"STUDY OF MICROALBUMINURIA IN HIV PATIENTS"

Submitted By

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in

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LIST OF ABBREVIATIONS

ADA	–	AMERICAN DIABETIC ASSOCIATION.
AIDS	–	ACQUIRED IMMUNO DEFICIENCY SYNDROME
ART	–	ANTI RETROVIRAL THEORAPY
CD4	_	CLUSTER OF DIFFERENCIATION
CDC	–	CENTRAL FOR DISEASE CONTROL AND PREVENTION
ELISA	–	ENZYME LINKED IMMONO SORBENT ASSAY
FBS	_	FASTING BLOOD SUGAR
FRAM	–	FAT REDISTRIBUTION AND METABOLIC CHANGES IN HIV INFECTION
GRID	–	GAY RELATED IMMUNO DEFICIENCY
HIV	–	HUMAN IMMUNO DEFICIENCY VIRUS
MA	_	MICROALBUMINURIA
MSBP	_	MEAN SYSTOLIC BLOOD PRESSURE
NNRTI	–	NON NUCLOSIDE REVERSE TRANSCRIPTASE INHIBITOR.
NSAID	–	NON STEROIDAL ANTI INFLAMMETRY DRUGS
RIA	–	RADIO IMMUNO ASSAY
RNA	–	RIBO NUCLEIC ACID
SIV	_	SIMIAN IMMUNODEFICIENCY VIRUS

ABSTRACT

BACKGROUD

HIV infection and AIDS is a global pandemic with cases reporting from virtually every country. The cardiovascular risk factors of increased systolic blood pressure and increase fasting blood sugar levels are strongly associated with MA in HIV patients. These results suggest that MA may be a sign of current endothelial dysfunction and microvascular disease and there is substantial risk of future cardiovascular disease events. The higher prevalence of MA among the HIV infected could be harbinger of future increased risks of both kidney and cardiovascular disease. Further study defining the prognostic significance of MA among HIV infected persons will be essential.

MATERIALS AND METHODS

The present study is done in 100 patients of HIV patients, non diabetic, non hypertensive, admitted to B.L.D.E.U's Shri. B.M. Patil Medical College, Bijapur from October 2009 to may 2011. The patients underwent detailed history and clinical examination. Early morning 5ml of urine sample was collected and MA was estimated by immunoturbidometry method. The relationship of MA with duration of HIV disease and severity with CD_4 count, mean systolic blood pressure, fasting blood sugar level and No. of hospital admission were assessed.

OBSERVATIONS AND RESULTS

The prevalence of microalbuminuria in this study is found to be 74%, in that 47 were male and 27 were female. We found out a significant association between MA and the duration of HIV (P = 0.043), longer the duration of HIV infection, more possibility of microalbumin in urine. Also there is a significant association between CD_4 Count and MA. We also found out significant high systolic blood pressure in patient of MA positive (P = 3.566E), also found higher fasting blood sugar level in MA positive (P = 1.037E-14).

CONCLUSION

The prevalence of MA in HIV patient is high in this part of the community. Early Screening of MA in HIV patient and aggressive management of positive cases might reduce the burden of cardiovascular disease and chronic kidney disease in the community.

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1. NEED FOR STUDY

HIV infection and AIDS is a global pandemic with cases reporting from virtually every country. HIV continues to be a common infection in developing country like India[1].

Microalbuminuria is a manifestation of HIV associated nephropathy. Therefore, microalbuminuria may be an early marker of HIV associated nephropathy, and screening for its presence may be beneficial[2]. A strikingly high prevalence of microalbuminuria among HIV infected patients has been described in various studies[3]. Risk factors for clinically significant proteinuria include, African - American race, higher HIV RNA level, lower CD_4 lymphocyte count[3]

The cardiovascular risk factors of increased systolic blood pressure and increase fasting blood sugar level are strongly associated with MA in HIV patient. These results suggest that MA may be a sign of current endothelial dysfunction and micro vascular disease and there is substantial risk of future cardiovascular disease events. Positive contributing factors include early kidney disease such as HIV associated nephropathy, a marker of end organ damage related to co morbidities of diabetes or hyperpertension, or more diffuse endothelial cells dysfunction. Nevertheless after adjustment for non HIV factors, HIV itself is a major risk factor[3].

The presence of HIV infection is independent risk to develop MA in HIV patient. Cardiovascular risk factors appeared to be stronger predictors of microalbuminuria than markers of HIV severity person with HIV infection and MA therefore appear to potentially bear the burden of two separate damage related to known vascular end organ damage related to know vascular risk factors, and HIV specific processes such as the direct viral infection of kidney cells[3].

The higher prevalence of MA among the HIV infected could be harbinger of future increased risks of both kidney and cardiovascular disease. Further study defining the prognostic significance of microalbuminuria among HIV infected persons will be essential[3].

Microalbuminuria seems to be a predictor of cardiovascular disease in diabetic and non diabetic subjects[4], hence it can also be used for early detection of micro vascular disease in HIV positive patients, thus can help to diagnose the disease at the earliest.

2. INTRODUCTION

HISTORICAL PERSPECTIVES

AIDS is a disease of human immune system caused by human immune deficiency Virus (HIV) [5, 6, 7]

This condition progressively reduces the effectiveness of the immune system and leaves individuals susceptible to opportunistic infections and tumors.

HIV is transmitted through direct contact of mucous membrane or blood stream with bodily fluids containing HIV such as blood, semen .vaginal fluid preseminal fluid and breast milk[8, 9]. This involves anal vaginal and oral sex and blood transfusion, and contaminated hypodermic needles, exchange between mother and baby during pregnancy, child birth, breast feeding or other exposure to one of the above bodily fluids. AIDS is now a pandemic[10] as of 2009, AVERT estimated that there are 33.3 million people worldwide living with HIV/AIDS, with 2.6 million new HIV infections per year and 1.8 million annual deaths due to AIDS[11] In 2007 UNAIDS estimated 33.2 million people had AIDS that year. AIDS killed 2.1 million people in the course of that year including 3,30,000 children and 76% of those death occurred in sub Saharan Africa[12]. According to UNAIDS 2009 reports, worldwide some 60 million people have been infected, with some 25 million deaths, and 14 million orphaned children in Southern Africa alone since the epidemic began[13]

Genetic research indicates that HIV originated in west central Africa during the late 19th or early 20th century [14,15] AIDS was first recognized by the US CENTRE FOR DISEASE CONTROL AND PREVENTION in 1981 and its cause, HIV, identified in

early 1980s16 Although treatments for HIV and AIDS can slow the course of disease, there is no known cure or vaccine. ART reduces both the mortality and morbidity of HIV infection, but these drugs are expensive and routine access to ART is not available in all countries.[17]. Due to difficulty in treating HIV infection, preventing infection is a key aim in controlling the AIDS pandemic, with health organization promoting safe sex and needle exchange programmes in attempts to slow the spread of virus. AIDS was first reported June 5,1981 when the US CDC recorded a cluster of pneumocystis carinini pneumonia in 5 active homosexual men in !os angeles.[18]. In the beginning, of the CDC did not have an official name for the disease .often referring to it by way of the disease that were associated with it, for example lymphandenopathy the disease after which the discoverer of HIV originally named the virus.[19, 20] They also used Kaposi sarcoma and opportunistic infections 1 By the name by which a task force had been setup in 1981.[21]. In general press, the term GRID, which stood for Gay related immune deficiency, had been coined.[22]. The CDC, in search of a name, and looking at the infected communities coined "the 4H disease". As it seemed to single out Haitians .homosexuals,hemophiliacs,and heroin users[23]. However, after determining AIDS was not isolated to homosexual community,[21] the term GRID became misleading and AIDS was introduced at a meeting in July 1982.[24]. By the September 1982 the CDC started using the name AIDS, and properly defined the illness [25]. The earliest known positive identification of HIV1 virus comes from the Congo in 1959 and 1960. Though genetic studies indicate it passed into human population from chimpanzees around 50 earlier[15] .A recent study states that a strain of HIV1 moved from Africa to Haiti and then entered the US around 1969.[26]. The HIV virus virus decends from the related simian immunodeficiency virus which infects apes and monkeys in Africa. There is evidence who participate in bush meat activities, either as hunters or as bush meet vendors,

commonly acquireSIV[26] however .only a few of these infections were able to cause epidemics in humans and all dead so in the late 19th and early 20th century to explain why HIV became epidemic only by that time, there are several theories, each invoking specific driving factors that may have promoted SIV adaptation to humans, or initial spread social changes following colonialism,[28] rapid transmission through unsafe or unsterile injections ,[29] colonial abuses and unsafe smallpox vaccinations or injections[30], or prostitution and the concomitant high frequency of genital ulcer diseases(such as syphilis) in nascent colonial cities.{[31,32]} A more controversial theory known as the OPV AIDS hypothesis suggests that the AIDS epidemic was inadvertently started in the late 1950s in the Belgian Congo by Hilary Koprowski's research into a poliomyelitis vaccine.[{33,34}]. According to scientific consensus, this scenario is not supported by the available evidence [{35, 36, 37}]

Clinical Categories (A--C) For Classifying the Natural Course of HIV Infection*[38]

Category **A:** asymptomatic disease, acute **HIV,** or **PGL** HIV positivity without any clinical signs or symptoms Acute, symptomatic (primary) HIV infection Persistent, generalized lymphadenopathy (PGL)

Category B: disease manifestations or illnesses that, although not AIDS-defining, nevertheless indicate impaired cellular immunity and are attributable to HIV infection

Bacillary angiomatosis

Pelvic inflammatory disease

Complications of tubal and ovarian

Abscesses

Herpes zoster affecting multiple dermatomes, or recurrent herpes zoster in a

Single dermatome

Idiopathic thrombocytopenic purpura (ITP)

Constitutional manifestations such as fever above 38.5°c **or** diarrhea for

Longer than 1 month

Listcriosis.

Oral hairy teukoplakia (ohi)

Oropharyngeal or vulvo-vaginal candidiasis that is cither chronic (>1 month)

Or intractable

Cervical dysplasia or carcinoma in situ

Peripheral neuropathy

Category C: AIDS-defining illnesses

Candidacies of the bronchi, trachea, lungs, or esophagus

CMV infection (except of the liver, spleen, or lymph nodes)

HIV- associated encephalopathy

Herpes simplex infection (for longer than 1 month; bronchitis, pneumonia,

Esophagitis)

Histoplasmosis (disseminated or extra pulmonary)

Isosporiasis, chronic, intestinal, **for** longer than 1 month

Kaposi's sarcoma

Coccidioidomycosis, disseminated **or** extra pulmonary

Cryptococcosis, extra pulmonary

Cryptosporidiosis, chronic (longer than 1 month), intestinal

Burkett's lymphoma

Immunoblastic lymphoma

Primary cerebral lymphoma

Atypical mycobacterium infection

Tuberculosis

Pneumocystis jirovecii pneumonia (pep)

Recurrent episodes of bacterial pneumonia (more than two in a single year)

Progressive multifocal leukoencephalopathy

Recurrent salmonella sepsis

Cerebral toxoplasmosis

Wasting syndrome

Invasive cervical carcinoma

INTRODUCTION HIV AND MICRO ALBUMINUREA

HIV-positive individuals have a significantly higher risk of having small quantities of a protein in their urine that indicates an increased risk of both cardiovascular and kidney disease, according to American researchers writing **in the** May 11TH edition *of AIDS*[39].

