PREVALENCE OF MICROALBUMINURIA AND ASSOCIATED FACTORS AMONG HYPERTENSIVE PATIENTS AT MUHIMBILI NATIONAL HOSPITAL DAR ES SALAAM

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled **PREVALENCE OF MICROALBUMURIA AND ASSOCIATED FACTORS AMONG HYPERTENSIVE PATIENTS AT MUHILIL NATIONAL HOSPITAL** in fulfillment of requirements for the degree of Master of Medicine (Internal Medicine) of Muhimbili University of Health and Allied Sciences.

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Prof. J. Lutale

(Supervisor)

Date: _____

DECLARATION AND COPYRIGHT

I, **Dr. Hussein Bhalloo** declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature…….....**.....** Date…….**....**……

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DEDICATED

This dissertation is dedicated to my dear wife, Dr. Fatima H. Mussa, my mother Mrs. Tahera Champsi, my son Ali Hussein, my brother Abbas Ali, my sister Mrs. Layla Fazle, and my late father, Asgher Bhalloo who have always been instrumental and inspirational in my career as a doctor.

ABSTRACT

Introduction:

Persistent microalbuminuria is the earliest indicator of chronic kidney disease (CKD) in patients with diabetes and hypertension. Patients with microalbuminuria have high risk for target organ damage resulting in stroke, retinopathy and adverse CV events.

Objective:

To determine the prevalence of Microalbuminuria among hypertensive patients at Muhimbili Hospital – Dar es Salaam.

Methodology:

This was a cross-sectional descriptive epidemiological study which comprised of a sample size of 341 hypertensives (mean age of 53.1 years with SD ± 1.58) from August 2012 to January 2013. Data was collected using a structured questionnaire. Variables that were entered in the equation were duration of diabetes mellitus (DM), type of DM, history of smoking, history of alcohol drinking and duration of drinking and BMI. In all participants urine albuminuria was measured in spot urine sample using initially urine dipstick, and if normoalbuminuria on dipstick, urine samples were further tested for microalbuminuria using microalbumin 2-1 combo strips to assess the albumin creatinine ratio. Other laboratory blood tests included lipid profile and random blood glucose measurements

Results:

The prevalence of microalbuminuria in hypertensives attending the Cardiac clinic at Muhimbili National Hospital was found to be 24% within the study group. The prevalence of microalbuminuria in males and females were found to be 27.4% and 21.6% respectively.

The prevalence of microalbuminuria was noted to be higher among males but was not statistically different (p=0.421).

Age group of greater than 61 years comprised of 24.5% of the microalbuminurics among the different age groups with the mean age of 53.1years with SD±1.586, but statistically, no significant difference was seen. p=0.518

.Cigarette smoking, alcohol consumption, BMI or lipid levels were statistically not associated with the occurrence of microalbuminuria among hypertensive patients.

Conclusion:

This study showed that the prevalence of microalbuminuria was 24% among hypertensive patients seen at the cardiac clinic at the MNH. When any form of albuminuria was considered the prevalence was almost 100%.

Almost all patients seen in this study had a form of proteinuria, either macro or micro which showed that majority of patients has already progressed to some form of albuminuria.

This suggests that microalbuminuria screening should be aggressively used as a screening tool to pick up early evidences of microalbuminuria in hypertensive patients.

There were no statistically significantly factors associated with the occurrence of microalbuminuria among the hypertensive patients

Recommendations:

Microalbuminuria is regarded as the earliest marker of capillary endothelial damage and therefore an important predictor of capillary injury in hypertensive patients; hence vigorous screening of this relatively inexpensive tool is essential which is underperformed at our centre.

It is hence important that in every hypertensive patient, this inexpensive test for urine albumin be measures routinely at every outpatient clinic at Muhimbili Hosp so as to detected early those at an in increased risk of vascular and cardiac morbidity and mortality and appropriate measures for its prevention or delay taken early.

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ABBREVIATIONS

MA	Microalbuminuria
AER	Albumin excrétion rate
ACE	Angiotensin converting enzyme Inhibitor
ARB	Angiotensin receptor blocker
BMI	Body mass index
WT	Weight
ACR	Albumin Creatinine Ratio
MNH	Muhimbili National Hospital
US	United States
TG	Triglycerides
LDL	Low density lipoprotein
HDL	High density lipoprotein
CHOL	Cholesterol
GFR	Glomerular filtration rate
UAE	Urine Albumin Excretion
UACR	Urinary albumin: creatinine ratio
CKD	Chronic Kidney Disease
ELISA	Enzyme-linked immunosorbent assay
NHANES	National Health and Nutrition Examination Survey
CVS	Cardiovascular system
RAAS	Renin Angiotensin Aldosterone System
OPD	Outpatient Department
WHO	World Health Organization
CVD	Cardiovascular disease

EMD	Emergency Medical Department
EGFR	Estimated Glomerular filtration rate
UTI	Urine tract infection
SPSS	Statistical Package for the Social Sciences

DEFINITION OF TERMS

Definition of HTN by WHO CRITERIA

Grade 1 HTN (SBP 140-159 or DBP 90-99)

Grade 2 HTN (SBP 160-179 or DBP 100-109)

Grade 3 HTN (SBP > 180 or DBP > 110)

ALBUMINURIA

Normoalbuminuria is defined by a urinary albumin excretion rate below 30 microgram per minute.

Microalbuminuria is defined by a urinary albumin excretion (UAE) rate higher than 30 but lower than 300 microgram per minute.

Macroalbuminuria is defined by a urinary albumin excretion (UAE) rate greater than 300 microgram per minute.

CHAPTER ONE

1.0 INTRODUCTION AND LITERATURE REVIEW:

Proteinuria has long been known as a major risk factor not only for renal disease but also for cardiovascular disease. However, in recent years the interest has focused on much earlier determinants of renal and cardiovascular disease as established by the presence of microalbuminuria [1-4] Microalbuminuria is a significant risk factor for progression to proteinuria and subsequent renal and cardiovascular disease as well as early mortality.

Therefore although proteinuria has long been part of a general screening program for virtually all types of patients, microalbuminuria has become equally, or perhaps even more, important as this measure makes intervention possible at a much earlier stage, usually before any decline in glomerular filtration rate (GFR) has occurred [4,5] In addition, as the clinical course of microalbuminuria has been fairly studied, patients are now being treated to accomplish optimal glycaemic [6] and blood pressure control [7,8], radically changing the so-called 'natural' history of renal and cardiovascular disease.

Microalbuminuria is typically defined as a 24-h urinary albumin excretion rate (UAE) of 30-300mg (20-200μg/min) or urinary albumin: creatinine ratio (UACR) of 2.5-30mg/mmol in men, 3.5-30mg/mmol in women; the lowest detection limit of proteinuria as measured by standard laboratory methods in the absence of UTI and acute illness.[9] Microalbuminuria is frequently seen in patients with established essential hypertension, and is considered a predictor of a higher risk for CVS and renal dysfunction.

An association between microalbuminuria and several CVS risk factors including dyslipidemia, endothelial dysfunction, insulin resistance, salt sensitivity, and increased renin-angiotensin system (RAAS) activity, has been widely demonstrated in hypertensive patients. Furthermore, increased UAE is associated with signs of subclinical organ damage, such as left ventricular hypertrophy and increased carotid wall thickness. Moreover microalbuminuria is a highly specific predictor of the simultaneous occurrence of both cardiac and vascular abnormalities. [10]

Epidemiological and experimental data confirm that high levels of UAE are associated with an increased incidence of all-cause and, in particular, cardiovascular mortality. [11-18]

1.1 Why do hypertensive patients with microalbuminuria have an increased risk of cardiovascular disease?

One explanation is that a number of studies show a striking clustering of metabolic and non-metabolic risk factors in these patients including : increased and prolonged BP levels and altered 24-h blood pressure profiles, insulin resistance and salt sensitivity, atherogenic serum lipid profile, systemic endothelial dysfunction & increased activity of the RAAS.
In addition, patients with MA show higher blood pressure levels compared to normoalbuminuric patients. [88]

In the Magic study, albuminuria was related to both diastolic and mean blood pressure. Other studies have shown an even stronger correlation between AER and 24-h ambulatory blood pressure. [19]

Macroalbuminuric patients are also characterized by several abnormalities in the circadian pattern of blood pressure, namely higher 24-h mean levels, lower day: night ratio and higher variability of pressure readings.

Furthermore, hypertensive target organ damage is more common in microalbuminuric patients[20-24]. Patients with elevated UAE have higher LV mass [25-28], a higher prevalence of hypertensive retinopathy [29], and an increased thickness and presence of plaques in the carotid artery [30, 31].

1.2 PATHOPHYSIOLOGY

1.2.1 Microalbuminuria and Cardiovascular risk.

Pathophysiologic processes that link microalbuminuria and CVD are unclear. Microalbuminuria could be a cause or a consequence of vascular disease. In the STENO hypothesis put forward by Deckert *ET al.*[32], albumin leakage into the urine reflected a widespread vascular damage, which were hypothesized to be due to endothelial dysfunction and chronic inflammations association between microalbuminuria and CVD [33, 34]. Chronic low-grade inflammation can be both a cause and a consequence of endothelial dysfunction,

and some studies used markers of inflammation such as C-reactive protein, IL-6, and TNF-α, which indicate that low-grade inflammation is associated with the occurrence and the progression of microalbuminuria and with an associated increased risk for atherosclerotic disease [35–36]. However, other studies indicate that although microalbuminuria, endothelial dysfunction, and low-grade inflammation are linked, they all are independently associated with risk for cardiovascular death [37, 38]. The inconsistency of these observations may reflect, in part, inadequate precision of the measurements of endothelial function and inflammation, or these markers may not be relevant to CVD risk in people with microalbuminuria.

