months.</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>0 - 2 visits</td>
<td>17 (60.7)</td>
<td>11 (39.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 – maximum visits</td>
<td>31 (56.4)</td>
<td>24 (43.6)</td>
<td>0.8 (0.33 - 2.11)</td>
<td>0.70</td>
</tr>
<tr>
<td>Insulin doses</td>
<td></td>
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</tr>
<tr>
<td>&lt; 0.8units/Kg</td>
<td>6 (50.0)</td>
<td>6 (50.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.81-1.2units/Kg</td>
<td>19 (57.6)</td>
<td>14 (42.4)</td>
<td>1.4 (0.36 - 5.11)</td>
<td>0.65</td>
</tr>
<tr>
<td>&gt; 1.2units/Kg</td>
<td>23 (60.5)</td>
<td>15 (39.5)</td>
<td>1.5 (0.42 - 5.66)</td>
<td>0.52</td>
</tr>
<tr>
<td>Insulin type:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soluble-Lente</td>
<td>30 (57.7)</td>
<td>22 (42.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixtard</td>
<td>18 (58.1)</td>
<td>13 (41.9)</td>
<td>1.0 (0.41 – 2.50)</td>
<td>0.97</td>
</tr>
<tr>
<td>Fulltime Insulin availability in 3mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>33 (53.2)</td>
<td>29 (46.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>15 (71.4)</td>
<td>6 (28.8)</td>
<td>2.2 (0.75 - 6.41)</td>
<td>0.14</td>
</tr>
<tr>
<td>Insulin insecurity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did not self ration</td>
<td>35 (52.2)</td>
<td>32 (47.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did self rationing</td>
<td>13 (81.2)</td>
<td>3 (18.8)</td>
<td>4.0 (1.03 -15.19)</td>
<td>0.04</td>
</tr>
<tr>
<td>History of hypoglycaemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7 (50.0)</td>
<td>7 (50.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>41 (59.4)</td>
<td>28 (40.6)</td>
<td>0.7 (0.21 - 2.16)</td>
<td>0.52</td>
</tr>
<tr>
<td>No albuminuria</td>
<td>1 (100)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 4.5 Factors associated with glycaemic control

Table 2 shows bivariate analysis for factors associated with sub-optimal glycaemic control. Among the factors associated with sub-optimal glycaemic control, insulin insecurity through self-rationing to ensure longer time of treatment was the most significant factor with [OR (95% CI), 4 (1.03 – 15.19)].

A multivariate analysis to control for the interactions among the factors was not possible because we had a finite sample size.
CHAPTER FIVE

5.0 Discussion

Introduction

A cross sectional study was conducted from November 2008 to March 2009 among children with type 1 diabetes attending Mulago hospital clinic. The aim of the study was to determine the prevalence of glycaemic control as measured by HbA1C and the prevalence of microalbuminuria. We also needed to determine factors associated with sub-optimal glycaemic control as a secondary objective.

We have reported a high prevalence of poor glycaemic control and a high prevalence of microalbuminuria; perhaps reflecting a complex environment, in which children with type 1 diabetes live in Africa.

Studies have shown that linear growth might be impaired in children with T1DM even when reasonable glycaemic control had been achieved\textsuperscript{78}, and this growth pattern is likely to be more pronounced in a setting in which control of diabetes is very poor. In fact, most of our children had short stature, mean height z-scores were low in all three age-groups (table 1) - 3.79 ± 1.63 with even lower rates in the pubertal -3.84 ± 1.43, and worst in the older age group -4.34 ± 1.37 (table 1). The contribution of other well-known factors such as malnutrition and chronic infections cannot be ruled out. Malnutrition leads to underweight, and subsequently to decreased height. Poorly controlled diabetes on the other hand can lead to stunting (normal weight for height or BMI, but poor linear growth)\textsuperscript{79}. 
5.1 Prevalence of glycaemic control

In this study, children received soluble- lente and mixtard insulin treatment regimen. The mean HbA$_1C$ was 9.95 ± 3.97% compared to 7.5 ± 1.9% reported in developed world$^{80,81}$. The high mean HbA$_1C$, represents poor glycaemic control with a prevalence of 57.8% compared to 8.5% in studies done in developed world$^{80,81}$. However, our findings were similar to a study done in Tanzania$^{53}$, where the prevalence of poor glycaemic control was 60.9% with a mean HbA$_1C$ of 10.65 ± 2.09%.