The investigators compared microalbuminuria - the presence of small amounts of the protein albumin in urine, a marker for both kidney and cardiovascular disease- in a cohort of HIV-positive patients and age-matched HIV-negative controls and found that the prevalence of elevated microalbuminuria was significantly higher in HIV-positive patients. The presence of microalbuminuria in HIV-positive patients was significantly associated with traditional risk factors for cardiovascular disease as well as HIV-related factors, most notably a weak immune system. Kidney disease, involving symptoms such as protein in urine or elevated creatinine output, has been well described as a complication of HIV infection. Studies conducted before potent anti- HIV therapy became available suggested that between 19% - 34% of HIV-positive individuals had elevated levels of albumin in their urine[39]. Investigators were interested in these observations because microalbuminuria has been associated with an increased risk of heart disease in the general population. As there is an increasingly robust body of evidence to show that antiretroviral therapy can increase the risk of cardiovascular disease, researchers wished to determine if microalbuminuria occurred with greater frequency in HIV-positive patients compared to age-matched HIV-negative controls. The researchers also wished to sec if any factors predicted an increased risk ofmicroaibuminuria in HIV-positive patients[39]. The study population consisted of individuals enrolled in the cross-sectional Study of 1-at Redistribution and Metabolic Change in HIV Infection (FRAM) cohort.

The control population Consisted **of a population-based sample** of healthy **white and** African-American men and women recruited to the **CARDIA** study. Albumin and keratinize concentrations were measured in spot urine tests, and the investigators calculated the albumin to keratinize **ratio** (ACR), **with** an **ACR** of above 30mg/g defined as microalbuminuria- **Data** were also gathered on measures of cardiovascular risk, **including** blood pressure, insulin and glucose **levels,** family **history** of heart disease and smoking. **For HIV**-positive **patients,** the investigators obtained **information** on **CD_4 cell** count and viral load. Microalbuminuria was present in l1%ofHIV-positive patients and 2% of controls, a statistically significant difference ($p < 0.001$)- This **difference remained** significant even after the investigators adjusted for **traditional** predictors **of microalbuminuria** ($p = 0.0008$). Significant predictors of microalbuminuria **in HIV-positive** patients were older **age** ($p = 0.02$). and African American race ($p = 0.001$). **Several factors** associated with an **increased** risk of cardiovascular disease were also strongly associated with microalbuminuria in patients **with HIV.** These were higher systolic blood pressure ($p = 0.01$). **a family** history of hypertension (p -- 0.03). and glucose in urine **(p** = 0.002). **Smoking was** not, however, significantly associated with microalbuminuria. **HIV-specific** factors associated **with** microalbuminuria were a **CD_4** cell count below 200 cells/mm^3 ($p = 0.05$). Current viral load ($p = 0.05$). **and treatment** with an **NNRTI** ($p < 0.05$). "This analysis demonstrated that **U1V** infection is a strong risk factor for the presence of microalbuminuria[39]. independent of the **risk** factors for **the** presence of renal disease", **write** the investigators.

The presence of markers for kidney or cardiovascular disease in HIV-positive patients with microaibuininuria. may be because of the increase in cardiovascular risk due to the metabolic complications caused by some antiretro viral s. The investigators conclude, "the high prevalence **of microalbuminuria** among the **HIV infected** could be a harbinger of future increased risks of both kidney and cardiovascular disease. Further study defining **the** prognostic significance of microalbuminuria **among HIV-infected** persons will be essential[39]."

PROTEIN HANDLING IN NORMAL KIDNEY

Normal barriers to protein filtration begins in the glomerulus. The normal glomerular endothelial cells forms a barrier and holds back cells and other particles. They are penetrated by large pores of 100nm called fenestrae that can be easily traversed by proteins. The glomerular basement traps most large proteins (>100Kda), while the foot process of epithelial cells (podocytes) cover the urinary side of the glomerular basement membrane and produce a series of narrow channels (slit diaphragm) to allow passage of small solutes and water. These slit diaphragm bridges the slits between the foot process of the glomerular basement membrane[40]. The visceral epithelial cells are covered with negatively charged heparan sulfate proteoglycans[41]. This negative charge and size selectivity of glomerular basement membrane impedes the passage of anion molecules such as albumin, globulin and large molecular weight protein across the glomerular wall. The smaller proteins that are filtered across the glomerular basement membrane are largely reabsorbed at the proximal tubule and only small amount are excreted.

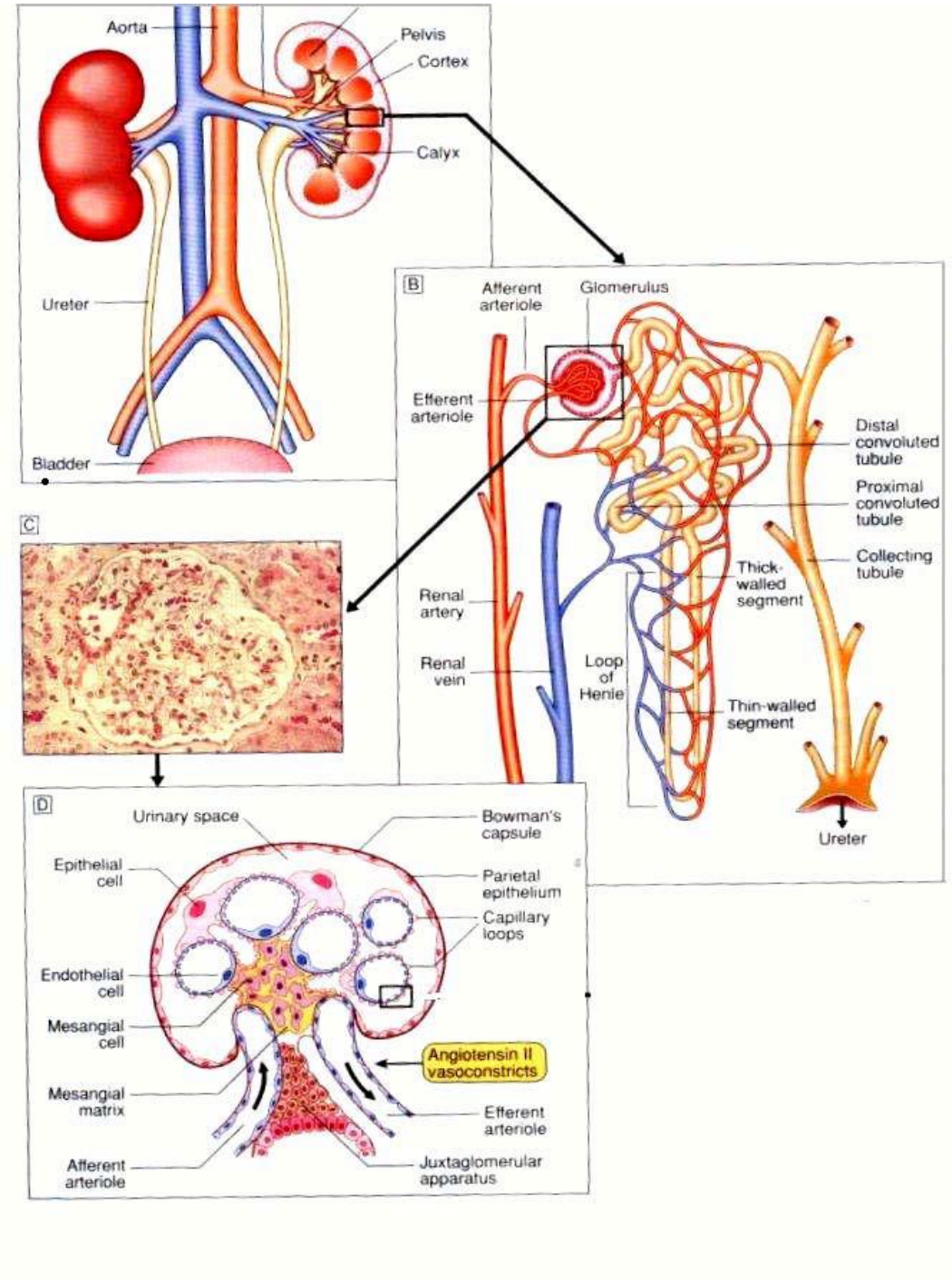


Fig.1 FUNCTIONAL ANATOMY OF KIDNEY

A: Anatomical relations of kidney **B: Single nephron**

C: Histology of normal glomerulus **D: Cross section of glomerulus**

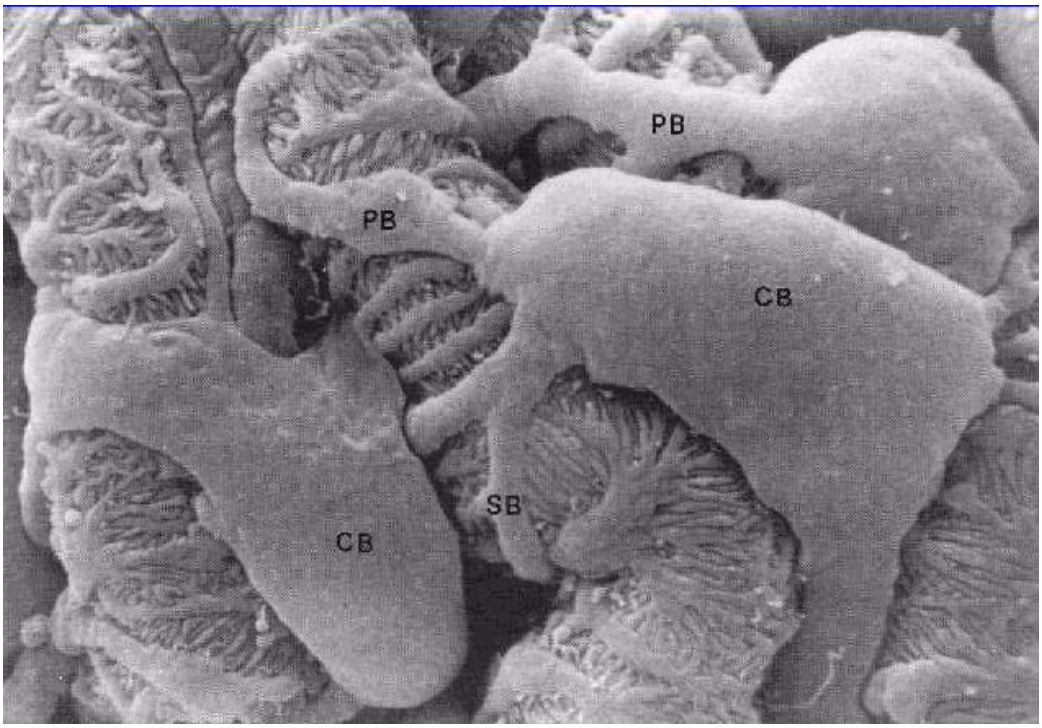


Fig.2 ELECTRON MICROSCOPY OF GLOMERULAR BASEMENT MEMBRANE

CB = capillary bed (tufts), Arrow = podocytes with fenestration slits

PATHOPHYSIOLOGICAL CLASSIFICATION OF PROTEINURIA

A) BENIGN

1. Postural Orthostatic proteinuria

2. Functional

3. Transient

4. Intermittent

B) PATHOLOGICAL

1. Glomerular

2. Tubular

3. Overflow

4. Secretory

A) BENIGN PROTEINURIA

This is a transient proteinuria that occurs with normal renal function, bland urinary sediment, and normal blood pressure and without any significant edema.24 hour urine albumin is usually less than 1 gram. They do not indicate any significant renal disease and disappears on repeated testing.