Other mechanisms linking MA and hypertension and other cardiovascular risk disease may be related to further increased transvascular leakiness of albumin in systemic as well as renal vessel; from several mechanisms like hyperfiltration, glomerular basal membrane abnormalities, endothelial dysfunction and nephrosclerosis.

Prolonged increased BP and increased systemic vascular permeability may be the pathogenetic mechanisms noted in hypertensives possibly due to endothelial damage, increasing the risk of cardiovascular damage.

Microalbuminuria is associated with a decreased size-and charge-selectivity of the glomerular vessel wall in clinically healthy subject [40], and is an independent marker of systemic transvascular albumin leakiness. [41] Furthermore; atherosclerotic vascular disease is associated with renal and systemic transvascular leakiness for albumin [42]. A defective endothelial permeability could then be the origin of microalbuminuria in the general population. Some recent findings support an eventual relationship between microalbuminuria and endothelial dysfunction in hypertension that includes a positive correlation of UAE and circulating von Willebrand Factor antigen, Factor VII hyperactivity, fibrinogen and endothelial cell damage [43, 44, 45]

However, when endothelial function was directly assessed through acetylcholine vasodilator action no correlation with UAE was found [46].

Others mechanisms include renal hemodynamic changes due to the direct transmission of increased systemic pressure to the glomeruli [47,48,49], perm selectivity changes of the glomerular filter and/or insufficient tubular reabsorption of albumin [48,50], and structural damage to the glomeruli and arterioles [49]. In favor of a significant role of elevated systemic blood pressure

facilitating the transglomerular passage of albumin is the significant positive correlation found between office blood pressure levels and UAE by most groups [5, 47,51 52, 53, 54, 55]. In this sense systolic blood pressure has been shown to be one of the most relevant determinants of microalbuminuria in the early stages of hypertensive disease [56.]

MA apart from predicting nephropathy is also commonly associated with increased early death from CV and cerebrovascular disease compared with diabetic patients with normal albumin excretion.

Meta-analysis studies showed that microalbuminuria is a risk factor for CV disease in type 2 DM patients and it doubles the risk for CV morbidity or mortality as well as total mortality.

1.3 EPIDEMIOLOGY:

Three large-scale, population-based studies; two in Europe and one in the USA; show broadly similar results for the prevalence of microalbuminuria in the general population, with or without the inclusion of people with concomitant diabetes and/or hypertension. [57]

For the total cohorts that included subjects with diabetes or hypertension, microalbuminuria was present in 7.2-7.8% of individuals. In those with neither concomitant diabetes nor hypertension, prevalence was 5.0-6.6%.

Advancing middle age made a significant contribution in all three studies. In the US study, higher prevalence was also found in the young (6-19 years) subgroup.

In the larger of the two European studies, prevalence of microalbuminuria was higher in males than in females for subjects aged 28-75 years. The reverse was true in the US study of subjects aged 6 years or more, suggesting that gender differences vary with age.

1.3.1 European data on the prevalence of microalbuminuria in the general population

The PREVEND study, conducted in the Netherlands, prospectively investigated the prevalence of microalbuminuria in the general population. In their study, about 40,000 adults aged 28-75 years were included and Microalbuminuria was found to be present in 7.2% of participants, with a higher prevalence among men (8.5%) than women (6.1%). Although microalbuminuria was also more prevalent in the subgroups with diabetes or hypertension, it was still evident in 6.6% of non-diabetic, non-hypertensive subjects. Presence of

microalbuminuria was also found to be independently associated with age, smoking, previous myocardial infarction and stroke.

In a Norwegian study, just over 2000 non-diabetic, non-hypertensive adults (>=20 years) were randomly selected from the population-based Nord-Trøndelag Health Study (HUNT). The overall prevalence of microalbuminuria was 5.0%. It was slightly more common in men (5.2%) than in women (4.7%), and, as with the PREVEND Study, was significantly associated with increased age.

1.3.2 Prevalence of Microalbuminuria in Hypertensives

No large population studies have specifically studied the prevalence of microalbuminuria in a hypertensive cohort. However, data from subgroup analyses of large general population studies have found microalbuminuria present in 11-16% of people with hypertension. [58]

In selected cohorts of hypertensives with left ventricular hypertrophy, this figure may be as high as 23%.59

Large-scale population-based studies in Europe and the USA PREVEND Study and NHANES III included similar numbers of people (4500-5000) with hypertension, defined as having systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg or currently taking antihypertensive medication. [90]

The prevalence of microalbuminuria in these hypertensive subgroups was 11.5% in the PREVEND Study and 16.0% in NHANES III.

A recent sub study of the LIFE Study assessed the relationship between albuminuria and left ventricular hypertrophy (LVH), both markers of cardiovascular damage, in patients with hypertension. This sub study involved a selected cohort (n=964) of subjects aged 55-80 years with hypertension (SBP ≥140 mmHg or DBP ≥90 mmHg) and ECG-verified LVH. Major exclusions included those with prior MI or stroke within six months, heart failure and renal insufficiency.[59]

Microalbuminuria (urinary albumin: creatinine ratio 30-300 mg/g) was present in 23% of subjects. Prevalence varied with left ventricular geometry, with significantly higher prevalence seen in patients with eccentric or concentric hypertrophy than in those with normal geometry.

The prevalence of microalbuminuria in people with hypertension and diabetes, as would be expected, is correspondingly high. Approximately 12-36% of patients with hypertension and diabetes have microalbuminuria.

In yet another study amongst Turkish hypertensive patients, the overall prevalence of MAU was 64.7% and there was no difference between genders. Most patients (82.5%) had uncontrolled hypertension, 35.6% had dyslipidemia, and 35.5% had diabetes, predominantly type 2. Almost one-third of the patients (26.4%) had at least one cardiovascular-related co morbidity, with 20.3% having documented coronary artery disease (CAD). [60]

1.3.3 Studies in Africa assessing the prevalence of microalbuminuria more notably have been done in Diabetics.

In a study by JK Lutale, in patients of African origin in Dar es Salaam it was seen that systolic and diastolic blood pressure among Type 2 Diabetic patients with abnormal albumin excretion rate were significantly higher than in those with normal albumin excretion rate. [61]

This cross sectional study conducted on type 1 and type 2 diabetic patients aimed at determining the prevalence of microalbuminuria among African diabetes patients in Dar es Salaam, Tanzania, and relate to socio-demographic features as well as clinical parameters.

Several prospective studies show an association between MA and the risk of future CV disease. The incidence of major CV events progressively increased with UAE. Anti-HT treatment reduces UAE and such effect may be detected after just a few days of treatment. ACE-I and ARB's are superior to other antihypertensive drugs in reducing UAE. As per most European Hypertension Guidelines, the determination of microalbuminuria is recommended in the initial work-up of subjects with hypertension.

In another study it was quoted that microalbuminuria is highly prevalent; in hypertensive and diabetic populations, its prevalence varies from 10 to 40%. It is interesting that microalbuminuria also is found frequently in seemingly healthy individuals (5 to 7%). The variable excretion of albumin in the urine is related to the risk for the individual to develop cardiovascular (CV) disease: Absence or very low levels of albuminuria is associated with low

CV risk, whereas the CV risk increases markedly with increasing amount of albumin in the urine. [62]

Prevalence of an elevated UAE increases with age, and with longer duration and a higher severity of hypertension. In treated patients prevalence can be as high as 25% when diuretics and beta-blockers are used.

Hypertensive target organ damage is more common in microalbuminuric patients..

In one study looking at target organ damage it was seen that the prevalence of normal Left Ventricle (LV) geometry was significantly higher in normoalbuminuric compared with microalbuminuric subjects (55 vs. 14%, $P < 0.001$) while the prevalence of concentric LV hypertrophy was significantly higher in microalbuminuric compared with normoalbuminuric subjects (32 vs. 5%, $P < 0.0001$) [63]

1.3.4. Ethnic Variations

There are several studies showing ethnic variations in terms of prevalence of microalbuminuria. In one study in USA, NHANES III (1988-1994), it was noted that ethnic minorities (patients without Diabetes) have greater odds of albuminuria than whites with and without diabetes, which persists primarily for those with an eGFR less than 60 mL/min/1.73 m2. This was significant only for blacks with or without DM for those with eGFR of 60ml/min/1.73m2 or more. [64]

In another study, NHANES, USA (1999 to 2006), participants with hypertension and prehypertension had a higher likelihood of microalbuminuria than those with normal BP, especially ethnic minorities, contributing to greater target organ damage. [65]

In a study of 109 patients with essential hypertension and without either diabetes mellitus or clinical proteinuria were examined to investigate possible racial differences in UAE rates. The black hypertensive patients were found to have significantly higher UAE rates compared with the white patients; in addition, a significantly greater proportion of the black patients than the white patients (32% *v* 14%) had microalbuminuria, defined as a urinary albumin excretion rate greater than 30 μg/minute. These differences could not be explained by age, blood pressure, body mass index, glycosylated hemoglobin, serum creatinine, duration of hypertension, or type of hypertension treatment. [66]

1.4 SOCIODEMOGRAPHIC FACTORS ASSOCIATED WITH MICROALBUMINURIA:

Sociodemographic factors have been shown to be associated with microalbuminuria which includes age, gender, and obesity, history of smoking or drinking. There are also interethnic and intra individual variations between different groups.