Most likely, the underlying causes of poor glycaemic control could be the interaction between limited insulin supply, lack of self-monitoring of blood glucose, and multiple infections. In addition to insulin insecurity, patients self rationed insulin doses to ensure longer periods of treatment as noted in table 2

5.2 Prevalence of microalbuminuria

An overall prevalence of microalbuminuria was 62.7% (figure 3). Chronic sub-optimal glycaemic control is an important factor in the pathogenesis of microalbuminuria$^{55-57}$. However, depending on the method used the prevalence of microalbuminuria in children and young adults varies world wide between 5% and 22%$^{34}$.

It is possible that the prevalence of microalbuminuria found in this study might have been overestimated, as confounders like standing for long hours at the clinic and walking long distances to the hospital might have been contributing factors. We acknowledge that these factors were not considered during analysis.

The prevalence of microalbuminuria reported in developed$^{34}$ world is from longitudinal studies were at least three samples of on spot urine collection one month apart were considered to report an average. In this study, we needed to establish the current state of glycaemic control and to
determine any possible renal complication. Therefore, a longitudinal study was not that was need since no information was available in the country to compare with.

5.3 Factors associated with poor glycaemic control

In this study, 25.3% children missed insulin doses at least once over the preceding three months (table 1). This problem was more evident among children with sub-optimal glycaemic control who had self rationing of insulin to ensure long time of treatment [OR (95%CI) = 4.0 (1.03 - 15.19). This situation may have been exacerbated by intermittent availability of supplies such as syringes, urine and blood testing strips, and, perhaps most crucially, by limited experience in the management of diabetes on the part of most health care workers.

The apparently low DKA prevalence of 1.2% is probably from lack of self monitoring, poor documentation and the arbitrary definitions used in the study. However, the most common cause of DKA is omitted insulin injections and intercurrent illnesses, but it is more likely to reflect lack of self monitoring.

Fourteen 14 (16.9%) children reported history of symptomatic hypoglycaemia, this low percentage of hypoglycaemic episodes found in the study, reflect perhaps a multiplicity of factors such as: recall bias, intercurrent infections, inappropriate feeding and low levels of general care. However, the true prevalence of severe hypoglycaemia remains unknown in our population. The percentage might again have been exaggerated and/ or under reported as we depended solely on self reporting or parental reporting of these episodes in the absence of self-monitoring of blood glucose. The prevalence of hypoglycaemia in the Tanzania’s study was (55.6%). Studies have reported that patients with type 1 diabetes, and have chronically poor glycaemic control perceive hypoglycaemia at higher levels than those with optimal glycaemic
control, suggesting the possibility that, children in this study might have had normal blood glucose levels when they had symptoms of hypoglycaemia.

5.4 Conclusions

In this study the following were ascertained;

✓ The prevalence of children with sub-optimal glycaemic was 57.8%, indicating a high incidence of poor glycaemic control.

✓ The prevalence of microalbuminuria was 62.7%, which is very high, indication that a large number of children already have early renal disease.

5.5 Recommendations

✓ Regular monitoring of glycaemic control and screening for microalbuminuria in Ugandan children with T1DM should start as soon as the diagnosis is made.

✓ And a longitudinal study should be carried out to monitor and screen for complications that may arise in early adulthood.

5.6 Study Limitations

✓ The limited sample size could not allow adequate description of factors associated with sub-optimal HbA1C.

✓ It was not possible to assess the correlation between the levels of glycaemic control and frequency of self-monitoring of blood glucose because only 49% children had glucometers, the majority of which were not functional. In addition, even those with glucometers did not have glucostrips.

✓ We used a single on spot urine collection to determining the prevalence of MA rather than at least three on spot urine collection recommended in longitudinal studies.
References


Microalbuminuria in Diabetic Adolescents and Children (MIDAC) Research group

Archives of Disease in Childhood 2000;83:239–43.


Appendices

Appendix 1: Study consent form

Study title:

GLYCAEMIC CONTROL AND PREVALENCE OF MICROALBUMINURIA AMONG CHILDREN WITH TYPE 1 DIABETES ATTENDING MULAGO HOSPITAL DIABETIC CLINIC.

Introduction

I am (representing) Dr Oburu Ofumbi Geoffrey from the Department of Paediatrics and child health, Makerere University Medical school, P. O. Box 7072, Kampala Uganda, Telephone number +256-772-540-226.