1) Postural /Orthostatic Proteinuria

This is seen in 3 to 5% of adolescents, especially in young males. It is characterized by increased protein excretion in the upright position and normal protein excretion during recumbency[42]. It is diagnosed by split urine protein excretion examination. In orthostatic proteinuria, the day time specimen typically has an increased concentration of protein, with night time specimen having a normal concentration usually less than 50 mg over eight hours[43]. In true glomerular disease there is reduced protein excretion in the supine position but it will not return to normal as with orthostatic proteinuria. Sp ringberg found that long term prognosis of orthostatic proteinuria is benign in virtually all cases over many decades[44]. Data on renal biopsies on orthostatic proteinuria are confusing. Some showed minor glomerular changes[45]. Posture affects urinary protein excretion, probably via an increase in glomerular capillary hydrostatic pressure and for change in permeability of the glomerular capillary walls. An alternate exp lanation[47] is entrapment of renal veins [47, 48]

2) Functional Proteinuria

It is a benign proteinuria due to changes in glomerular ultra filtration pressure and/or membrane permeability. It is seen in fever, exercise, cardiac failure, emotional stress and acute illness. It is usually less than 0.5 gm/day but may be as heavy as 5.0 gm/day (following marathon running). It disappears with the resolution of causative disorder[49]. Kallmeyer et al

found that recent exercise can induce several gram of protein per liter of urine, sometimes together with hematuria and even casts so called jogger's nephritis[50]. Post exercise proteinuria is about 15 to 20 times the resting range of proteinuria and require about 4 hours to regain resting value in the recovery period[51]. Poortmans et al found that proteinuria was influenced mostly by 35 the intensity of exercise rather than its duration[52].

3) Idiopathic Proteinuria

This is seen in young healthy adults. This dipstick positive proteinuria disappears spontaneously by next clinical visit.

4) Intermittent Proteinuria

This benign proteinuria is found in half of their different urine samples in absence of other renal or systemic abnormalities.

B) PATHOLOGICAL PROTEINURIA

This is persistent proteinuria that is detected on multiple ambulatory clinical visits. This is seen in both recumbent and upright position and usually signals a structural renal disease.

1) GLOMERULAR PROTEINURIA

It is the most common cause of proteinuria in clinical practice. It is characterized by a disproportionate amount of albumin in urine[53]. Due to preservation of selectivity and large concentration of albumin in blood glomerular proteinuria is 85 to 90 % albumin, accompanied by pre-albumin, transferrin and relatively low molecular weight proteins since it contains mostly albumin. They are readily detected by stick or turbidometric methods. Glomerular proteinuria ranges from few hundred mg per 24 hours to 100 gms per 24 hours. McConnell et al on evaluation of proteinuria found that urinary excretion of more than 2 gm per 24 hours is usually a result of glomerular disease[54]. In glomerular proteinuria there is increased glomerular capillary permeability to high molecular weight anionic plasma proteins. How the glomerular barrier is damaged so that it leaks more than normal remains unclear[55]. This may be due to:

-Loss of fixed anionic charge (Congenital nephrotic syndrome, minimal change nephropathy)

- Detachment of epithelial podocytes from basement membrane[56].
- Immune aggregates.
- Increase in glomerular capillary pressure.

The filtered protein, that reach the tubules overwhelm the limited capacity of tubular reabsorption and cause these proteins to appear in urine. Glomerular disease is classified as primary when the pathology is confined to the kidney and secondary when it is a part of multi system disorder.

Glomerular proteinuria is of two types:

a) Selective Proteinuria

b) Nonselective Proteinuria

In selective proteinuria the clearance ratio of immunoglobulin to albumin or transferrin is less than 0.10(<10%).In nonselective proteinuria the clearance ratio of immunoglobulin to albumin or transferrin is more than 0.50(>50%).

GLOMERULAR PROTEINURIA -CAUSES

Primary Glomerulonephropathy:

- Minimal change disease

- Focal segmental glomerulonephritis

- Idiopathic membranous glomerulonephritis

- Membranoproliferative glomerulonephritis

- IgA nephropathy

Secondary Glomerulonephropathy :

- Diabetes mellitus

- Amylodosis

- Collagen vascular disease (Eg-Lupus nephritis)

- Infections

- HIV

- Hepatitis B and C infection

- Post streptococcal

- Syphilis

- Malaria

- Infective Endocarditis

- Drugs

- NSAIDS

- Penicillamine

- Lithium

- Heroin

- Heavy metals

- Gastrointestinal and lung cancers

- Lymphoma

2) TUBULAR PROTEINURIA

Proteinuria results from the damage of proximal tubule so that normally reabsorbed protein, principally of low molecular weight pass into the urine. This usually occurs as part of the fanconi syndrome of proximal tubular dysfunction. Tubular proteinuria usually does not exceed 2gm per day[57, 58]. Beta 2-microglobulin is one of the many micro globulin which make up tubular proteinuria. Normal level of Beta 2-microglobulin in urine is less than 0.4 mcg/L. It can be assessed by RIA or ELISA. The urinary albumin and Beta 2-microglobulin

ratio of 10 to 1 suggests the presence of Beta 2-microglobulin. Further measurement of Beta 2 lysozy me may help in distinguishing type of urinary tract infection besides diagnosis of heavy metal poisoning[59, 60]. Urinary protein electrophoresis and/or immuno electrophoresis may aid in distinguishing tubular and glomerular proteinuria.

TUBULAR PROTEINURIA – CAUSES

- Hypertensive nephrosclerosis

-Tubulo intestinal diseases

-Fanconi syndrome

-Heavy metals

-Uric acid nephropathy

-Acute hypersensitivity

-Interstitial nephritis

-Sickle cell disease

-Drugs (NSAID, antibiotics)

3) OVERFLOW PROTEINURIA

It is due to filtration by normal glomerulus of an abnormally large amount of low molecular weight proteins, which exceeds the capacity of the normal tubules for reabsorption. It is characterized by the presence of abnormal peak or spike on urinary electrophoresis. Most often, this is a result of the immunoglobulin over production that occurs in multiple myeloma. The resultant light change immunoglobulin fragments (bence jones proteins) produce a monoclonal spike in the urine electrophoresis[61, 62].

OVERFLOW PROTEINURIA – CAUSES

-Multiple myeloma

-Myoglobinuria

-Rhabdomyolysis

-Lymph proliferative disorders

4) **SECRETORY PROTEINURIA**

It occurs due to secretion of proteins into the urine after glomerular filtration. About 20 to 30 mg/24 hours of non plasma protein is contributed by renal tubules and lower urinary tract. Mostly they are formed by Tamm-Horsfall proteins[44]. Some secretary IgA is added by lower urinary track including the urethral glands together with trace quantity of protein of prostatic or seminal vesicular organ[63, 64]. Tamm- Horsfall protein is secreted by the ascending thick limb and early distal convoluted tubule into the tubular fluid. It is an easily polymerized glycoprotein.

They form the major constituent of renal tubular casts[65], along with albumin and traces of many plasma proteins, including immunoglobulins[66]. In myeloma, casts contain par proteins polymerized with Tamm-Horsfall protein, and may show a micro fibrillar structure that will stain positive with Congo red, even though no amyloid is present in renal tissue.

(According to daily protein excretion)

Causes - 0.15 **– 2.0 gm** Mild glomerulopathies Tubular proteinuria

Overflow proteinuria 2.0 **–3.5 gm**

Usually glomerular 3.5 **gm** always glomerular

3. AIM AND OBJECTIVES

TO STUDY INCIDENCE OF MICROALBUMINURIA IN HIV PATIENTS AND ITS RELATION WITH CD4 COUNT.

4. REVIEW OF LITERATURE:

Microalbuminuria

Microalbuminuria or dipstick negative albuminuria is conventionally defined as urinary albumin excretion between 30-300 mg/24 hour for timed 24 hours urine collections and between 20-200 mg/L for untimed samples[68]. High normal. albuminuria is defined as morning urinary albumin concentration up to 30 mg/l. Low- normal albuminuria is morning urinary albumin concentration of less than 10 mg/l.

Normoalbuminuria = <30 mcg/min.

Microalbuminuria (Incipient nephropathy) = 30 – 300 mcg/min.

Macroalbuminuria (Clinical nephropathy/ Overt nephropathy**)** > 300 mcg/min.