In one study, Pearson correlation of microalbuminuria with age showed significant linear relationship ($r = 0.529$, $P < 0.001$) [91]

In yet another study, there was a dramatic increase in albuminuria prevalence in those aged 70 or more regardless of gender, race/ethnicity obesity, and hypertension. [92]

Another study looked at both age as well as gender association with microalbuminuria showing that there was a difference with females versus males in the fourth decade, males versus females in the fifth and sixth decades, and then becoming equal with age greater than 70 years old. [93]

In addition, Patients with microalbuminuria are older and exhibit predominant male gender, as compared with normoalbuminuric subjects. [67]

Smoking is also independently associated with albuminuria. In another study, smokers had a higher median albumin excretion than nonsmokers and were more likely to have microalbuminuria and high normal albuminuria with elevated or decreased GFR. After adjustment for several potential confounding factors, persons who smoked 20 or fewer cigarettes/d and persons who smoked more than 20 cigarettes per day, respectively, showed a dose-dependent association between smoking and high normal albuminuria. [68]

An association between smoking, alcohol intake and microalbuminuria has also been shown. [67]

Central obesity is the single most important risk factor for increased urinary albumin excretion in nondiabetic South Asian subjects. This relationship was even strengthened after correction for BMI, underscoring the critical role of visceral fat in this relationship.

The pathogenesis is unclear and could be mediated primarily by adipogenic inflammation and endothelial dysfunction giving microalbuminuria or secondarily by hypertension and hyperglycemia, which accompany central obesity. [94]

Our study suggests obesity as an independent risk factor for the development of microalbuminuria and this association is particularly alarming.

The prevalence in alcoholics (which included both smoker-alcoholics and non-smoker-alcoholics) was found to be 35%, whereas in the smoker group (which included both alcoholic-smokers and non-alcoholic-smokers) it was found to be 42%.

This suggested that both smoking and alcohol add insult to renal function in hypertensive patients.

1.5 DIAGNOSIS OF MICROALBUMINURIA

1.5.1 Different Methods of Urine Collection:

For the diagnosis of Microalbuminuria, there are different methods of urine collection techniques:

The first is a timed collection which measures the Albumin Excretion Rate (AER).

By this method the issues of diurnal variability in albumin excretion are overcome, but however, this method of collection is subject to errors and is cumbersome.

The measurement of AER in a timed urine sample collection remains the gold standard for the definition of microalbuminuria.

The second method is a Random or first morning spot collection which is used to determine the Albumin Creatinine ratio.

As per the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines it is this ACR measurement in a first-morning spot urine collection that is adequate and a timed urine collection is not necessary.

1.5.2 Assessment of microalbuminuria:

Assessment of microalbuminuria can be performed by three methods:

1. Measurement of the albumin-to-creatinine ratio in a random spot collection

2. 24-h collection with creatinine, allowing the simultaneous measurement of creatinine clearance.

3. Timed (e.g., 4-hour or overnight collection) The first method is often found to be the easiest to carry out in an office setting and generally provides accurate information; morning collections are preferred because of the known diurnal variation in albumin excretion, but if this timing cannot be used, uniformity of timing for different collections in the same individual should be employed. Because reagent strips only indicate concentration and do not correct for

creatinine as the spot urine albumin-to-creatinine ratio does, they are subject to possible errors from alterations in urine concentration. All positive tests by reagent strips or tablets should be confirmed by more specific methods. There is also marked day-to-day variability in albumin excretion, so at least two or three collections done in a 3-6 month period should show elevated levels before designating a patient as having microalbuminuria.

Microalbuminuria is said to be present if urinary albumin excretion is 30 mg/24 h (equivalent to 20 g/min on a timed specimen or 30 mg/g creatinine on a random sample). Screening with reagent tablets or dipsticks for microalbuminuria may be carried out if these assays are not available, as they show acceptable sensitivity (95%) and specificity (93%) when done efficiently.

Microalbuminuria results may also be dependent on the type of urine collection.

The optimal collection would have minimal inter-individual and intra-individual variability and the highest diagnostic sensitivity and specificity.

It is suggested that at least three urine collections are necessary because of high intra-individual variation and hence at least two of three collections done in a 3 to 6 month period should show elevated levels before designating a patient as having microalbuminuria.

1.5.3 Determination:

Analysis of microalbuminuria is conducted semi quantitative and quantitative. Influence of irregular rhythm of urination is possible to regulate by standardization with creatinine ratio in urine, as creatinine is a stable parameter. It is acceptable to determine albumin in at least 3 occasions due to high intra individual variations.

1.5.3.1 Semi quantitative analysis:

Test strip: good for screening, possible false negative results in non diluted urine sample Latex agglutination tests (inhibit test): titer is adapted in a way that drop of antihuman albumin falls one by one and attach all connection places of albumin in urine in concentration 30 mg/L and more Micro-albumin test: bromphenol blue remains albumin concentration over 40 mg/L, but it is not specific enough Micral: immunochemical reaction between albumin and monoclonal antialbumin IgG class (in complex with ß-galactosidase) gives conjugate. It promotes

enzymatic reaction and the intensity of nascent red color is proportional to albumin concentration.

1.5.3.2 Quantitative analysis:

There are many reactions for measuring albumin concentration in urine but all of them use the same principle; immunochemical reaction between antibody to antihuman albumin and albumin. Difference only being in preparing the reaction: RIA, ELISA, RID, immunoturbidimetry, and electrochemiluminescence. The choice depends of equipment in laboratory, the number of samples and experience. All of these methods have mostly well-balanced and good analytical precision, sensitivity and detection area. Methods based on color bounding or protein precipitation are not specific neither sensitive.

1.6 TREATMENT:

The aim of early intervention or aggressive treatment of hypertensive patients found to have microalbuminuria is to slow down or reverse the progression to end stage renal disease or overt nephropathy and thereby improve CV and renal outcomes and, consequently, a reduced burden on the healthcare resources.

1.6.1 Treatment approaches for microalbuminuria and the prevention to progression of macroalbuminuria:

Renin-angiotensin system (RAS)-blocking agents, which provides sustained 24-h BP control, reduces microalbuminuria independently of BP lowering.

As a result, microalbuminuria reduction has been shown to be greatest with intensive antihypertensive regimens that provide effective blockade of the RAS.

Guidelines for the treatment of hypertension stipulate that a BP target of at least <130/80mmHg should be achieved in patients with hypertension and type II diabetes. [69, 70, 71]

British Hypertension Society guidelines advocate that this should be even lower (125/75mmHg) in patients with proteinuria ≥1g in 24h. [72]

Studies have demonstrated that angiotensin II blockade can reduce albuminuria and the progression of renal disease and that the antiproteinuric effects of ARB's such as Losartan and irbesartan translate into CV and renoprotective benefits beyond BP lowering in patients with

diabetic nephropathy. In the DETAIL study, (investigating progression from microalbuminuria to overt renal disease), the treatment with ARB's or ACE inhibitors was associated with a very low number of events. [73]

European guidelines recommend that, to provide the greatest reduction in microalbuminuria and to lower BP, an ARB or ACE inhibitor should be used as first-line therapy, either as monotherapy or in combination with another antihypertensive agent (either low-dose thiazide diuretics or calcium channel blockers), particularly if the patient has diabetes.

Studies have shown that the ACE inhibitors such as captopril, fosinopril, lisinopril, enalapril and ramipril effectively reduce microalbuminuria in patients with hypertension, type II diabetes, or both. It is not clear, however, whether these effects are independent of BP lowering. There is, however, a stronger case for ARBs than ACE inhibitors in patients with hypertension and microalbuminuria when renal end-points are used.[74, 75]

ARBs have been demonstrated to provide CV and renoprotective benefits in proteinuric diabetic nephropathy independent of BP reduction. Within the ARB class, efficacy in terms of reduction of microalbuminuria independent of BP lowering has been shown with irbesartan, losartan [76,] valsartan, candesartan and telmisartan.

In a study of the ARB Losartan vs. the ACE inhibitor enalapril in patients with hypertension, type 2 diabetes and early nephropathy, both patient groups experienced a significant reduction in mean UAE ($p<0.001$ for both) at 1year. This reduction was associated with decreased SBP and DBP. Short-term studies in patients with type I diabetes and overt nephropathy has demonstrated similar beneficial effects on UAE, BP and renal hemodynamic with losartan and ACE inhibitors. Losartan also lowered UAE in patients with type 2 diabetes mellitus and microalbuminuria.