E-mail address; oburuofumbi@yahoo.com

You are being requested to allow your child to take part in this study. The purpose of this study is to determine the level of sugar control, factors associated with sub-optimal sugar control and whether your child might be having early kidney disease.

Study procedure: Your child has been identified to participate in this study and requires your consent. You will be asked questions about your child’s illness and a physical examination will be carried out on your child. Blood and urine samples will be obtained from the child upon your permission for laboratory tests for a random/fast ing blood sugar, level of glucose control, urine protein and creatinine. These are used to determine the level of diabetes control and they reflect the likelihood for your child developing early kidney disease.

An on-spot fresh urine sample of approximately 2.0mls will be collected at the out patient reception on the day of a regular visit. Two millitres of blood will be drawn from vessels between the upper and fore arm joint for analysis of sugar control.

Rights of the patient: Entry into the study is entirely voluntary and no penalty will be incurred for non-participation. Should you choose that your child withdraws from the study anytime for
any reason, you are free to do so and this will not affect the management of your child. In case you are not happy with your child’s treatment, you may contact any of my supervisors:

**Dr Edison Mworozzi:** Senior Consultant paediatrician Makerere University medical school department of paediatrics and child health

P. O. Box 7072 Kampala- Uganda.

Tel; 0772 619 355

**Dr Israel Kalyesubula**

Consultant paediatrician Makerere University medical school department of paediatrics and child health

P. O. Box 7072 Kampala- Uganda.

Tel; 0772 674 707

**Dr. Amos Odiit**

Consultant paediatrician Makerere University medical School department of paediatrics and child health

P O Box 7072, Kampala-Uganda

Tel; 0772 520 991

For questions about the rights of the participants you may consult the chairman of the faculty of medicine research and ethics committee Dr. Charles Ibingira on telephone 0414530020.

Benefits and risks: The tests done and results obtained will help the team of medical workers managing your child to know the level of glucose control and how many are currently developing early kidney disease. The results will be used to institute appropriate measures to prevent progression to end stage kidney disease. No serious risks are associated with this study, however, drawing blood from the child will be a little painful but bearable for your child. All laboratory tests will be free during the study period for the participants.
Confidentiality: The identity of your child as well as yours will not be revealed in any presentation or publications of this study. Confidential information will only be used for research purposes only. The information obtained in the course of the study will only be communicated to the medical team managing your child and to no one else without your written permission. This study carries no risk to the participants. However, the participant will experience little pain on drawing blood.

Consent statement: I have been informed of the study to determine the glycosylated haemoglobin and the prevalence of microalbuminuria among children and adolescents with type 1 diabetes mellitus attending Mulago hospital.

The purpose and nature of the study, the benefits and risks to my child have all been explained to me. I was made aware that tests on blood and urine will be done on my child and that these tests are free of charge. I was also informed that the information given will be kept confidential and that my child’s participation in this study is entirely voluntary and no consequences will result if I refuse to participate or withdraw from the study.

I hereby give my informed consent to participate in this study.

....................................................................................................................................................................................

Name of parent/care taker       Caretaker’s signature or thumb print       Date
....................................................................................................................................................................................

Name of investigator/           Signature       Date

Research assistant.................Name signature Date
Appendix 2: Luganda version consent form

OKUNOONYEREZA KUKUZIYIZA OBULWADDE BW’ENSIGO MUBAANA ABALINA OBULWADDE BWA SSUKAALI, ABALINA EBIRAGA NTI BAFUNYE OBULWADDE BW’ENSIGO, NGA BAJJANJABIRWA MU DDWAALIRO E MULAGO.

Ebyanjula:

Ndi wano kulw’omunoonyereza omukulu, Dokita Oburu Ofumbi, asinzidde mu kitongole ekijjanjaba abaana wano mu Mulago.

Ekigendererwa mukunoonyereza kuno kwekuzuula ebyo ebitera okulaga nti omwana omulwadde wa ssukaali afunye ekirwadde ky’ensigo, nga kyakatandika.

Enkola:

Omwana wo azuuliddwa nga alina ebisanyizo by’okunoonyereza kuno. Singa omukkiriza ojja kubuzizibwaayo ebibuuzo ku by’obulwadde bwe ate era omusawo ajja kumwekebejja omubiri gwonna, wagwa nookumugggyako omusaayi n’omusulo nabyo bikeberwe bulungi mu laboratory. Kino kijja kuyamba abasawo okuzaula ebiraga nti omwana afunye obulwadde bw’ensigo nga bwakatandika era kibasobozese okuziyiza ebyandivudddemu.