Mechanism of microalbuminuria

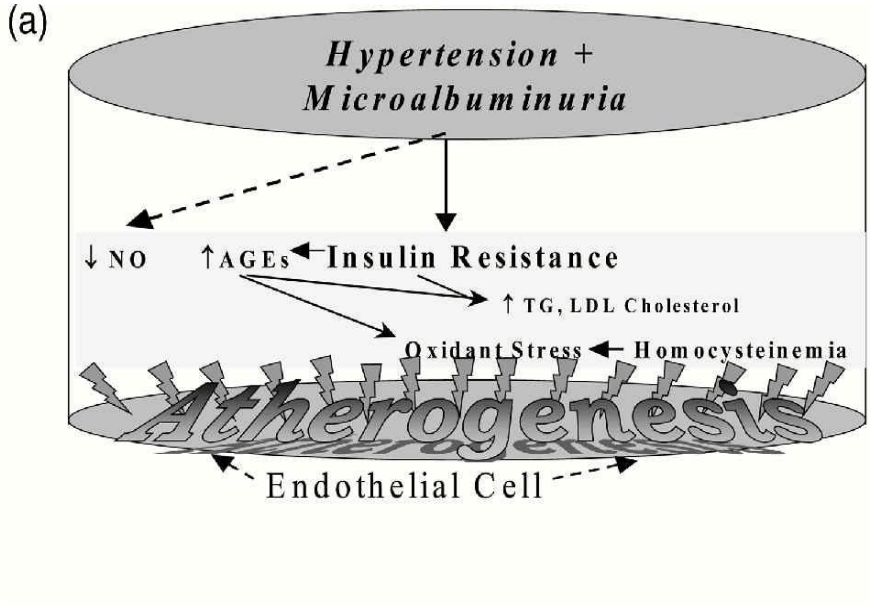
The intimate relationship between low-level albumin excretion and vascular permeability makes urinary albumin excretion highly sensitive to the presence of any inflammatory processes. Pathophysiological processes associated with microalbuminuria:

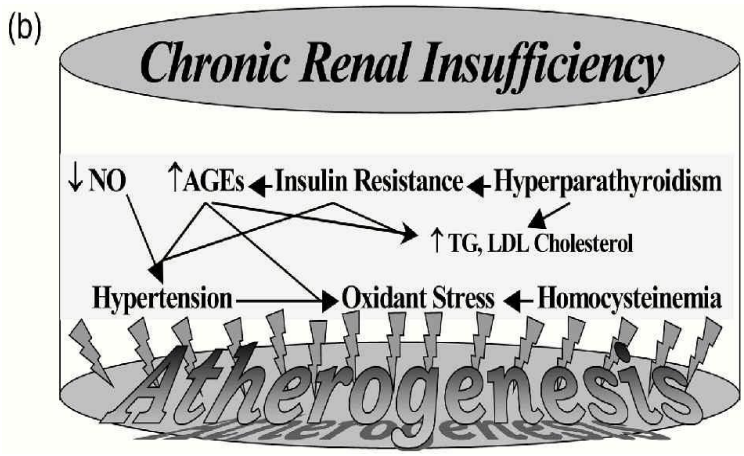
Local process

1. Increased intraglomerular capillary pressure
2. Increased shunting of albumin through glomerular membrane pores

Systemic process

1. Activation of inflammatory mediators
2. Increased transcapillary escape rate of albumin
3. Vascular endothelial dysfunction





(AGE = glycated end products)

The kidney is ideally placed to amplify any small changes in the systemic vascular permeability. The glomeruli receive 25% of the cardiac output. Of the 70 kg of albumin that pass through the kidneys every 24 hours, less than 0.01% reaches the glomerular ultra filtrate (i.e. less than 7g/24 hour) and hence enters the renal tubules. Almost all the filtered albumin is absorbed by the proximal tubule via a high affinity, low capacity endocytotic mechanism, with only 10-30 mg/24 hr appearing in the urine. Assuming that 7 gm of albumin is filtered every 24 hour, 1% increase in systemic vascular permeability in response to an inflammatory stimulus would result in an additional 70 mg of albumin passing into the

filtrate. Since tubular mechanisms for albumin reabsorption are near saturation, urinary albumin excretion would increase from a maximum of 30 to approximately 100 mg/24 hour[69]. Glomerular permeability to albumin is dependent on endothelial charge selectivity as well as size selectivity. The negative charge conferred on the glomerular membrane by its consistent glycoprotein plays a role in restricting the permeability of anionic proteins. Loss of glomerular charge selectivity has been found in both diabetic and non-diabetic population with microalbuminuria[70]. Other possible mechanisms of microalbuminuria include the following:

1. Systemic transvascular albumin leakage: TERalb is defined as the fraction of the intravascular mass of albumin going through the vascular bed per unit time. The transcapillary escape rate of albumin is an overall measure of macromolecular permeability of the vascular bed in vivo. As microalbuminuria reflects systemic transvascular leakiness for albumin, which may also allow for a higher degree of lipid in sudation into the large vessel wall, the is may link microalbu minuria to atherogenesis[71].

2. Role of sialic acid: Sialic acid has been reported to affect several hematological factors, transvascular permeability and accumulation of lipid in the arterial wall. Studies showed that in subjects without diabetes mellitus, an elevated serum concentration of sialic acid is predictive of atherosclerotic vascular disease in presence of concomitant elevation of urinary albumin excretion[71].

3. Impaired arterial dilatory capacity: Slightly elevated urinary albumin excretion is associated with impaired conduit arterial dilatory capacity in clinically healthy subjects, and this impairment may be explained by a reduced dilatory response to nitric oxide of both endogenous and exogenous origin. Impaired arterial dilatory capacity may contribute to the increased cardiovascular risk in subjects with elevated urinary albumin excretion[72].

4. Elevated Von Willebrand Factor concentrations and other prothrombotic factors: Studies showed that prothrombotic factors like fibrinogen and factor VII C, von willebrand factor antigen are elevated in patients with type 1 diabetes complicated by microalbuminuria, so also in hypertensive patients. These were considered potential markers of endothelial dysfunction[73, 74].

5. Hyperinsulinaemia: In vitro insulin has been shown to cause smooth muscle cell proliferation. It stimulates LDL binding to smooth muscle cells, fibroblasts and monocytes and stimulate cholesterol synthesis in monocytes[75]. Hyperinsulinaemia and microalbuminuria are components of metabolic syndrome and are associated with a highly abnormal cardiovascular risk factor pattern.

6. Hyperhomocysteinaemia: The enhanced risk of cardiovascular and cerebrovascular disease with microalbuminuria may also be due in part to an association with hyperhomocysteinemia, a risk factor for atherosclerosis[76].

REVIEW OF LITERATURE:

Microalbuminuria signifies abnormal vascular permeability and its presence may be considered as kidney's notice for markedly enhanced cardiovascular risk[77].The importance of microalbuminuria was first appreciated in the early 1980s when two landmark studies in London and Denmark independently reported that it was predictive of development of overt diabetic nephropathy and progressive renal failure[78, 79]. Since then, various studies have established the significance of Microalbuminuria in several conditions:

1) Morten Baekken, Ingrid Os[5], in 2008. studied microalbuminuria associated with indicators of inflammatory activity in an HIV positive population. Study based on three prospective urine sample in an unselected non hypertensive, no diabetic HIV positive cohort, analyzed the prevalence of microalbuminuria and compared the Caucasian share with that of a nonhypertensive, nondiabetic population-based control group. Significant predictors for microalbuminuria were analyzed within the HIV positive cohort. Result prevalence of microalbuminuria was 8.7% in HIV infected cohort, which is three to five times higher than the general population. Concluded the development of microalbuminuria with respect to increasing risk of developing coronary vascular disease or renal diseases and mortality, the high prevalence of microalbumiuria in HIV infected individuals warrants special attention.

2) Szczech, Lynda Anne[3], in 2007 did cross sectional study over microalbuminuria in HIV infection and concluded microalbuminuria was present in 11% of HIV infected than that of 2% control participant.

3) Chioma Pedro Emem , Fatiu Arogundade[6], in 2007 assessed renal disease in HIV seropositive patients in Nigeria, In order to determine the pattern of renal disease and risk

factors for renal disease in HIV infected Nigerians, studied 400 consecutive HIV/AIDS patients (210 males, and 190 females) Aged between 18 and 65 years (mean ± SD; 34.6 ± 9.4 years), and examined renal disease factors attributable to the infection. Diagnosis of renal disease was based on the consistent presence of at least 1+ albuminuria and/or elevated serum creatinine. As

4) T M Han, S Naicker[2], in 2006 did a cross sectional study of HIV seropositive patients with varying degrees of proteinuria in south Africa and evaluated early detection of HIV associated nephropathy may be beneficial in evaluating early treatment. This study examined the pattern of renal diseases in HIV infected South Africans and also attempted to diagnose HIVAN at an early stage. In this single-center cross sectional study 615 HIV infected patient were screened for proteinuria. 30 patients with varying degrees of protenuria underwent renal biopsy. Patients with diabetes mellitus, uncontrolled hypertension, known cases of chronic kidney disease, and serum creatinine above 250µ mol/l were excluded. HIVAN was found in 25 (83%) patients, 6 (24%) of them had microalbuminuria. Then they concluded microalbuminuria is a manifestation of HIVAN in their study patients. Therefore, microalbuminuria may be early marker of HIVAN and screening for its presence may be beneficial, renal biopsy may be considered in seropositive patients who present with persistent microalbuminuria, especially with low CD4 counts irrespective of good renal function. This will allow diagnosis and treatment of HIVAN at an early stage and may prevent further disease progression.

5) Lynda Anne Szczech, Stephen J. Gange[7], in 2002 did prospective cohort includes 2059 women enrolled in the Women's interagency HIV study, Found result of 2057 HIV positive women, 32% had proteinuria on initial evaluation. And concluded establishment the association between both increasing HIV RNA level and decreasing CD4 lymphocyte

count with the presence of proteinuria and occurrence of renal failure.

6) Several studies have shown that microalbuminuria in diabetic patients predicts diabetic nephropathy as well as increased cardiovascular and overall mortality[80]. Persistent microalbuminuria in these patients also correlates with the presence of hypertension, obesity and dyslipidemia[81]. American Diabetes Association has adopted cut off values for diagnosis of diabetic nephropathy[82]. In 1998, ADA included positive microalbuminuria as the risk factor for coronary artery disease in diabetic Subject[83].

7) Studies have shown that the prevalence of microalbuminuria is enhanced in hypertensive subjects, in particular in those with blood pressure characteristics that are associated with enhanced cardiovascular risk, such as salt sensitivity and an abnormal diurnal blood pressure rhythm. Microalbuminuria possibly identifies at an early stage, hypertensive patients with an enhanced risk of developing the well-known renal and cardio vascular hypertensive complications[84].

8) Studies have documented the relationship between the presence of Microalbuminuria and other atherosclerotic risk factors such as hypertension, dyslipidaemia and smoking in the general population. Studies have revealed the significance of microalbuminuria as predictor of increased mortality in elderly Persons[85].

9) Microalbuminuria is detected early in the course of acute myocardial infarction and is considered as an independent predictor of early mortality in this condition. Microalbuminuria has been found to be proportional to the size of the infarct. Gosling et al suggested that early rise in urinary albumin concentration is useful in distinguishing myocardial infarct from angina[86]. Spyridon K et al found that microalbuminuria is a strong independent predictor of 3 year adverse prognosis in patients who has sustained acute myocardial infarction[87].

10) Roine et al demonstrated that microalbuminuria distinguished bacterial meningitis from aseptic meningitis with specificity of 94%[88].

11) Shearman et al found that microalbuminuria peaked 36 hours after admission in patients with acute pancreatitis and that serious complications developed later, only in those with the higher values of microalbuminuria[89]

.