Among the ARB antihypertensive class, there is strong clinical evidence for microalbuminuria and low-grade inflammation reduction with irbesartan: an effect that has been shown to be independent of its antihypertensive effect. [77]

Additionally, a placebo-controlled study of Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria (IRMA-2) showed that treated patients were significantly less likely to develop diabetic nephropathy, defined as a UAE >200μg/min and at least 30% higher than the baseline level, than those in the placebo group ($p<0.001$). In the IRMA-2 study, irbesartan

significantly prevented the development of clinical proteinuria in individuals with microalbuminuria and delayed the progression of nephropathy in individuals with proteinuria. Secondary analysis showed that SBP and baseline and end-point proteinuria were the major factors for predicting renal outcomes, and, notably, renoprotective effects of irbesartan were found to be independent of the effect on BP. [78]

The MicroAlbuminuria Reduction with VALsartan study in 332 patients with type 2 diabetes and microalbuminuria (with or without hypertension) showed that a greater proportion of patients reverted to normoalbuminuria with valsartan than with the calcium channel antagonist amlodipine (29.9% vs. 14.5%; p=0.001) within 24weeks treatment. Both treatments were associated with the same level of attained BP and the same degree of BP reduction. [79]

1.7 Dyslipidemia and microalbuminuria

MA is associated with increased serum total cholesterol and reduced serum HDL cholesterol. The most consistent association between lipoprotein abnormalities and MA is with a low HDL. This suggests that clearance of LDL cholesterol may be as important as lower levels of this lipoprotein lessen cellular injury. Thus, the apparent association between microalbuminuria and CVD may be related to this adverse risk factor profile. Dyslipidemia is evident at the onset of MA in people with diabetes and accelerated processes of nephropathy. Intervention to improve the abnormal lipid profiles delays this atherosclerotic process.

The hazard ratios for regression of microalbuminuria were significant for younger age and microalbuminuria of shorter duration. A low level of either cholesterol or triglycerides alone approximately doubled the chance of the regression of microalbuminuria by Bruce A. et al 2003 involving 386 participants in US with persistent microalbuminuria.

1.8 Obesity and microalbuminuria

Central obesity reflected by a high waist-to-hip ratio (WHR) has only recently received more attention as a potential risk factor for renal disease in nondiabetic subjects. The pathogenesis is unclear and could be mediated primarily by adipogenic inflammation and endothelial dysfunction giving microalbuminuria or secondarily by hypertension and hyperglycemia, which accompany central obesity.

1.9 Smoking and microalbuminuria

Cigarette smoking especially when accompanies poor glycemic control is considered to be a risk factors for diabetic nephropathy particularly in type 1 diabetes. However, the association to the onset of this complication is not yet established.

Patients with type 1 diabetes who smoke with their HbA_{1c} maintained >8% have the highest risk of onset of microalbuminuria with incidence rate of 3.3/100 person-years by Laura J. et al 2001 (US). [80]

Smoking was found to cause both poor glycaemic control and microalbuminuria in patients with diabetes, independently of other characteristics in a study done in Sweden aimed to determine the association between smoking, glycaemic control, and microalbuminuria by P M Nilsson ET all (2001) [94]

CHAPTER TWO

2.0 STATEMENT OF THE PROBLEM:

Due to the multisystem involvement and complications of hypertension, early diagnosis of the disease and picking up the earliest signs of vascular damage (by detecting MA) is a crucial step towards reducing mortality.

Early detection techniques like microalbuminuria detection would therefore be useful for preventing costly and the debilitating complications of hypertension

2.1 RATIONALE:

The increase in the incidence of HT and high risk CV patients in our population justifies the compelling need to perform early and regular screening for MA. As evidence suggests, the periodic evaluation of this simple, inexpensive and predictive marker is valuable and cost-effective. Hence screening and early case detection in a resource poor country will encourage aggressive multifactorial treatment to reduce BP and other CV risk factors in these patients.

2.2 STUDY OBJECTIVES:

2.2.1 Broad Objectives:

To determine the prevalence of Microalbuminuria among hypertensive patients at Muhimbili Hospital – Dar es Salaam.

2.2.2 Specific Objectives:

1 To assess the prevalence of microalbuminuria in hypertensive patients at Muhimbili Hospital Cardiac Clinic

2 To describe the socio-demographic factors in hypertensive patients associated with microalbuminuria and

3 To determine the risk factors in hypertensive patients associated with microalbuminuria.

CHAPTER THREE

3.0 METHODOLOGY:

3.1 Study Design:

Descriptive Cross-sectional Clinic based epidemiological study

3.2 Study Population:

This included all hypertensive patients attending the Muhimbili National Hospital (MNH) – Cardiac OPD as per the inclusion criteria. At MNH, the cardiac out-patient clinic is conducted on every Tuesdays and Wednesdays, with about 40 patients attending per clinic day. The clinic consisted of a team of 2 nurses, one of whom being a head nurse, and the second – a nursing assistant. About 3 Consultant physicians with 2 resident physicians conduct the clinic from 2pm to 5:30pm. Patients encountered at the cardiac OPD included hypertensive patients, patients with chronic heart failures and referrals from other departments (ie gastroenterology/neurology).

During visits, patient's vital signs including blood pressure, pulse rate, and weight were charted and recorded.

3.5 Study Duration:

5 months (August 2012-January 2013), convenient sampling. (15-20 pts/week) with a sample size of 340 hypertensive patients

3.6 Sample Size Calculation:

Sample size for the required study was calculated using the formula as stated below:

$$N = \frac{Z^2 p (1-p)}{d^2}$$

Where N = sample size

Z = 5% significance level (1.96)

P = prevalence of microalbuminuria = 15% [81]

(Prevalence was obtained from a study as cited 'Microalbuminuria in the US population: third National Health and Nutrition Examination Survey'. This was estimated as for the

general worldwide population as generally prevalence among different areas and regions vary

d = precision level of .04%

N = 305 + adding 10% (Loss to f/u) = 336 ~ 340

3.7 Inclusion Criteria:

1. All known consenting hypertensive patients n
2. Newly diagnosed HT with BP >140/90
3. Age of 18 or more years

3.8 Exclusion Criteria:

1. Patients with UTI documented as the presence of nitrites, pus cells, leukocytes and hematuria.
2. Any febrile illness/episode at the current visit
3. Recent surgery within two weeks
4. Female patients on their menses on the clinic day of sample collection.
5. Documented cases of thyroid diseases [82][84]
6. Congestive heart failure(CHF) in New York Heart Association(NYHA) classes 2-4
7. Known CKD patients

3.9 Recruitment of Study Participants:

At Muhimbili National Hospital – Cardiac clinic is conducted on Mondays, Tuesdays and Wednesdays. About 30 patients on average attend on clinic days. Mondays are reserved for alular clinics. Cardiomyopathy clinics and regular outpatient follow up and new patients are seen on both Tuesday and Wednesday clinics. For the purpose of the study, recruitment of the study participants was consecutively done on Tuesdays and Wednesdays. These patients would first pass through the nursing station where vital signs including pulse rate, blood pressure in sitting position, temperature and respiratory rate were recorded. Also height and weight was measured and recorded. The BMI was obtained by dividing the weight in kg to height in meter^2. The nurses were instructed to ask the patients if they had any history of hypertension so that controlled hypertensives were not missed out in the study.

After patients had passed through the nurse station, they were consecutively recruited in the study after an informed consent.

Patients were given written consent form to read. Illiterate patients had the consent form read to them by the investigator. A signed consent was obtained from each patient upon agreeing to participate. The aim of the study and procedures involved were explained to the patients.
In each clinic day about 15 to 20 hypertensive patients were recruited into the study. Data was collected by principal investigator and an assistant. A structured questionnaire was used to collect sociodemographic and clinical data of the patients.

3.10. Clinical Assessment

3. 10. 1. Measurement of Blood Pressure:

BP was measured from the right arm with the patient seated up by using Riester aneroid sphygmomanometer mimimus®II Germany, BHS Validated. Two BP readings were taken, being 5 minutes apart and the average of the two was taken as the BP of the patient on that day. BP was categorized as Grade 1 hypertension 140/90-159/99 mmHg, Grade 2 hypertension as BP 160/100-179/109mmHg, Grade 3 hypertension as BP >180/100 mmHg.

3.10.2. Body Mass Index Measurement

Weight was measured using Secca weighing scale without shoes and recorded to the nearest 0.5 kg. Height was measured using height measuring rod and written to the nearest 0.5 cm. BMI was calculated by the formula: weight (in kilograms) divided by height (in meters) squared.

3.10.3. Urine Collection and Testing

Patients were given urine containers to collect a fresh sample of urine. They were instructed to collect urine on the spot into a clean plastic bottle aseptically. Urine specimen was sent to the clinic within an hour of collection. Urine specimens which were unlikely to be analyzed within one hour of collection were planned to be kept refrigerated at 4^0C and analyzed not more than 18 hours from collection. However in the study, all urine specimens were analyzed within 1 hour in the clinic.

Urine test strips were used to screen urine specimens for the presence or absence of

proteinuria and that of hematuria and leukocyte esterase if present. All urine test strips yielded clear and accurate results in less than 30 seconds. Results were interpreted using visual comparison of the reagent pads to the color chart.