Kijja kwetaagisa nookufuna omusulo gw’omwana gwa mirundi esatu oguwe abasawo abali mukunooyereza kuno.

Omusulo ogunaasooka ojja kuguggya ku mwana ku lunaku lwe mulina okudda okulaba omusawo mukilinika.

Eddemde lyo nga nnakyewa (this means volunteer you may need to introduce it in the English version too):

Okwenyigira mu kunoonyereza kuno kwa kyeyagalire, tewali kuwalirizibwa kwonna, woyagalira okubivaamu nga obadde wewandiisizza, woobiviiramu, era kino tekikosa bujjanjabi bw’ofuna okuva mu kilinika eno.

Bwe wabaawo kyeweebuza kukunoonyereza kuno, osobola okukuba essimu nooyogera noomunoonyereza omukulu, Dokita Oburu Ofumbi ku namba ya ssimu, 0772540226, oba omu ku abo abalabirira okunoonyereza kuno;

1) Dokita Mworozi Edison ku namba yassimu, 0772619355,
2) Dokita Israel Kalyesubula ku namba yassimu, 0772674707
3) Dokita Odiit Amos ku namba yassimu, 0772520991

Bano bona bali kukasanduuko ka posta namba, 7072, Kampala.
Emigaso n’akabi ebiri mu kunoonyereza kuno

Ebinaava mu kunoonyereza kuno bijja kuyamba abasawo abajjanjaba omwana wo okusobola okumanya okukuuma ssukaali we nga ali wansi ate nookumanya omuwendo gw’abaana abatandise okufuna obulwadde bw’ensigo. Okunoonyereza kwa kuyamba abasawo okusobola okuziyiza abaana okutuuka mu mbeera embi ennyo eyoobulwadde bw’ensigo. Tewali ky’ofiirwa nga wetabye mu kunoonyereza kuno okujjako, wajja kubaawo obulumi obutali bwamanyi okuva kukayiso akaggyako omusaayi,

Enkuuma yebiandiiko mu kunoonyereza:

Ebibakwataako nga abantu, ggwe n’omwana wo, bijja kuba bya kyama era nga byakukozebwa abo bokka abali mukuonyereza, sibyakuwandiikako oba okukozebwa mulujjudde olwengeri yonna okujjako nga gwe owadde olukusa olwo.

Ensasula:

Tewajja kuba kusasulwa kwonna singa wabaawo ekituuka ku mwana mu kiseera ky’anaamala nga ali mu kunoonyereza kuno, wabula kyonna ekisoboka okumuwa obujjanjabi obwetagisa, kyakukolebwa.

Okussaako omukono:

Ntegezebbwa byonna ebikwata ku kunoonyereza kuno byonna, ensonga lwaki kwetaagisa, bye nnyinza okuganyulwamu, oba okufiirwa. Ntegeezebbwa nti kijja kwetaagisa okuggya ku mwana, omusaayi noomusulo, eby’okunoonyerezebwako, era nti ebifa kukunoonyereza bya kukuumibwa nga bya kyama ate nga nookwetaba mu kunoonyereza kwa kyeyagalire. Wenjagalira nsobola okubivaamu nga tewali kye nfiirwa kubujjanjabi omwana bw’afuna mukirinika.

Nzikirizza omwana wange okwetaba mu kunoonyereza. ……………………………

(Errinnya ly’omuzadde/omujjanjabi) (Ekinkumu) …………….Olunaku/omwezi/omwaka

Name of investigator/research asst Signature Date
Appendix 3: Assent form

Study title

GLYCAEMIC CONTROL AND PREVALENCE OF MICROALBUMINURIA AMONG CHILDREN WITH TYPE 1 DIABETES ATTENDING MULAGO HOSPITAL DIABETIC CLINIC.

Introduction

I am (representing) Dr. Oburu Ofumbi Geoffrey from the department of paediatrics and child health, conducting a study to find out the level of sugar control, factors associated with sub-optimal sugar control and the presence of early kidney disease in children attending Mulago hospital clinic.

The findings of this study will help health worker provide appropriate treatment to children with diabetes that may be having early kidney disease.

Procedures

During the study you will be asked questions about your illness such as fever, length of disease, and age when first diagnosed with diabetes. You will under go a full examination, blood and urine samples will be taken for laboratory for analysis.