12) Pallister et al found that microalbuminuria levels 8 hours after admission in trauma victims predicted the development of acute respiratory distress syndrome with a positive predictive value of 85% and a negative predictive value of 95%[90].

13) Microalbuminuria has been found to be associated with wide variety of inflammatory conditions like rheumatoid arthritis, inflammatory bowel disorder, and surgery etc[91, 92].

14) Highly significant association between microalbuminuria and carotid artery intima-media thickness has been reported a finding which suggests that microalbuminuria may be a marker for early development of carotid artery atherosclerosis and points to a possible linkage between microalbuminuria and atherothrombotic stroke mechanism[93].

Microalbuminuria is unlikely to be a marker for susceptibility to the development of clinical nephropathy but it is more likely to be a sign of early disease.

TESTS FOR ALBUMINURIA

In 1963, Keen and Chlouveraskis described the first specific RIA for albumin in urine[94]. Since then several methods have been described for measurement of urinary albumin excretion with emphasis on inexpensive, easy to apply, rapid tests which can be used on a large scale population. The various methods used are:

1. Dipstick method.
2. Semi quantitative method.
   - Chemical precipitation (Sulphosalicyclic acid trichloroacetic acid)
   - Immuno precipitation (Micral Test).
3. Photometric method, Immunoturbidimetric assay
4. Nephelometric method.
5. Sensitive Quantitative methods
   - Radio immuno assay.
   - Cellulose acetate, agarose gel electrophoresis.

The procedures of various important methods include the following:

1. Dipstick method: Chemically impregnated dipstick contains methyl red and bromophenol blue with buffering salts. The later dissolve on contact with urine and protein in the urine lowers the pH turning it green. It was traditionally known to detect albuminuria >300 mg/L and hence not advocated for screening for microalbuminuria. But, in a study by Alfredo Pegoraro et al, they found that the combination of sulfosalicylic acid testing and chemstrips was as good as and less expensive than micral-test in ruling out microalbuminuria[95].

2. Chemical precipitation (Sulphosalicylic acid test): 5 drops of 20% sulphosalicylic acid is added to 3 ml of urine in one test tube. This test tube is compared with test tube of untreated urine held against a dark background, immediately and turbidity is taken to indicate proteinuria[96].

3. **Immunoprecipitation (Micral test)**: It is based on color shift of monoclonal antibody to human albumin labeled with gold. Here gold labeled optically read Immuno assay detects microalbuminuria. A specimen of the urine sample passes via the wick fleece into the conjugate fleece. Any albumin present in the urine binds itself specifically to the gold labeled antibodies. Excess antibodies are bound byn immobilized albumin in the capture matrix. Only antibodies bound to albumin from the urine sample can pass through the capture matrix. These gold-labeled antibodies flow to the detection pad and turn it red. Test is performed on early morning random urine sample by immersing the strip for 5 sec and reading the result at 2 min, visually comparing with color blocks on vial (0 mg/l, 20mg/l, 50 mg/l and 100 mg/l albumin)[96].

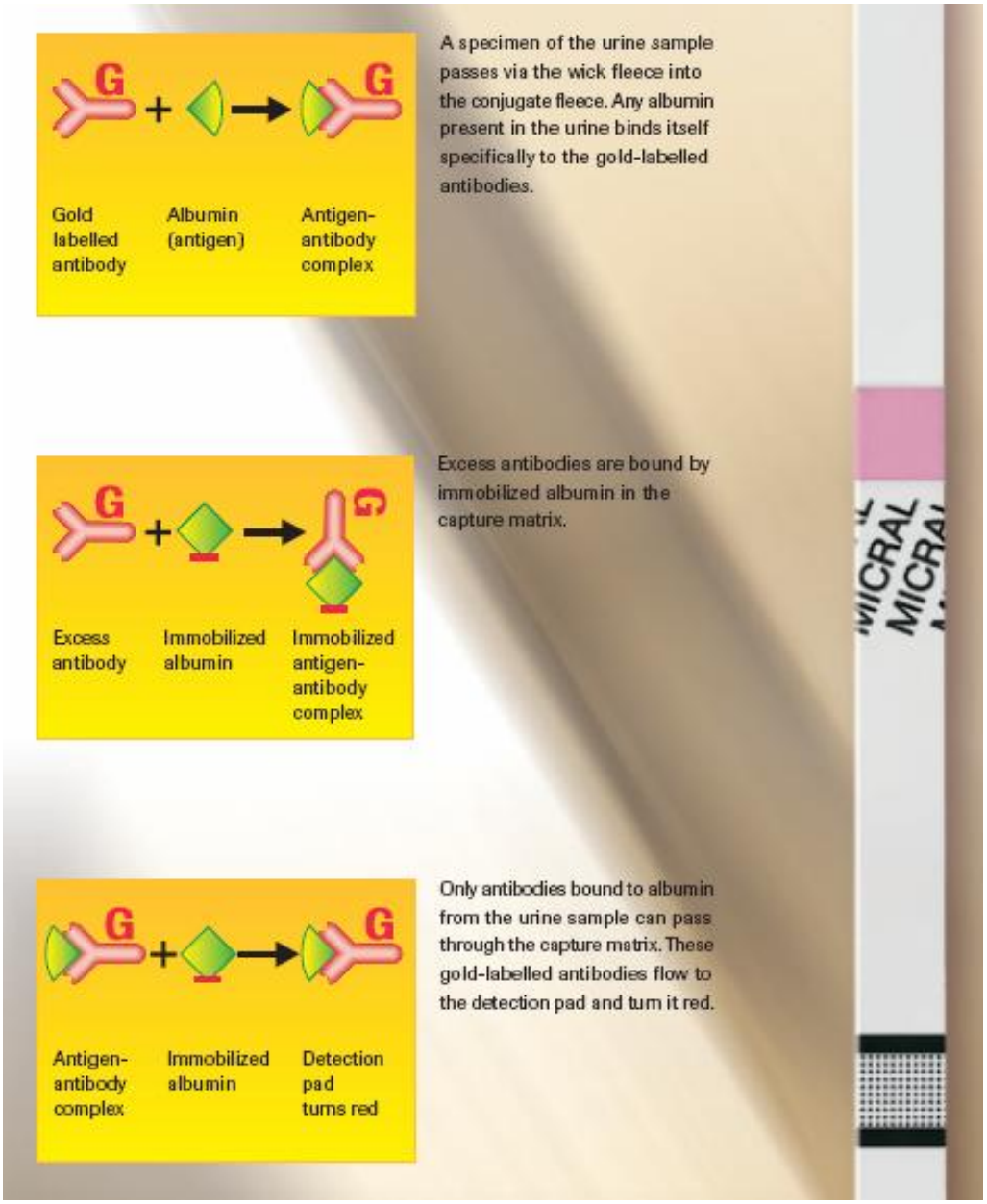


Fig.3. Principle of micral Test

The absorbed urine enters a zone on the test strip containing a conjugate fleece. Albumin in the urine binds itself specifically to gold labeled antibodies. These flow into detection pad, which in the presence of albuminuria turns the white detection to a shade of red.

4. Radioimmuno assay: It is the "gold standard" for estimation of albuminuria. It is a double antibody technique where albumin in the sample has to compete with the fixed amount of 125 labeled albumin for the binding sites of the specific antibodies. Bound and free albumin is separated by addition of a second antibody immuno absorbent followed by centrifugation and decanting. The radio activity in the pellet is measured with a C-counter, Albumin concentration in the sample is inversely proportional to the radioactivity. The sensitivity for radio immune assay method was 0.3 mg/l.

METHOD OF URINE COLLECTION

For the diagnosis of microalbuminuria, a 24-hour urine collection is the gold standard. Because of the effort involved, it is not the method of choice for screening. The second best is a timed overnight urine collection. Again, because this requires collection of urine over a given time period, this may be acceptable for screening specific patient groups such as p patients with diabetes or hypertension, but it is less feasible for population screening. The next best is a first-morning urine sample. This has the advantage over a spot-urine sample because it is always performed at the same time of the day, and it is least influenced by hydration status and physical activity of the patient, reducing the variability that is caused by these factors. In clinical practice however, a spot-urine sample is collected when the patient visits either the general practitioner or the health care office, where the screening takes place.

To express albuminuria, preferably the excretion of albumin per unit of time should be used {UAE per 24 hours or per minute (in case of timed overnight collections)}.For untimed samples; the albumin-to-creatinine ratio is advocated[97].

The albumin-to-creatinine ratio however, introduces the need to use different definitions for an abnormal value for men and women. Moreover, creatinine excretion in the urine depends not only on gender but also on age and race[98, 99]. This may explain why urinary albumin concentration from a spot sample performs equally well for the definition of microalbuminuria as albumin-to-creatinine ratio[100].

In this study a kit was used to detect micro albumin in urine. First morning mid stream urine sample that was collected in a sterile container was used for determining microalbuminuria. Also it has the advantage over a spot-urine sample because it is always performed at the same time of the day, and it is least influenced by hydration status and physical activity of the patient, reducing the variability that is caused by these factors. By quantitative immunochemical and turbidometric method, the turbidity formed was measured at 340 nm and the levels of micro albumin in urine was detected.

Reference (cut off) values of micro albumin in urine = 0 to 30 mg / liter

Microalbuminuria = 30 to 300 mg / liter

When someone is found to be positive for microalbuminuria, one first should confirm the positive test by repeated testing. It has been argued that two of the three tests need to be positive. Repeated urine for micro albumin , twice to be done in period of 3 to 6 months and after that if 2 or 3 tests become positive, then only microalbuminuria should be treated, as depicted in the fig no.6.

TREATMENT OF MICROALBUMINURIA

1. Control of Blood pressure: Systolic BP is one of the most relevant determinants of microalbuminuria. Studies of secondary prevention have shown that blood pressure reduction effectively reduces the albumin excretion rate. Among anti-hypertensive, ACE inhibitors and ARB's seem to be particularly effective[101]. The target BP should be < 140/90 mmHg in non-diabetics and < 130/80 mmHg in diabetic patients.

2. Glycemic control: Intensive ant diabetic therapy can significantly reduce the risk of development of microalbuminuria and overt nephropathy in people with diabetes[102].

3. Treatment of Dyslipidemia: Statins modify endothelial dysfunction, inflammatory response, plaque vulnerability and thrombus formation. Their usage is known to slow progression of microalbuminuria and is associated with stabilization of UAE[104].

4. Smoking cessation: Smoking should be strongly discouraged in patients with microalbuminuria not only to retard the progression of microalbuminuria but also to guard against cardiovascular disease.

5. Protein restriction: Animal studies have shown that restriction of dietary proteins intake reduces hyper filtration and intraglomerular pressure hence retarding the progression of microalbuminuria. The general consensus s is to prescribe a protein intake of 0.8 g/mg/day in patients with overt nephropathy.