An urines sample which tested negative for proteinuria using the dipsticks strips were tested for microalbuminuria using a Microalbumin 2-1 Combo Strips , TC-URS-2M-25, CPT CODE 82044QW (FDA 510K#: K061419). The Microalbumin 2-1 combo Strip is a plastic strip to which two test pads are affixed testing for Microalbumin and Creatinine**.**

One test being that at constant pH, albumin binds the sulfonephthalein dye to develop a blue color. The resulting color ranges from pale green to aqua blue. The test for creatinine urine assay, in an alkaline condition forms a purplish-brown color complex. The concentration of creatinine is directly proportional to the color intensity of the test pad. The Microalbumin 2-1 Combo Strips automatically gives out albumin and creatinine levels in the urine which are later used to calculate the albumin -creatinine ratio (ACR). An ACR of <30mg/g meant the patient was normoalbuminuric, an ACR of 30-300mg/g meant the patient was microalbuminuria while an ACR of >300mg/g meant the patient was macroalbuminuria.

All investigation results were communicated back to the patients and the attending physicians.

For the purpose of analyses, for all patients urine dipstick was performed which then characterized the patients into either proteinuria positive or absent proteinuria. Those patients with proteinuria signified over proteinuria hence were not included into the study.

If a patient had an absent proteinuria via urine dipstick, he/she would be then subjected to another urine dipstick by using the microalbumin sticks which is a semi-quantitative method of measuring urinary creatinine and albumin levels.

By getting these two values it was thus possible to calculate the albumin creatinine ratio.

ACR (albumin creatinine ratio) subdivided the patients into 3 categories:-

Microalbuminuria, normoalbuminuria and microalbuminuria.

Of note that microalbuminurics signified patients with overt proteinuria, (these were false negatives that were missed out by the conventional urine dipstick analyses.)

The ***microalbuminurics*** as assessed by the ACR were used for data entry into the SPSS.

3.12. Laboratory Investigations:

Blood lipids which included total cholesterol, low density lipoproteins, high density lipoproteins and triglycerides were measured for all participants at the hospital centrally biochemical lab using Cobas Integral 400 machine

Random Blood Glucose was measured using Accu-CHEK® Aviva plus System for all patients as they were screened for the presence of albuminuria.

3.11. Data Analysis:

Data was entered, cleaned and analyzed using SPSS version 16 Software. SPSS Inc. Patients demographic characteristics, risk factors and impact of the disease on daily life were summarized using frequency distribution tables.

Data analysis SPSS (Statistical Package for Social Sciences) ver. 16.0 for continuous variables- mean and standard deviation, median was computed. Categorical variables numbers and percentages were computed.

3.13. Ethical Consideration

The proposed study posed no risks to the study community; rather it aimed at preventing future risks of cardiovascular compromise as has been stipulated above. The aims of the study and expected outcomes and utility of knowledge derived from this study were explained to patients and guardians. Study participants were enrolled after the participant/guardian gave written informed consent which would be administered by the principal investigator or the research assistant. Participants who decline to consent would receive the same quality of care as those who consent to participate in the study.

All data collected during the study was treated with strict confidence. The findings of the urine tests, blood tests for lipid profile and the prognosis and future preventive methods was clearly explained to the participant as well as any further investigations that would warrant were explained to the study participant. With the results appropriate treatment were also administered.

Ethical clearance to carry out this study was obtained from the Research and Publications Committee of MUHAS and the director of clinical services of MNH.

Patient Disposal: patients with asymptomatic UTI would be advised urine for culture and sensitivity on the same day of visit and advised to follow-up with their respective Outpatient department (OPD). Symptomatic UTI were prescribed Quinolones therapy as per the WHO guidelines.

CHAPTER FOUR

4.0 RESULTS

In this study, from August 2012 to January 2013, a total of 726 patients attended the cardiac clinic. Of these, 321 did not meet the inclusion criteria. Sixty four (64) patients were excluded due to refusal to consent, menstruation, hyperthyroidism, urinary tract infection (UTI) and CCF stage 3 or 4. A total of 341 patients were recruited into the study and analyzed. (Figure 1)

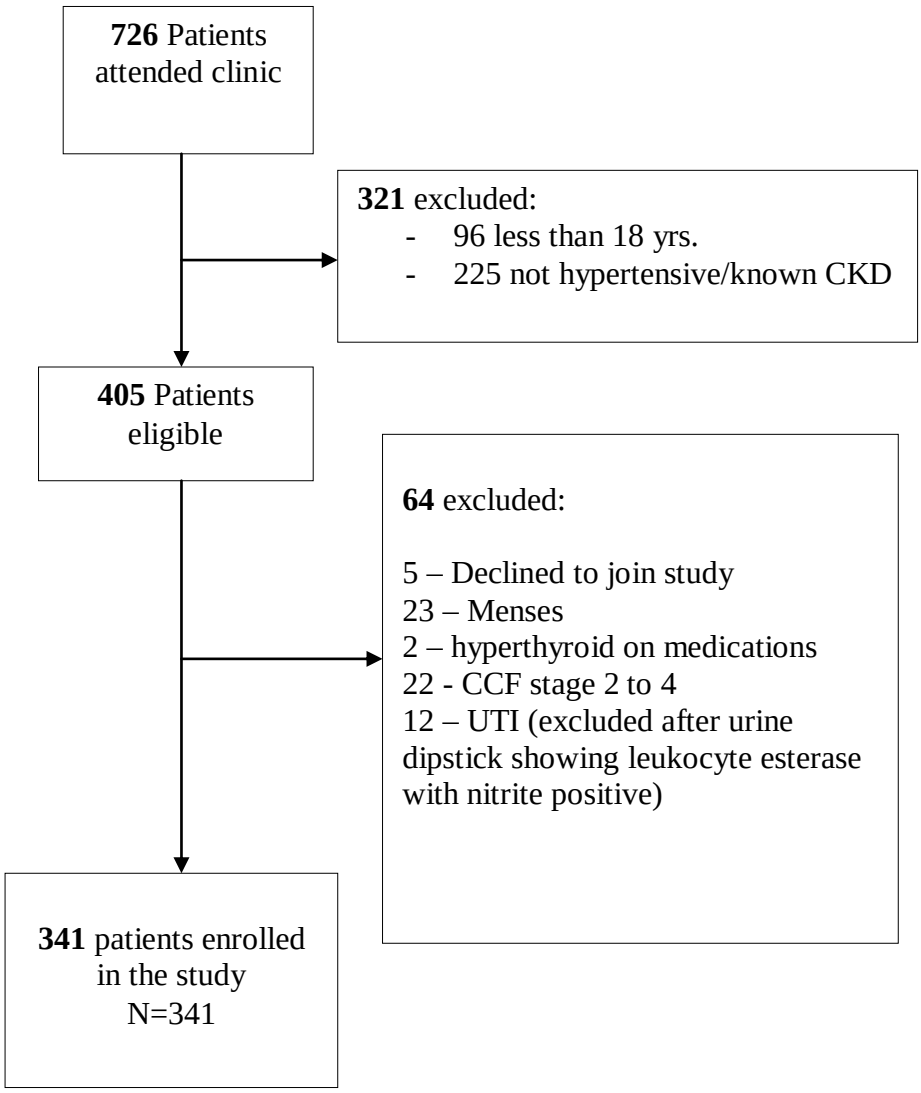


Figure 1: Flowchart showing the patient recruitment into the study (Aug 2012-Jan 2013)

Table 1: Sociodemographics of hypertensive patients attending MNH cardiac clinic from August 2012-Jan 2013 N=341

Parameters	Frequency	Percentage
Sex:		
Female	199	58.40
Age:		
18-30	115	33.70
31-60	104	30.50
≥ 61	122	35.80
Employment:		
Peasant/farmer	92	27.00
Unskilled worker	141	41.30
Private sector	24	7.00
Self employed	11	3.20
Unemployed	73	21.40
BMI:		
<18.5	87	25.50
18.5-24.9	89	26.10
25-29.9	88	25.90
>30	77	22.60
Non smokers:	279	81.80
Smoking duration:		
1-5 yrs	32	51.60
6-10 yrs	16	25.80
11-15 yrs	4	6.40
16-20 yrs	6	9.60
>20 yrs	4	6.40
Cigarette number per day:		
1-10	45	72.50
11-20	16	25.80
21-30	1	1.60
Alcohol users:		
No	253	74.20
Alcohol use duration:		
≤10 yrs	72	81.80
11-20 yrs	10	11.30
>20 yrs	6	6.80
Diabetes mellitus:		
No	299	87.70
Diabetes type:		
Type 1	9	21.40
Type 2	33	78.50
Diabetes Duration:		
1-5 yrs	28	66.60
6-10 yrs	7	16.60
11-15 yrs	4	9.50
16-20 yrs	3	7.10

4.1 Sociodemographic of hypertensive patients attending MNH cardiac clinic Aug 2012-Jan 2013 (n=341)

Table 1 shows the Sociodemographic characteristics of the study population. Females comprised 58.4% of the study population. Majority (35.8%) of the patients were aged 61 years or older. The mean age was 53 ± 1.58 SD years.

Most of the patients 78.5% were employed, with 41.3% being people doing unskilled works. There were 18.2% smokers among the study population. Most of the smokers (51.6%) had smoked between 1 and 5 years only 6% had smoked for more than 20 years. 72.5% smokers smoked 1-10 cigarettes per day. 48.5% of the study population was overweight or obese and a quarter of the study population was underweight.