You will also be asked to collect an on-spot fresh urine sample that you will collect and deliver on the day of your next regular hospital visit.

Risks and benefits

There may be some discomfort caused by the needle prick when drawing blood. Emphasis will be put on ensuring that blood is drawn under aseptic conditions. The laboratory tests will be carried out free of charge and results obtained will be helpful both to the patient and to the health workers caring for children with diabetes and early kidney disease.

Patient’s rights

Participation in this study is voluntary. Refusal to participate in this study will no way affect your treatment. You are free to withdraw from the study at any stage. In case of any queries contact Dr.Oburu Ofumbi from the department of paediatrics and child health, Mulago hospital Tel. 0772-540-226. Or any of his supervisors:

Dr Edison Mworazi
Senior Consultant paediatrician Makerere University Medical School Department of Paediatrics and Child Health

P. O. Box 7072 Kampala- Uganda.

Tel; 0772 619 355

Dr Israel Kalyesubula

Consultant paediatrician Makerere University medical school department of paediatrics and child health

P. O. Box 7072 Kampala- Uganda.

Tel; 0772 674 707

Dr. Amos Odiit

Consultant paediatrician Makerere University medical School department of paediatrics and child health

P O Box 7072, Kampala-Uganda

Tel; 0772 520 991

For questions about the rights of the participants you may consult the chairman of the faculty of medicine research and ethics committee Dr. Charles Ibingira on telephone 0414530020.

Statement of assent

I have been informed about the nature of this study. I understand that questions will be asked of me and I will undergo a physical examination. Urine and blood samples will be taken off for laboratory analysis. All laboratory tests will be free of charge during the study period.

Participation is voluntary and refusal to participate in the study will be no way affecting my treatment. I am free to withdraw from the study at anytime. I therefore, sign below as proof of my assent.

......................................................... ......................................................

Name: Signature/Thumbprint.... Date/month

...............................................................

Name: Signature
Appendix 4 Luganda version of assent form:

OKUNOONYEREZA KUKUZIYIZA OBULWADDE BW’ENSIGO MUBAANA ABALINA OBULWADDE BWA SSUKAALI, ABALINA EBRIRAGA NTI BAFUNYE OBULWADDE BW’ENSIGO, NGA BAJJANJABIRWA MU DDWAALIRO E MULAGO.

Ebyanjula:

Ndi wano kulw’omunoonyereza omukulu, Dokita Oburu Ofumbi, asinzidde mu kitongole ekijjanjaba abaana wano mu Mulago.

Ekigendererwa mukunoonyereza kuno kwekuzuula ebyo ebitera okulaga nti omwana omulwadde wa ssukaali afunye ekirwadde ky’ensigo, nga kyakatandika.

Enkola:

Okuyita mu kiseera ky’onomala nga wenyigidde mu kunoonyereza kuno, ojja kubuuzibwa ebikwata kubulamu bwo, gamba nga omusujja, ebbanga lyoomaze ne ssukaali, ne ddi lwewasooka okumanya nti olina ssukaali. Ojja kufuna okwekebejjebwa omubiri gwonna, era oggyibweko omusaayi n’omusulo bisobole okukeberebwa obulungi.

Kijja kwetagisa okutuwa omusulo kw’olwo lw’onodda okulaba omusawo mu kilinika.

Emigaso n’akabi ebiri mu kunoonyereza kuno Wajja kubaawo obulumi obutali bwa maanyi okuva kukayiso akaggyako omusaayi, naye nga omutindo gw’obuyonjo ogwokukozebwa mu kino gujja kuba gwawaggulu ddala. Okukebera okunetagisa kwonna, kijja kuba kwa bwereere, ate nga ebinaava mu kunoonyereza byakuyamba abasawo okusobola okujjanjaba abana ababa bakafuna obulwadde bw’ensigo.

Eddemde lyo nga nnakyewa

Okwenyigira mu kunoonyereza kuno kwa kyeyagalire, tewali kuwalirizibwa kwonna, woyagalira okubivaamu nga obadde wewandiisizza, wooribiviiramu, era kino tekikosa bujjanjabi bw’ofuna okuva mu kilinika eno.
Bwe wabaawo kyeweebuuza kikunoonyereza kuno, osobola okukuba essimu nooyogera
noomunoonyereza omukulu, Dokita Oburu Ofumbi ku namba ya ssimu, 0772540226, oba omu
ku aho abalabirira okunoonyereza kuno;

1) Dokita Mworazi Edison ku namba yassimu, 0772619355,
2) Dokita Israel Kalyesubula ku namba yassimu, 0772674707
3) Dokita Odiit Amos ku namba yassimu, 0772520991

Bano bonna bali kukasanduuko kaposta namba, 7072, Kampala.