MICROALBUMINURIA: A PRACTICAL PERSPECTIVE

Several pathways may link microalbuminuria and vascular disease. Several factors that cluster with microalbuminuria include insulin resistance, central obesity, low levels of high-density lipoprotein cholesterol, high triglyceride levels, systolic hypertension, and lack of nocturnal dip in blood pressure on 24 hour monitoring, salt sensitivity, endothelial dysfunction, hypercoagulability, impaired fibrinolysis and renal dysfunction. This provides enough proof to support the role of microalbuminuria as a predictor or vascular events in high-risk population. Hence, screening for microalbuminuria on a regular basis may help to identify a subgroup of patients who are at high risk for cardiovascular disease and need more intensive therapy and closer follow-up because they could benefit from early intervention and treatment[104].

MATERIALS AND METHODS

1. SOURCE OF DATA:

The material for the present study is collected from HIV infection patients who attended to BLDEU'S Shri B. M. Patil's medical college hospital and research centre, Bijapur .Period of study is from October 2009 to May 2011.

2. METHOD OF COLLECTION OF DATA:

By history

By clinical examination.

By analyzing case papers.

3. SAMPLE SIZE:

Prevalence of HIV infection in India is a 0.91%,[6] and $\pm$ 2 Margin of error at 5% risk. The work out and sample size is 87 by using statistical.

$$n = \frac{(1.96)^2 (p) (1-p)}{d^2}$$

Hence minimal sample size = 87

4. INCLUSION CRITERIA:

Registered case of HIV/AIDS (according to WHO Criteria) out patients and in patients.

5. EXCLUSION CRITERIA:

Diabetic patients

Hypertensive patients

Patient who underwent an antibiotic treatment since 3 days for urinary tract infection.

6. STATISTICAL METHOD:

Diagrammatic presentation

Mean ± SD – Presentation

Proper statistical test. (If necessary)

Z test

Chi – square test

METHODS OF TEST

ESTIMATION OF MICROALBUMINURIA IN URINE -

Microalbuminuria is defined as presence of albumin in the range of 30 to 300 mg/day, in 24 urine sample. Five ml of first voided early morning sample of urine will be collected for the study. The patients will be asked to avoid exercise prior to urine collection. In women, urine examinations will be done during the non menstrual phase. A kit will be used to detect micro albumin in urine. By quantitative immunochemical and tubidometric method, the turbidity formed will be measured at 340 nm and the levels of microablumin in urine will be detected.

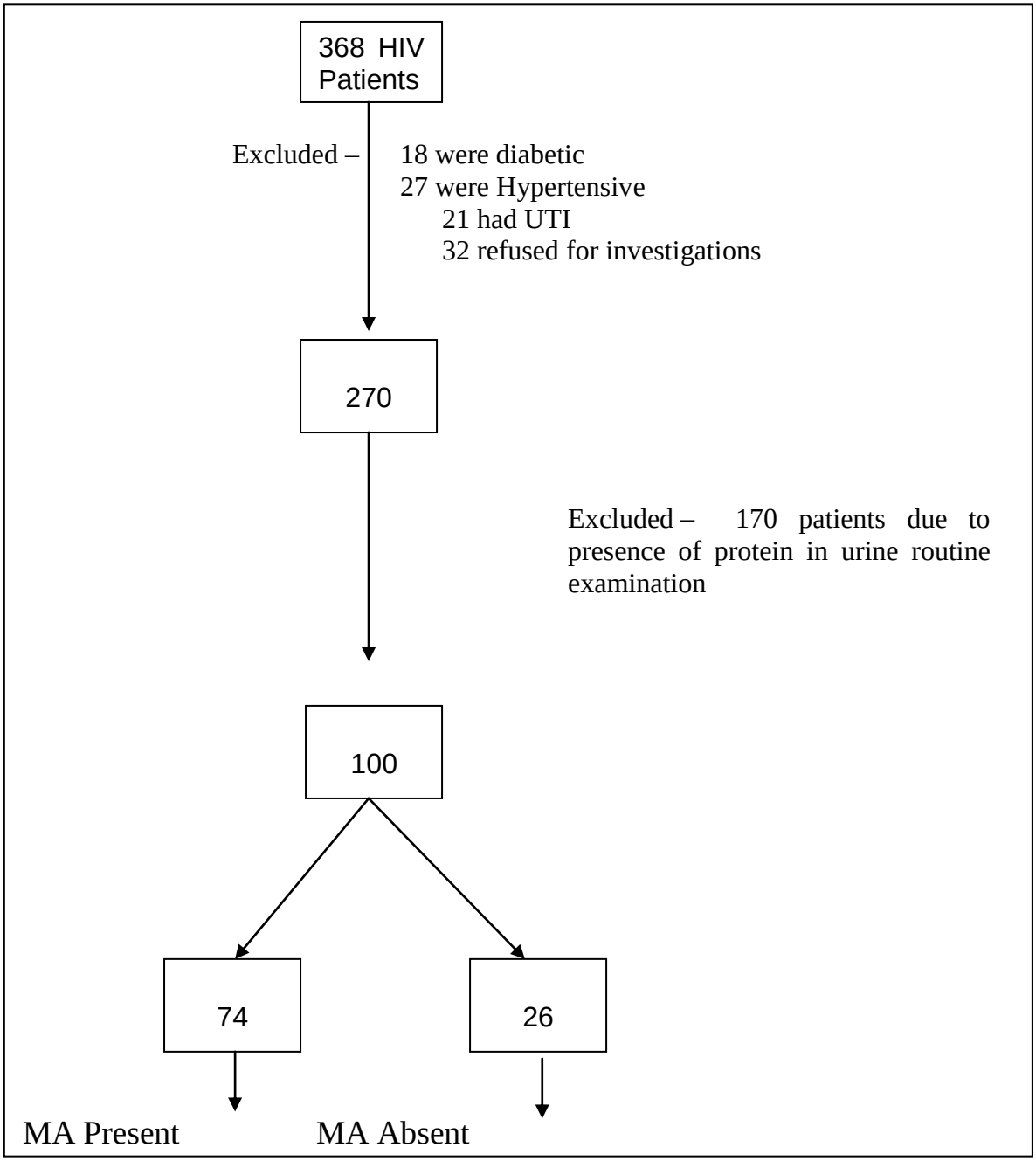
Reference (cut off) values of micro albumin in urine = 0 to 20 mg/liter

Microalbuminuria = 20 to 200 mg/liter.

5. OBSERVATION & RESULTS

Incidence of microalbuminuria in HIV patients.

Table No 1.

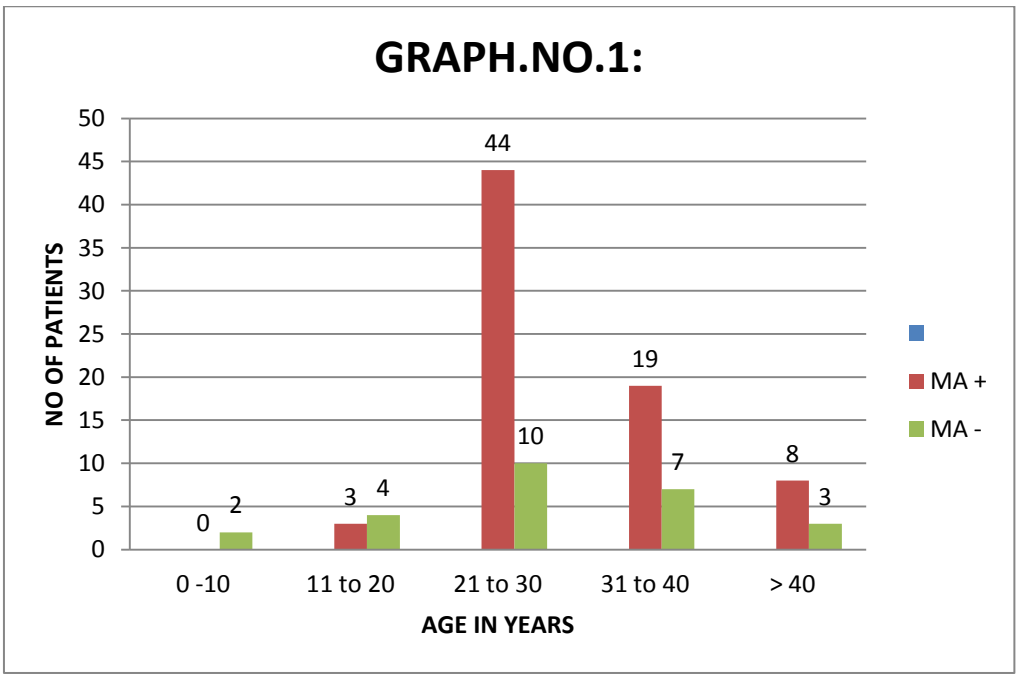


Hence incidence of microalbuminuria in HIV patients = 20.16%

Table No. 2.

	MICROALBUMINUREA					CF - CUMULATIVE FREQUENCY	
S.No	AGE(Years)	MA +	%	MA -	%	CF +	CF -
1	0 -10	0	0	2	7.692308	0	2
2	11 to 20	3	4.054054	4	15.38462	3	6
3	21 to 30	44	59.45946	10	38.46154	47	16
4	31 to 40	19	25.67568	7	26.92308	66	23
5	> 40	8	10.81081	3	11.53846	74	26
	TOTAL	74	100	26	100		

Graph. 1.