Of the hypertensives, 25.8% consumed alcohol, with the majority 81.8% having used alcohol for less than 10 years. There were 12.3% diabetics among the study population. Type 2 diabetics were seen in 78.5% of patients. Sixty six of diabetics had lived with diabetes for 1-5 years. Only 7.1% diabetics had their diabetes for more than 16 years (Table 1).

It is of note that normoalbuminuric constituted the vast minority with only 4 patients in the normoalbuminuric range. (1.17%) and hence has not been represented in the above table

Prevalence of microalbuminuria

Of the 341 urine samples tested, 29% tested negative for proteinuria by the dipstick reagent. These samples were further tested for microalbuminuria using the Micro Combo 2-1 strips for evaluating microalbuminuria and creatinine. Out of the 99 samples tested, 1.4% was normoalbuminuric, 82.8% of the samples were microalbuminuria range and 13.1% were macroalbuminuric. The overall microalbuminuria in the study population was 24%. (Figure 2 and table 2).

Two forty two out of the initial 71% samples were detected to proteinuria positive (macroalbuminuria) by dipstick testing. These samples were not tested further with the micro Combo 2-1 strips (Figure 1).

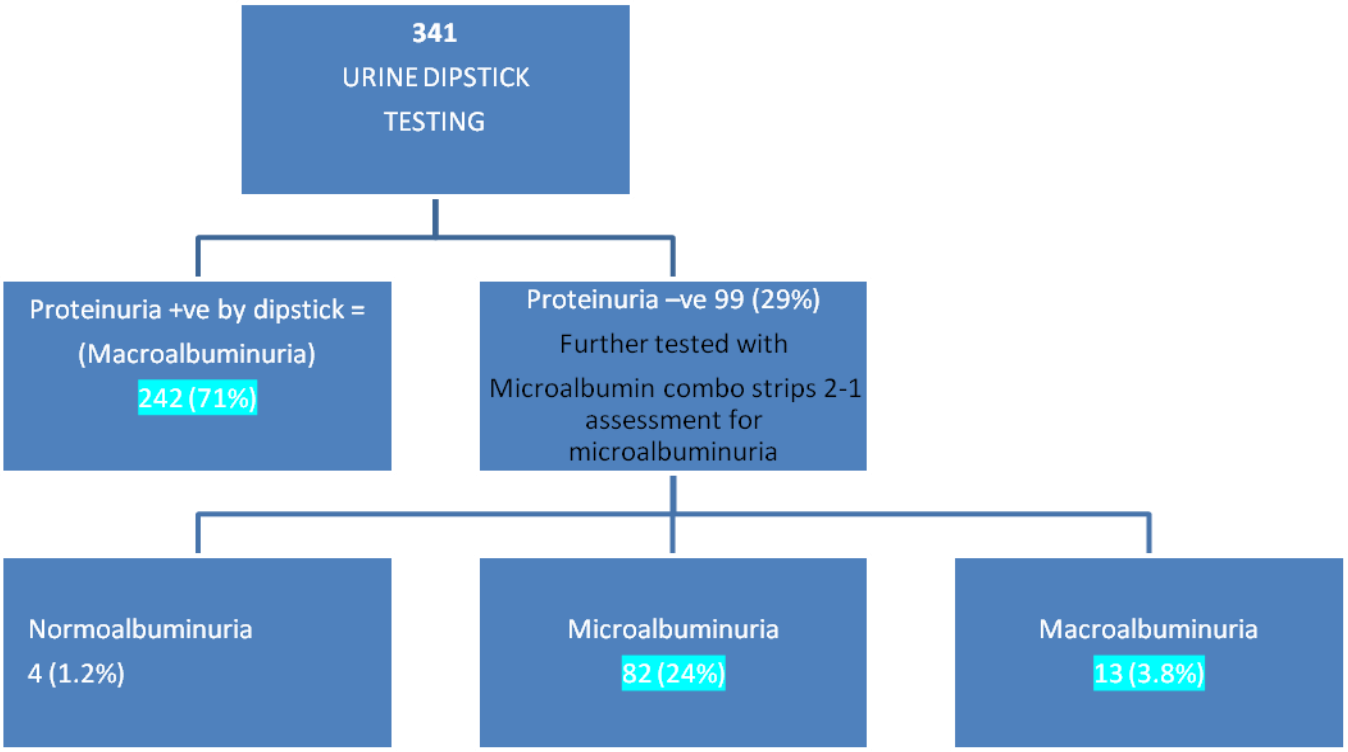


Figure 2: Flowchart showing the patient recruitment into the study (Aug 2012-Jan 2013)

Table 3: Description of risk factors among hypertensive patients with microalbuminuria at MNH cardiac clinic – Dar-es-salaam

Parameters	N	Microalbuminuria N=82(24%)	Macroalbuminuria N=255(74.7%)	P Values
Sex:				
Female	199	43(21.6%)	154(77.3%)	0.421
Male	142	39(27.4%)	101(71.1%)	
Age:				
18-30	115	27(23.4%)	88(76.5%)	0.518
31-60	104	25(24%)	78(75%)	
≥ 61	122	30(24.5%)	89(72.9)	
Smoking duration:				
Non smoker	279	73(26.1%)	202(72.4%)	0.086
Smoker	62	9(14.5%)	53(20.7%)	
1-10 yrs	32	4(12.5%)	28(87.5%)	0.642
>10 yrs	30	5(16.6%)	25(83.3%)	
No of cigarettes smoked per day:				
<10	45	8(17.7%)	37(82.2%)	0.236
>10	17	1(5.8%)	16(94.1%)	
BMI:				
<18.5	87	23(26.4%)	64(73.5%)	0.638
18.5-24.9	89	16(17.9%)	71(79.7%)	
25-29.9	88	22(25%)	65(73.8%)	
>30	77	21(27.2%)	55(71.4%)	
Alcohol duration:				
No alcohol	253	62(24.5%)	189(74%)	0.520
Alcohol	88	20(22.7%)	66(75%)	
Alcohol for 1-10yrs	72	17(23.6%)	53(73.6%)	0.951
Alcohol for >10 yrs	16	3(18.7%)	13(81.2%)	
DM Duration:				0.423
Non diabetic	299	69(23%)	226(75.6%)	
Diabetic	42	13(15.8%)	29(11.3%)	
≤10 yrs	35	10(28.5%)	25(71.4%)	0.813
>10 yrs	7	3(42.8%)	4(57.1%)	
TG mmol/L				
≤1.7	113	23(20.3%)	88(77.8%)	0.176
>1.7	228	59(25.8%)	167(73.2%)	
Total cholesterol mmol/L				
≤5.2	114	27(23.6%)	84(73.6%)	0.652
>5.2	227	55(24.2%)	171(75.3%)	
LDL mmol/L				
≤2.6	79	22(27.8%)	55(69.6%)	0.594
>2.6	262	60(22.9%)	200(76.3%)	
HDL mmol/L				
≤1.3	124	31(25%)	93(75%)	0.386

CHAPTER FIVE

5.0 DISCUSSION:

5.1 Summary of the study findings

The prevalence of microalbuminuria in hypertensives attending the Cardiac clinic at Muhimbili National Hospital was found to be 24% which was 27.4%% in male and 21.6% in female hypertensive patients.

In this study it was seen that there were no statistically significantly factors associated with the occurrence of microalbuminuria among the hypertensive patients.

5.2 Factors associated with microalbuminuria in hypertensives:

The prevalence of microalbuminuria was noted to be higher among males (p=0.421), with the age group of greater than 61 years comprising the majority of microalbuminurics among the different age groups. p=0.518

There were more non-smokers with microalbuminuria compared to smokers. p=0.085.

It was noted that those who smoked greater than 10 years had higher levels of microalbuminuria though not statistically significant p=0.642

Most of the microalbuminurics smoked less than 10 cigarettes per day. p=0.236

BMI in the overweight group had higher prevalence of microalbuminuria p=0.638.

Non Alcohol consumers were found to have a higher prevalence compared to alcohol consumers. p=0.520

Diabetics had higher prevalence of microalbuminuria compared to non diabetics p=0.423.

Duration of Diabetes of greater than 10 years demonstrated higher prevalence of microalbuminuria p=0.813

Triglyceride levels greater than 1.7mmol/L was associated with high prevalence of microalbuminuria p=0.176.

While Total cholesterol levels above 5.2mmol/l was associated with higher prevalence of microalbuminuria. p=0.652, Low density lipoproteins and triglyceride levels were not associated with high prevalence of microalbuminuria. p=0.594 & p=0.386.

The prevalence of microalbuminuria among hypertensive patients varied from study to study probably due to different urine collection times.

In this study due to the cumbersome process of obtaining a morning spot random sample as has been mentioned in the methodology, a spot random test was taken and assessed immediately per patient.

As per the study done by Rajvit Kaur et al, the incidence of Microalbuminuria was found to be (N=174) 33.3%.

This was a cross sectional study in which morning random urine samples of clinically documented hypertensive patients attending Civil OPD of Command Hospital (SC), Pune and Military Hospital (Cardio-Thoracic Centre), Pune was used and assessed for microalbuminuria.

Similar findings were noted by study of Rosa, Cerasola, and Agrawal. [83]

The prevalence is comparatively similar to the studies by Hornych (6-24%), Mimran, Halal, Col M, and MAGIC Study (Microalbuminuria: A Genoa Investigation on Complications) [84]. Despite the fact that in this study urinary albumin was estimated within 4 hours of voiding of urine without adding any preservatives and storage of samples, as storage has been reported to reduce urinary albumin, there wasn't much difference in the prevalence between our studies and the latter.