Ebikwata ku kunoonyereza nga kukyagenda mu maaso oba nga kuwedde, osobola okukubira
Dokita Ibingira Charles, 0414530020, ono nno nga yesentebe wokunoonyereza nookukwasisa
empisa mu Uganda.

**Okussaako omukono:**

Ntegezebbwa byonna ebikwata ku kunoonyereza kuno byonna, ensonga lwaki kwetaagisa, bye
nyinza okuganyulwanu, oba okufirwa. Ntegeezebbwa nti kija kwetaagisa okuggya ku mwana,
omusaayi noomusulo, eby’okunoonyerezebwako, era nti ebifa kikunoonyereza bya kukuumbwa
nga bya kyama ate nga nookwetaba mu kunoonyereza kwa kyeyagalire. Wenjagalira nsobola
okubivaamu nga tewali kye nfiirwa Kubujjanjabi omwana bw’afuna mukirinika.

Erinnya)/(Ekinkumu) ..................................................................Olunaku/omwezi/omwaka

..........................................................................................................

Name (Ekinkumu)
Appendix 5: Questionnaire

GLYCAEMIC CONTROL AND PREVALENCE OF MICROALBUMINURIA AMONG CHILDREN WITH TYPE 1 DIABETES ATTENDING MULAGO HOSPITAL DIABETIC CLINIC.

A. Sociodemographics

Child’s study number.......................... File No.......................... Date of visit..........................
Age (years)............................. Sex Female [ ] Male [ ]
Address LCI.............................. LCIII................................. Tel..............................
District Kampala [ ] Wakiso [ ] Mukono [ ] Other [ ]

Education and behavior

Level of education of caretaker.............. Level of education of the patient..........................
Do you smoke cigarettes, No [ ] Yes [ ] if yes how many sticks per day..............
Do you drink alcohol Yes [ ] No [ ], if yes how many bottles per sitting..............
How long have you had diabetes?............. At what age where you? ..............

B. Clinical history (tick were appropriate)

Reason for clinic visit: routine visit [ ] Complaint [ ] No complain [ ]
If complaint tick as appropriately Yes No
❖ Fever (Temperature) [ ] [ ]
❖ Vomiting [ ] [ ]
❖ Abdominal pain/ menses [ ] [ ]
❖ Joint pains [ ] [ ]
C. Current diabetes management

- Insulin.................Insulin usage: Number of injection per day [  ]
- Units of insulin per day [  ] Number of days without insulin [  ].
- Number of days you had to take less insulin [  ], Number of days in last three months without insulin [  ]. Having a glucometer at home Yes [ ] No [  ],
- Having glucose-test strips........ Having a Blood pressure machine..................

Clinical care:

Frequency of the following in 3- months:

- Clinic visits [  ] HbA1C measurement [  ], other diabetes clinic visited............
- Other medication taken....................Diabetes education provided [  ].
- No of education received in last 3-months [  ]

D. Past medical history

Diabetes acute complications: A scale of 1-5 will be used for hypoglycaemic episodes (1- single, 2- double, 3- triple, 4- quadruple and 5- more than five times).

- Acute: Number of episodes of severe hypoglycaemia in the preceding 3 months [  ]
- coma [  ] Convulsion [  ] Assistance of another person for Rx [  ]
- Young children: Confusion [  ], Drowsiness [  ] Requiring immediate Rx [  ]
E. Physical examination

*Anthropometric indices:*

- Weight (Kg) [ ], Height (m) [ ], Weight (%) [ ] Height (%) [ ].

*Respiratory system exam*

- Respiratory rate: Normal [ ], Abnormal [ ]
- Chest in drawing [ ], Crepitations [ ] others.............................

*Cardiovascular system*

- Blood pressure (mmHg) using percentile values for age, sex and height [ ]
- Pulse rate [ ], Blood pressure [ ] Heart sounds............................

*Central nervous system*

- Conscious [ ] Not conscious [ ], Current diagnosis other than T1DM..........................