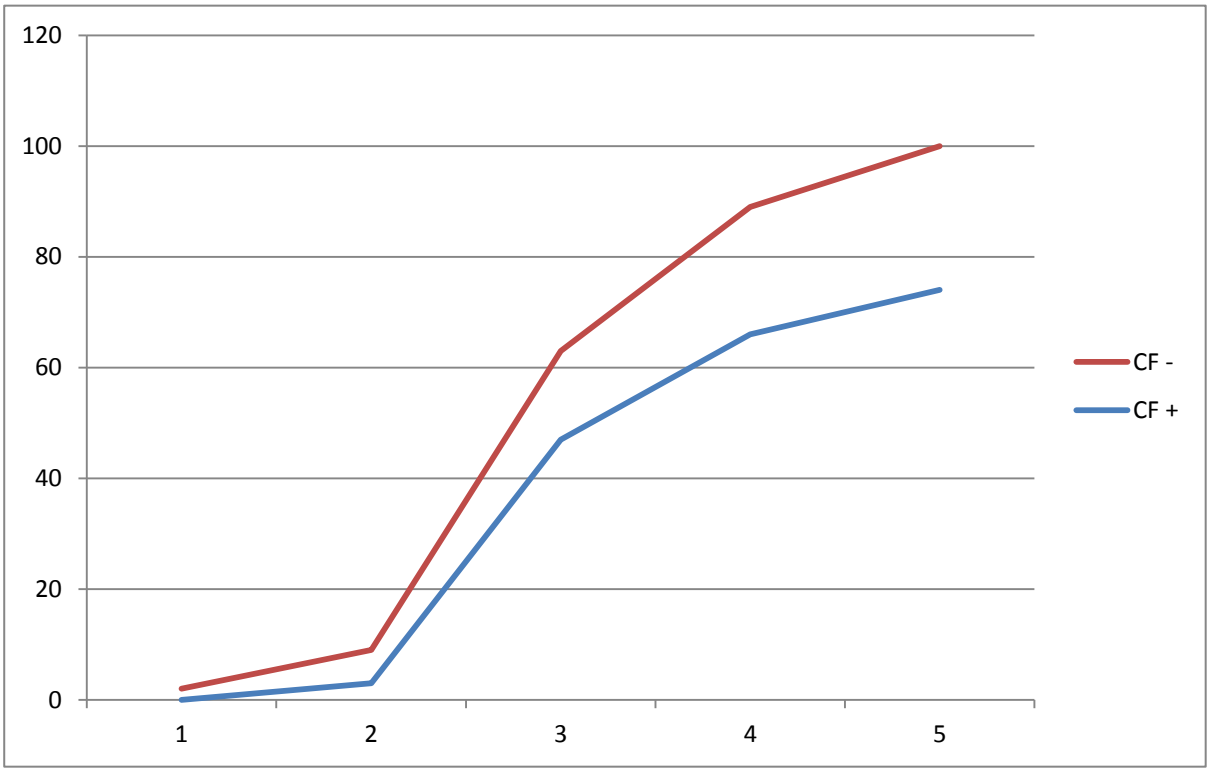
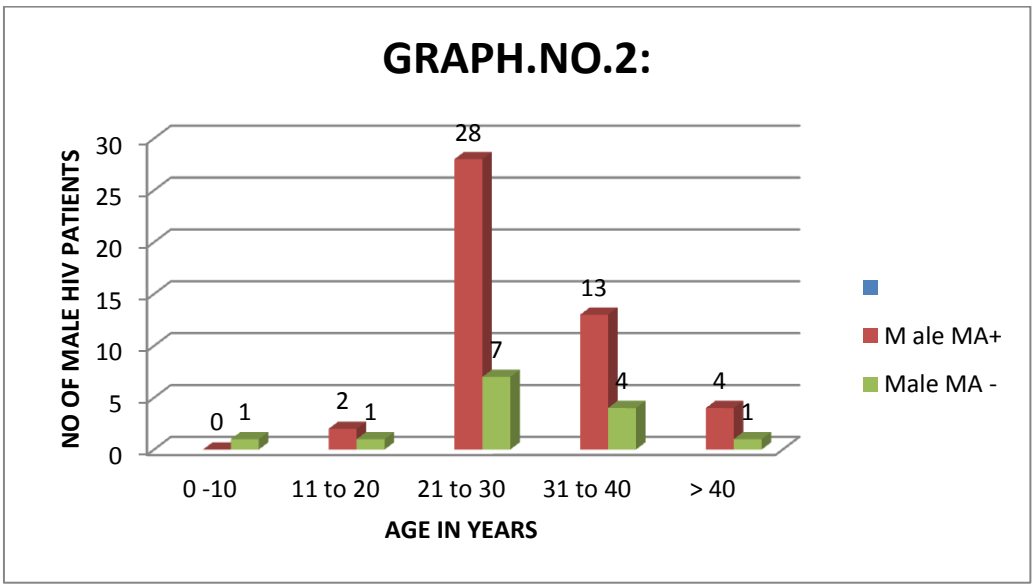

120
100
80
60
40
20
0
1
2
3
4
5
CF -
CF +

Table. 3.

AGE	M ale MA+	%	Male MA -	%	CF	CF
0 -10	0	0	1	7.142857	0	1
11 to 20	2	4.255319	1	7.142857	2	2
21 to 30	28	59.57447	7	50	30	9
31 to 40	13	27.65957	4	28.57143	43	13
> 40	4	8.510638	1	7.142857	47	14
TOTAL	47	100	14	100		

Graph. 2.



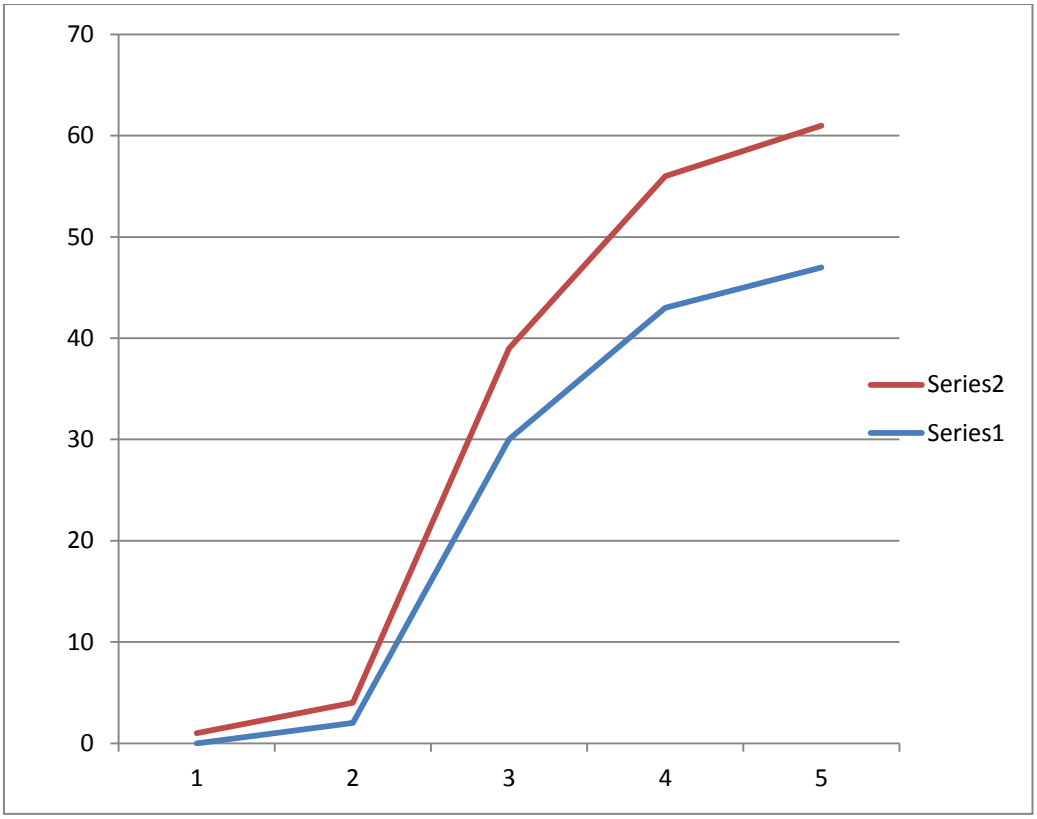
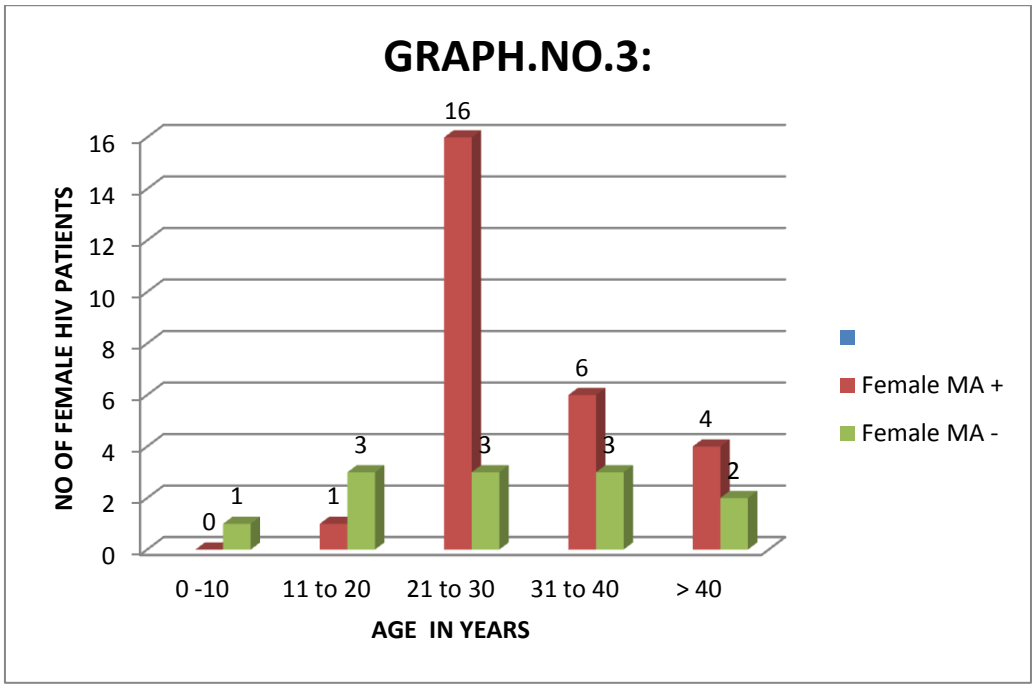

70
60
50
40
30
20
10
0
1
2
3
4
5
Series2
Series1

Table. 4.

AGE	Female MA +	%	Female MA -	%	CF	CF
0 -10	0	0	1	8.333333	0	1
11 to 20	1	3.703704	3	25	1	4
21 to 30	16	59.25926	3	25	17	7
31 to 40	6	22.22222	3	25	23	10
> 40	4	14.81481	2	16.66667	27	12
TOTAL	27	100	12	100		

Graph. 3.