However, large variation has been reported in various published studies.

The large study on the prevalence of microalbuminuria by Bigazzi et al in 1992 reported the figure of 40% (N=123), while subsequent studies reported the variation from 4.7% to 40% [85].

In yet another study by Bibek ET al, the prevalence of microalbuminuria was assessed to be 51.8%, in which they studied the prevalence of microalbuminuria in newly diagnosed hypertensives.

Shrader J and Luders ET all in the MARPLE study found the prevalence of microalbuminuria to be 30%; this was a prospective long term studies. [86]

Other studies, showed an even higher prevalence as was noted by Losito, and also similarly in another study by Gianconi S.

In yet another study, which studied the association of cardiovascular risk factors with microalbuminuria in hypertensive individuals – iSEARCH global study, the prevalence of microalbuminuria was found to be 58.4% (Journal of Hypertension, 2007). [87]

However, in the MAGIC study, it was seen that the prevalence of microalbuminuria among hypertensive patients was 6.7% which was considerably lower as compared to the above stated studies as by Palatini, Graniero, Mattrei and others including this study.

These discrepancies are most likely due to different criteria in patient selection (ie, the severity of hypertension, age, race, coexistence of renal disease, and the techniques used for the detection of albuminuria). In the magic study, the urine was kept to freeze overnight and this is associated with a modest reduction in albumin levels.

In a Nigerian Study, it was seen that 28% non dippers (Hypertensives whose BP readings fail to drop during the night); prevalence of microalbuminuria was found to be 57.1%
In this study, the difference in prevalence are expected as the differences can also be due to differences in definition of microalbuminuria (i.e. cut off values), method of urine collection (timed versus random), quality of albumin assay and mode of expression of urinary albumin (excretion rate, ratio to creatinine, or concentration), size of study (small cohort versus large population based) and ethnic background of patients.

Non-compliance could be another reason including intra-ethnic variations that can contribute to the difference in microalbuminuria prevalence among the different studies.

In this study cohort of hypertensive patients, descriptive analysis to describe the relationship between age, sex, smoking duration, alcohol drinking, obesity, dyslipidemia toward the progression of microalbuminuria was analyzed.

The prevalence of microalbuminuria was noted to be higher among males which amounted to 27.4%. Statistically there was no significant difference noted. (p=0.421).

Age group of greater than 61 years comprised of 24.5% of the microalbuminurics among the different age groups with the mean age of 53.1years with SD±1.586, but statistically, no significant difference was seen. p=0.518

On further analyses it was seen that 26.1% were non-smokers with microalbuminuria compared to smokers at 14.5%. The difference between the two groups was statistically insignificant. p=0.086. However smokers who smoked greater than 10 years were seen to have greater prevalence's of microalbuminuria (16.6%) but statistically this was not validated. p=0.642

Further looking into the number of cigarettes smoked per day, of those who smoked between 1 to 10 cigarettes per day, (17.7%) had microalbuminuria compared to those who smoked more than 10 cigarettes per day but yet again this failed to attain statistical significance p=0.638

Comparing our study to others; Ravjit Kaur Sabharwal found the prevalence in the smoker group (which included both alcoholic-smokers and non-alcoholic-smokers) it was found to be 42%; and that of alcoholics (which included both smoker-alcoholics, and non-smoker-alcoholics) was found to be 35%.

Hypertensive smokers have a worse cardiovascular risk profile than non-smokers as smoking has been hypothesized to impair the pharmacological effects of antihypertensive drugs.

The prevalence in this study *as well as our study* could not be statistically validated due to the small sample size of the subgroups. In his study there was a trend toward greater prevalence of microalbuminuria in smokers and alcoholics alike. But in our study it was noted that microalbuminuria was more prevalent in the non-smoker group, this could be possibly due to the small sample size or other possible confounders, and due to the fact that this was a descriptive study not designed to study associations.

Non alcohol drinkers in our study had a higher prevalence of microalbuminuria amounting to 74%, versus alcohol drinkers 22.7%. p=0.520

However, in terms of duration of alcohol drinking, 18.7% had been drinking alcohol for greater than 10 years, but these findings failed to achieve statistical significance. p=0.951

This was on the contrary to the study of Rajvit Kaur et al due to the small sample size in our study that was designed to be descriptive.

When we look at BMI, those hypertensives that were overweight were noted to have a higher prevalence of microalbuminuria of about 21(27.2%) but this was not statistically validated. p=0.638

In comparison, Rajvit Kaur ET all's study looked at association of BMI with that of microalbuminuria and found no statistical significance.

This however was in contradiction to the study by Redon where correlation was reported between BMI and albumin excretion. Redon found that Microalbuminuria was found more frequently in obese hypertensives but he reports that this association is explained by higher blood pressure more than insulin resistance, *this could probably explain the findings of our study.*

In a study by Martin Thoenes, BMI was NOT identified as an independent marker of renal and cardiovascular risk by using MAU as a surrogate marker, thereby confirming the findings from INTERHEART and Canoy and colleagues in a large sample of hypertensive patients.
Obesity may be linked to microalbuminuria in that there is an increased cardio metabolic risk, frequently associated with atherosclerotic cardiovascular disease or diabetes.

There is an ongoing discussion on the particular importance of abdominal obesity, associated with an accumulation of visceral fat tissue, as an important component of the metabolic syndrome and its associated complications.

Studying the other factors of associating dyslipidemia in hypertensives with microalbuminuria, no significance in this study was noted in terms of Total Cholesterol, LDL and HDL in hypertensives with microalbuminuria, although an increasing prevalence of microalbuminuria was noted with triglyceride levels as seen in Table 3 but this failed to achieve statistical significance. (p=0.176)
The relationship between dyslipidemia and microalbuminuria is inconsistent. Atherosclerotic vascular disease is associated with increased endothelial permeability that leads to transvascular albumin leakage and enhanced lipid accumulation in the vessel wall. [88]

Increased UAE in parallel with dyslipidemia was found in diabetic patients. In both types of diabetes, dyslipidemia and low HDL-cholesterol levels may impair endothelial function. It was demonstrated that hypertriglyceridemia and low HDL-cholesterol were associated with

microalbuminuria. Molitch *et al*. tried to determine whether high levels of HDL-cholesterol accompanied lower prevalence of albuminuria. They found that type 1 diabetic patients with higher HDL-cholesterol concentrations were much less likely to have albuminuria. In another study, a significant association was found between albuminuria and duration of diabetes, hypertension and HDL-cholesterol concentration. The protective role of higher HDL-cholesterol level against the development of albuminuria in patients with type I diabetes still needs explanation.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion:

This study showed that the prevalence of microalbuminuria was 24% among hypertensive patients seen at the cardiac clinic at the MNH. When any form of albuminuria was considered the prevalence was almost 100%.

Almost all patients seen in this study had a form of proteinuria, either macro or micro which showed that majority of patients has already progressed to some form of albuminuria.

This suggests that microalbuminuria screening should be aggressively used as a screening tool to pick up early evidences of microalbuminuria in hypertensive patients.

There were no statistically significantly factors associated with the occurrence of microalbuminuria among the hypertensive patients.

6.2 Recommendations:

Microalbuminuria is regarded as the earliest marker of capillary endothelial damage and therefore an important predictor of capillary injury in hypertensive patients; hence vigorous screening of this relatively inexpensive tool is essential which is underperformed at our centre.

It is hence important that in every hypertensive patient, this inexpensive test for urine albumin be measures routinely at every outpatient clinic at Muhimbili Hosp so as to detected early those at an in increased risk of vascular and cardiac morbidity and mortality and appropriate measures for its prevention or delay taken early.

6.2.1 Study Limitation

Ideally microalbuminuria should be assessed by a morning spot test which was not possible in our cases so variation in albuminuria levels may be explained due to that although assessing random tests in cumbersome situations has been validated.

6.2.2 Study Strength

The urine dipstick and microalbumin combo strips were assessed at the clinic, no preservation of urine samples was done either refrigerating or using any preservatives thereby reducing the possibilities of reduction in albumin levels which happens otherwise.

The patients were consecutively picked up at the cardiac clinic hence reducing the possibility of selection bias.

This study serves to alert us that the number of patients leading into endothelial damage and hence eventual target organ failure is rampant and therefore all efforts should be made toward being able to pick these patients early to prevent future complications. It gives a direction to further studies in this regard.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion:

This study showed that the prevalence of microalbuminuria was 24% among hypertensive patients seen at the cardiac clinic at the MNH. When any form of albuminuria was considered the prevalence was almost 100%.

Almost all patients seen in this study had a form of proteinuria, either macro or micro which showed that majority of patients has already progressed to some form of albuminuria.

This suggests that microalbuminuria screening should be aggressively used as a screening tool to pick up early evidences of microalbuminuria in hypertensive patients.

There were no statistically significantly factors associated with the occurrence of microalbuminuria among the hypertensive patients.

6.2 Recommendations:

Microalbuminuria is regarded as the earliest marker of capillary endothelial damage and therefore an important predictor of capillary injury in hypertensive patients; hence vigorous screening of this relatively inexpensive tool is essential which is underperformed at our centre.