*Urinalysis*

Sugar.................................................................................................................................
Ketones..............................................................................................................................
Leukocytes........................................................................................................................
PH.........................................................................................................................................
Nitrites..................................................................................................................................

*Laboratory Request Form*

- Random blood sugar [ ] mg/dl or mmol/l.
- Urine albumin [ ] mg/dl.
- Urine creatinine.................mmol/l.
- Urine albumin/creatinine ratio [ ]
- Microalbuminuria [ ], No microalbuminuria [ ].
Appendix 6: Urinary protein calorimetry

GLYCAEMIC CONTROL AND PREVALENCE OF MICROALBUMINURIA AMONG CHILDREN WITH TYPE 1 DIABETES ATTENDING MULAGO HOSPITAL DIABETIC CLINIC.

Determination of urinary protein using the calorimetric method based on the buiret’s reaction

**Principle**

Alkaline copper solution reacts with the peptide bonds in the protein molecule, production a violet colour which is directly proportional to the amount of protein present.

**Reagents**

- 20% trichloroacetic acid
- 1M sodium hydroxide, 40mg per litre of water
- Standard protein solution: 5.0g /l in 0.9% NaCl
- Stock Buiret’s reagent. Dissolve 45g of sodium potassium titration in approximately in 400ml of 0.2M sodium hydroxide. Add with constant stirring 15g of copper sulphate; when in solution add 5g of KI and dilute to 1.0 litre with 0.2M NaOH.

**Methods**

**Test**

To 1.0 or 2.0ml of urine add equal volume of trichloroacetic acid

Mix well and allow stand for 3 minutes.

**Centrifuge**

Decant the supernatant fluid without disturbing the deposit.
Dissolve the precipitated protein in 1.0ml of 1.0M NaOH.

Add 2.0ml of distilled water.

**Black**

3.0ml of distilled water

Standard

3.0ml of standard protein solution

To all the three tubes add 5.0ml of working Buiet’s solution mix thoroughly and place them in the 37 °C water bath for 10 minutes. After colour development allow the tubes to cool and compare the absorbencies in photoelectric absorptiomer, using a green filter.

Use blank to zero the instrument.

**Calculation**

The urine protein concentration (mg/dl) is determined by the following formula;

\[
\text{Protein mg/dl} = \frac{\text{Abs (test)} \times \text{standard conc} \times 1000}{\text{Abs (standard)} \times \text{urine volume}}
\]
Appendix 7: Normal ranges for of glycaemic control and Insulin types

<table>
<thead>
<tr>
<th>Age range</th>
<th>Target optimal HbA1C</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 years</td>
<td>8.5 – 9.5%</td>
</tr>
<tr>
<td>2 – 5 years</td>
<td>8.0 - 9.0%</td>
</tr>
<tr>
<td>6 – 16 years</td>
<td>7.0 – 8.5%</td>
</tr>
<tr>
<td>Above 16 years</td>
<td>6.0 – 7.5%</td>
</tr>
</tbody>
</table>

Insulin préparations

<table>
<thead>
<tr>
<th>Type</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>½ -1hr</td>
<td>2-3 hr</td>
<td>4-8 hr</td>
</tr>
<tr>
<td>Analogue</td>
<td>10 -15min</td>
<td>60-90 min</td>
<td>3-5 hr</td>
</tr>
<tr>
<td>NPH/Lente</td>
<td>2 -4hr</td>
<td>4 -12 hr</td>
<td>12-16 hr</td>
</tr>
<tr>
<td>Detemir</td>
<td>2 -4hr</td>
<td>6 – 12 hr</td>
<td>12 – 20 hr</td>
</tr>
<tr>
<td>Glargine</td>
<td>2-4hr</td>
<td>‘4 -8 hr’</td>
<td>20-24 hr</td>
</tr>
</tbody>
</table>

Analog: Humalog, NovoRapid, Apidra

Regular: Humulin R; Actrapid

Intermediate: Humulin N; Protaphane

Pre- mixed insulin’s are a mixture of the above and share characteristics of both components:

30:70 Ratio of rapid/short to intermediate acting

Actraphane = actrapid and Protaphane

Humulin 30/70 =Humulin R and Humulin NPH (Mixtard)

NovoMix30 = Novorapid and Protaphane

25:75 Ratio of rapid to intermediate acting

Humalog Mix 25 = Humalog and NPL

50:50 Ratio of intermediate to rapid acting

Humalog Mix 50= Humalog and NPL