It is hence important that in every hypertensive patient, this inexpensive test for urine albumin be measures routinely at every outpatient clinic at Muhimbili Hosp so as to detected early those at an in increased risk of vascular and cardiac morbidity and mortality and appropriate measures for its prevention or delay taken early.

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93. Central Obesity Is an Independent Risk Factor for Albuminuria in Nondiabetic South Asian Subjects Prataap K. Chandie Shaw, MD, Stefan P. Berger, MD, PHD, Marko Mallat, MD, Marijke Frölich, PHD, Friedo W. Dekker, MD, PHD and Ton J. Rabelink, MD, PHD April 24, 2007, doi: 10.2337/dc07-0028

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APPENDIXES

Appendix i: QUESTIONAIRE (ENGLISH VERSION)

DEMOGRAPHIC DATA AND BACKGROUND INFORMATION:

Serial number: _____

Name: _____

Telephone contact: _____

Date of birth (dd/mm/yy): _____

Sex: M ☐ F ☐

Body weight _____

Height: _____

BMI: _____

Daily medications (If any): _____

Marital status: _____

Relationship of caregiver to the patient

☐ Husband/wife

☐ Mother

☐ Father

☐ Sibling

☐ Other – specify _____

SOCIOECONOMIC ASSESSMENT:

Occupation

☐

☐

Unemployed

Casual laborer ☐

Formal employment (unskilled work)

Formal employment (skilled job) ☐

Business owner with employees ☐

What is your usual mode of transport on foot

Bicycle ☐

Motorbike

Public transport

Private car ☐

Highest level of education completed

None ☐ Primary ☐ Secondary ☐ College / University ☐

Have you ever been diagnosed to have any diseases (tick one)

Hypertension ☐ …… ……

Diabetes ☐ …….. ……..

Hypercholesteremia ☐ ……..

(If yes state the medications, duration of usage and regularity)

Any history of:

Smoking: **IF YES** SPECIFY…….....

Alcohol: **IF YES** SPECIFY……..

Tobacco: **IF YES** SPECIFY ……

The following data will be filled by the principal investigator.

1: Clinical Data of the patient

BP: _____ PR: _____ HR:_____

2: Symptoms and Signs _____

3: Results

Urinalysis	Microalbuminuria	Fasting blood glucose	Lipid profile

Appendix ii: QUESTIONARRE (KISWAHILI VERSION):

Idadi ya Watu takwimu na taarifa USULI:

Namba ya faili yako: _____

Jina: _____

Namba yako ya simu: _____

Tarehe ya kuzaliwa (dd/mm/yy): _____

Jinsia: M ☐ F ☐

Uzito wa mwili: _____

Urefu: _____

BMI: _____

Dawa za kila siku (kama unatumia eleza hapa): _____

Hali ya ndoa: _____

Uhusiano wa Mtoaji huduma kwa mgonjwa:

☐ Mume/Mke

☐ Mama

☐ Baba

☐ Ndugu

☐ Au mtu asiyehusika, eleza taarifa yake: _____

Kijamii na kiuchumi TATHMINI

Taarifa ya kazi:

Wasio ajiriwa ☐

Msaidizi ☐

Mfanyakazi bila ya ujuzi ☐

Mfanyakazi mwenye ujuzi ☐

Mwenye Biashara au Kampuni ☐

Usafiri wako wa Kawaida ni vipi ?

Unatembea kwa miguu ☐

Baskeli ☐

Usafiri wa umma (dala dala) ☐

Piki piki ☐

☐

Gari ya Kibinafsi

Kiwango cha juu cha elimu kukamilika?

Hakuna	Misingi	Sekondari	Chuo / Kikuu
☐	☐	☐	☐

Jee, umewahi kukutwa kuwa na magonjwa yoyote (weka alama kwenye kiboksi chini)

Shinikizo la damu ☐ ……

Ugonjwa wa kisukari ☐ ……

Mafuta kwenye mwili ☐ ……

(Kama ndiyo hali ya dawa, muda wa matumizi na utaratibu)

Historia yoyote ya:

Sigara: Kama jibu **ni ndio**, eleza hapa: …….....

Pombe: Kama jibu **ni ndio**, eleza hapa: …….....

Tumbaku: Kama jibu ni ndio, eleza hapa: ……...

Taarifa zifuatazo lazima itolewe na mpelelezi mkuu wa Hospitali.

Maelezo rasmi ya mgonjwa:

BP: _____

PR: _____

HR: _____

Dalili na Ishara:

_____
_____
_____
_____
_____
_____

Matokeo:

Urinalysis	Microalbuminuria	Fasting blood glucose	Lipid profile

Appendix iii: INFORMED CONSENT FORM

ID no…….

Consent to participate in the study on the on 'the prevalence of microalbuminuria in hypertensive patients and associated factors at Muhimbili National Hospital – Daresalaam.'

Greetings! My name is Dr. Hussein Bhalloo, a postgraduate student at MUHAS, investigating the prevalence of microalbuminuria in hypertensive patients

What participation involves:

Should you agree to participate in the study, an interview, and a detailed clinical history regarding your health will be requested.

Confidentiality:

All information collected on questionnaires will be entered into a computer with special identification number. The questionnaires will be handled with greater secrecy in order to maintain your confidentiality.

Risks

There is no risk associated with this study

Right to withdraw and alternatives

Participating in this study is completely a voluntary choice. You are allowed to withdraw from the study any time and yet continue to receive all services that are normally provided in the hospital.

Benefits: Participating in this study allows you to know your kidney status and options for treatment in case there is a kidney disease.

In case of any injury

No harm is anticipated.

Whom to contact

If you have any question about the study or in case of further information, you may contact Dr. Hussein Bhalloo on 0717355250/0786355250; or the Supervisor/Coordinator Prof. Lutale on 0655292485. If you have questions about your rights as a participant you may contact Prof. M. Aboud, Chairman of MUHAS Research and Publications Committee.
P.O.BOX 65001 Dar es Salaam. Tel 2150302-6

Signature

Do you agree?

Participant agrees…….. Participant does NOT agree……

I …… have read and understood the content of this form. My questions have been answered and I voluntarily agreed to participate in this study.

Signature of participant…….

Signature of witness…….....…… Date of signed consent…….

Appendix IV: FOMU YA RIDHAA (SWAHILI VERSION)

Nambari ya usajili …….

Idhini ya kushiriki katika utafiti juu ya maambukizi ya /microalbuminuria kwa wagonjwa katika Hospitali ya Muhimbili – Daresalaam, Tanzania.

Salaam! Mimi naitwa Dr. Hussein Bhalloo, ni mwanafunzi wa shahada ya udhamili - Chuo Kikuu cha Sayansi za Afya na Tiba – Muhimbili. Nafanya utafiti kuhusu kuchunguza tatizo/ ugonjwa wa figo kwa wagonjwa wenye kisukari.

Madhumuni ya utafiti

Jinsi ya kushiriki

Kama utakubali kushiriki katika utafiti huu, utaombwa kujibu maswali kadhaa na pia kufanyiwa vipimo vya damu na figo.Vipimo vitafanyika bure bila wewe kuchangia pesa.

Utunzaji wa siri

Taarifa zote zitatunzwa kwa siri kwa kutumia herufi maaulum au nambari badala ya jina la mgonjwa.

Madhara /Athari

Hakuna athari au madhara aina yeyote yanayotegemewa kutokana na ushiriki wako katika utafiti huu. Vipimo hivi ni salama kwa afya ya kina mama na watoto na wala hakitoi mionzi inayohatarisha afya.

Uhuru wa kushiriki

Una uhuru wa kushiriki au kutoshiriki kwenye utafiti huu, pia unaweza kujitoa wakati wowote kama hujaridhika. Hata kama ukichagua kutokushiriki au kujitoa kwenye utafiti huu matibabu yako utaendelea kupata kama kawaida.

Faida ya utafiti

Vipimo hivi vya gharama kubwa vitafanywa bure, mgonjwa atafaidika kwa kuhudumiwa na mtafiti pamoja na kupewa rufaa ili ajiunge na clinic ya madaktari bingwa wa magonjwa ya figo.

Ni matumaini yangu kwamba utafiti huu utasaidia kuboresha tiba kwa wagonjwa wengine siku za baadae.Kuna kamati ya kusimamia udhibiti wa utafiti Kamati hii hutoa taarifa za matokeo ya utafiti ambayo huytoa elimu kubwa kuhusu tatizo hili.

Taarifa

Endapo unahitaji kupata maelezo kuhusu haki zako au taarifa zaidi ,wasiliana na Dr. Hussein Bhalloo, Mtafiti, kupitia namba ya simu 0717355250/0786355250 au Msimamizi / Mratibu Prof Lutale 0655292485 aw Prof M M Aboud Mwenyekiti wa Kamati ya Utafiti, MUHAS S.L.P 651001,Dar es salaam, Simu 2150302-6.

Jee unakubali kushiriki kwenye utafiti huu? weka alama ya vema(√)

Ndiyo..... Hapana.....

Mimi .....nimesoma na nimeelewa maelezo iliyeandikwa hapo juu na ninakubali kwa khiari yangu kushiriki kwenye utafiti huu.

Sahihi ya mgonjwa .....

Sahihi ya ndugu/shahidi .....

Sahihi ya Mtafiti ..... . Tarehe……