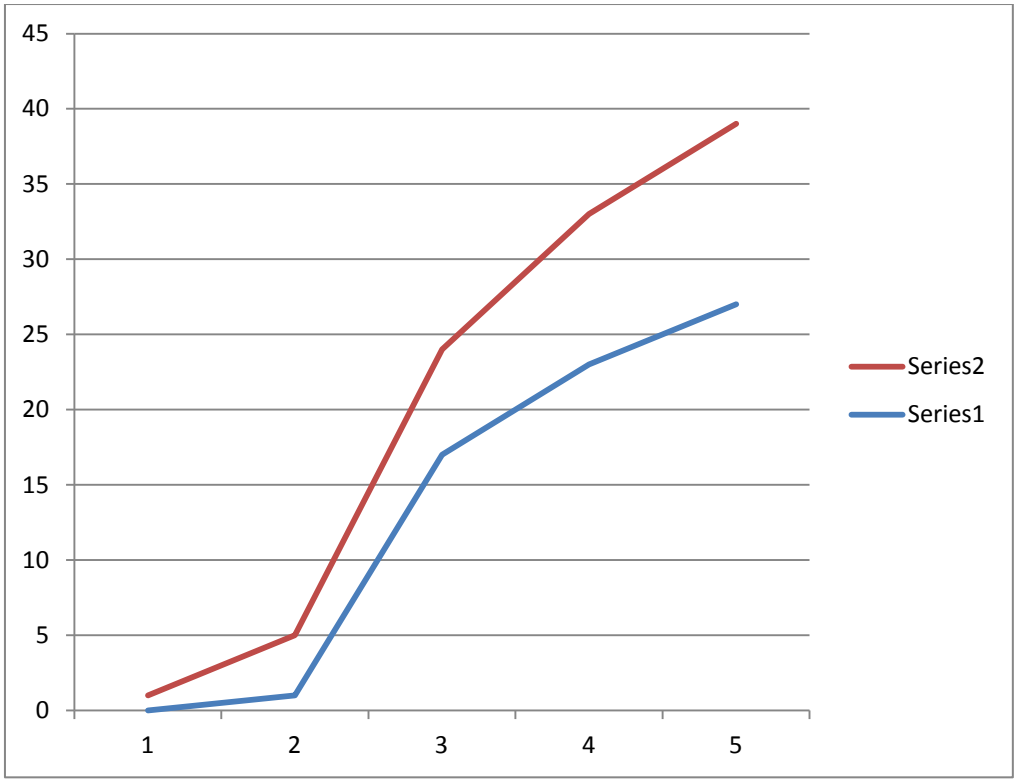
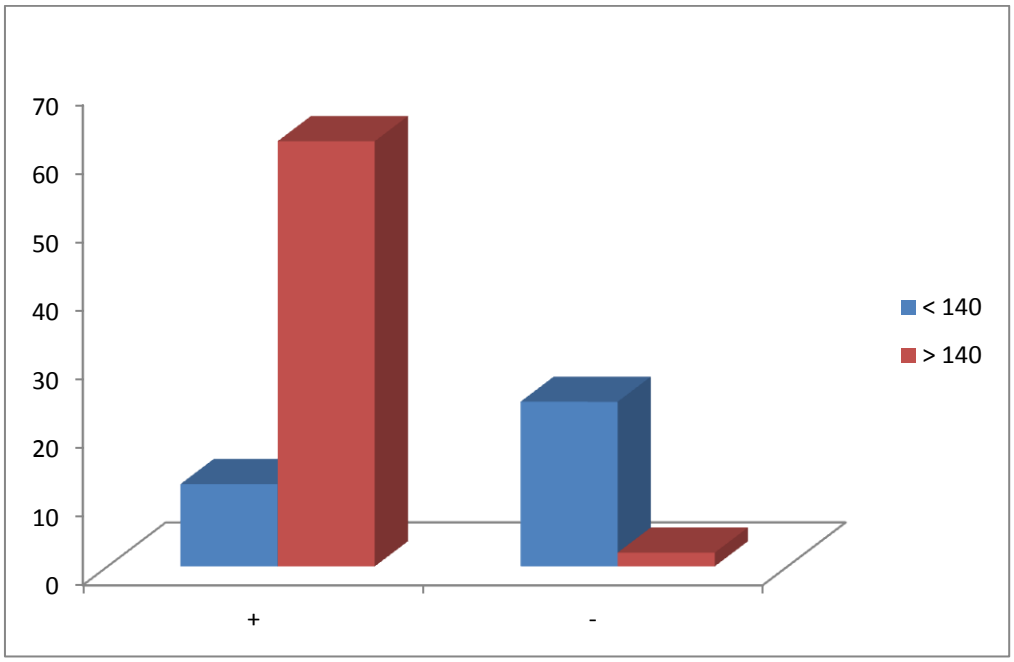

45
40
35
30
25
20
15
10
5
0
1
2
3
4
5
Series2
Series1

Table. 5.

MSBP	MA+	MA-	P VALUE	
< 140	12	24	3.56582E-12	S
> 140	62	2	3.56581E-12	S
	74	26		

Graph. 4.



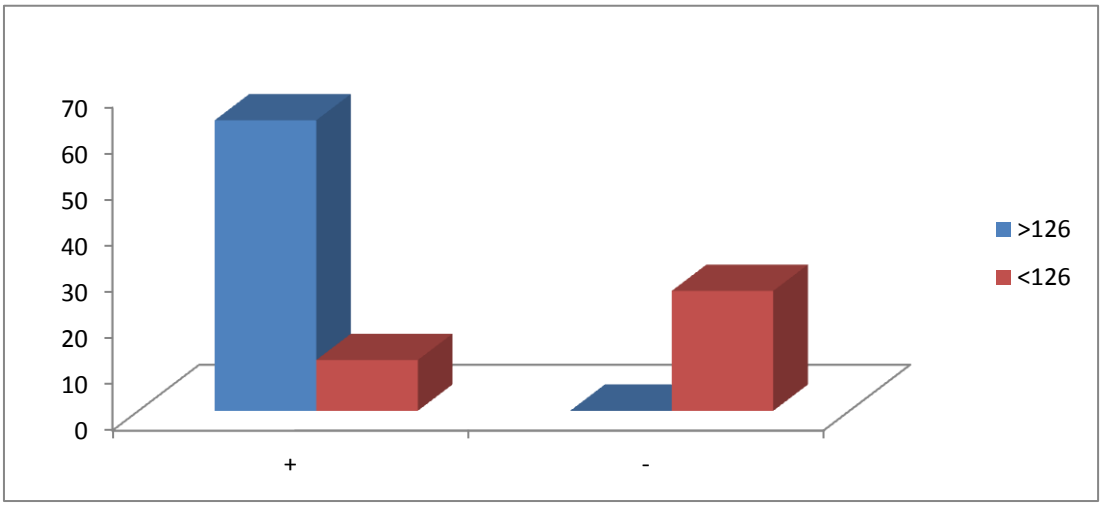
mean		MA +	MA -
	MSBP	144.2703	133.1538462

Subjects with MA are having high mean systolic blood pressure as compare to MA negative HIV person, which is matching with the results, a study done by Szczech LA et al MA associated with higher systolic blood pressure in HIV patients.

Table. 6.

			Z - TEST	
GFBS	MA+	MA-	p	
>126	63	0	0.0000	S
<126	11	26	1.03694E-14	S
	74	26		

Graph. 5.

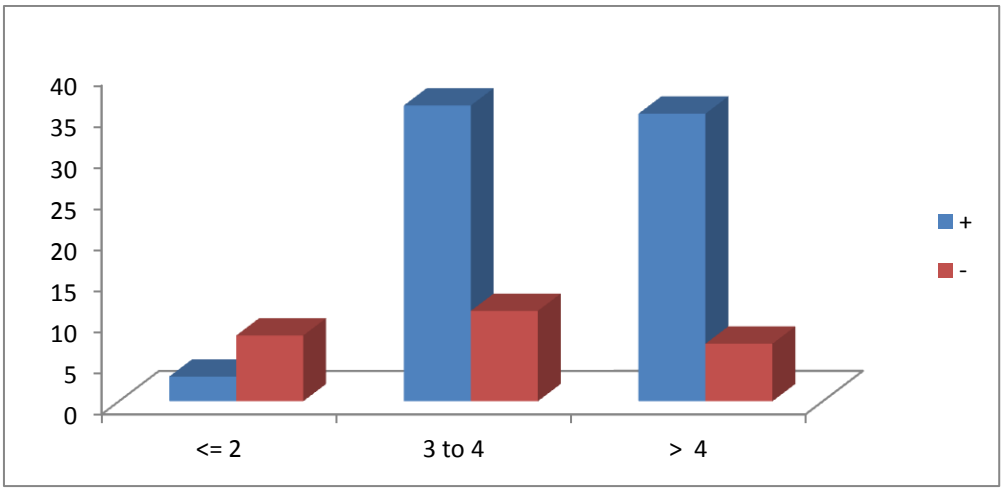


Subject with MA is having high fasting blood sugar as compare to MA negative patients which is matched with the study done by Szczech LA et al in 2002.

Table. 7.

No of Hospital Admission	MA+	MA-		
<= 2	3	8	0.000180286	S
3 to 4	36	11	0.5773	NS
> 4	35	7	0.070188343	S
	74	26		

Graph. 6.



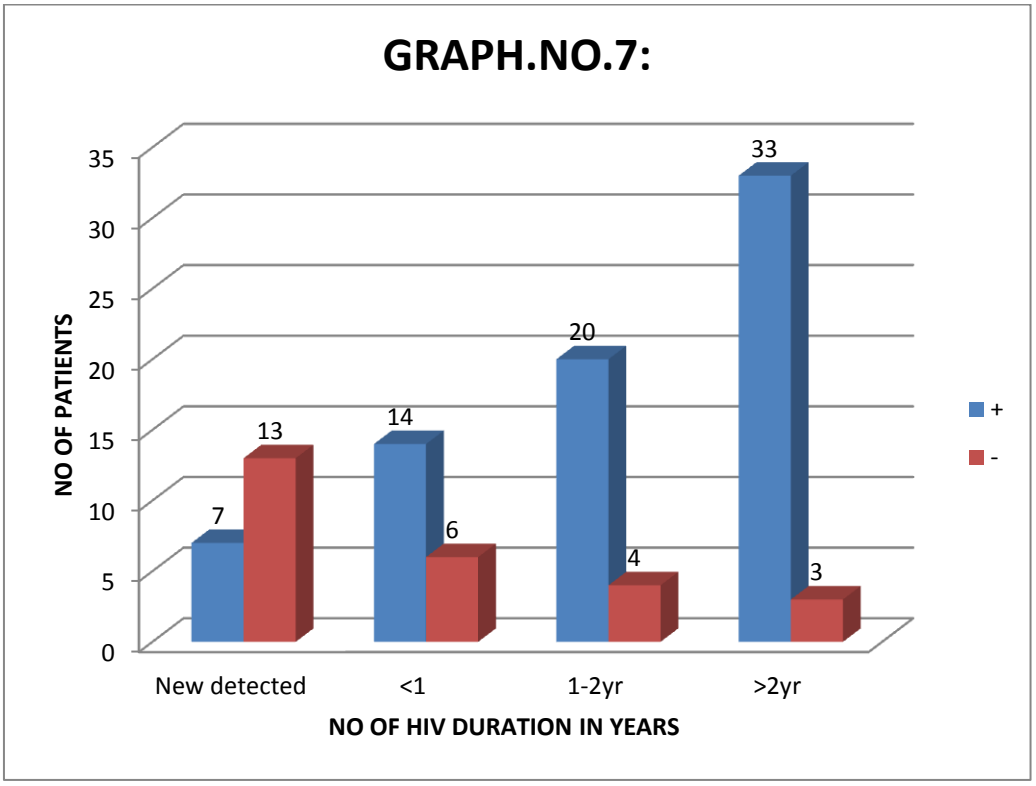
mean		MA +	MA -
	NO. HA	4.324324	3.346153846

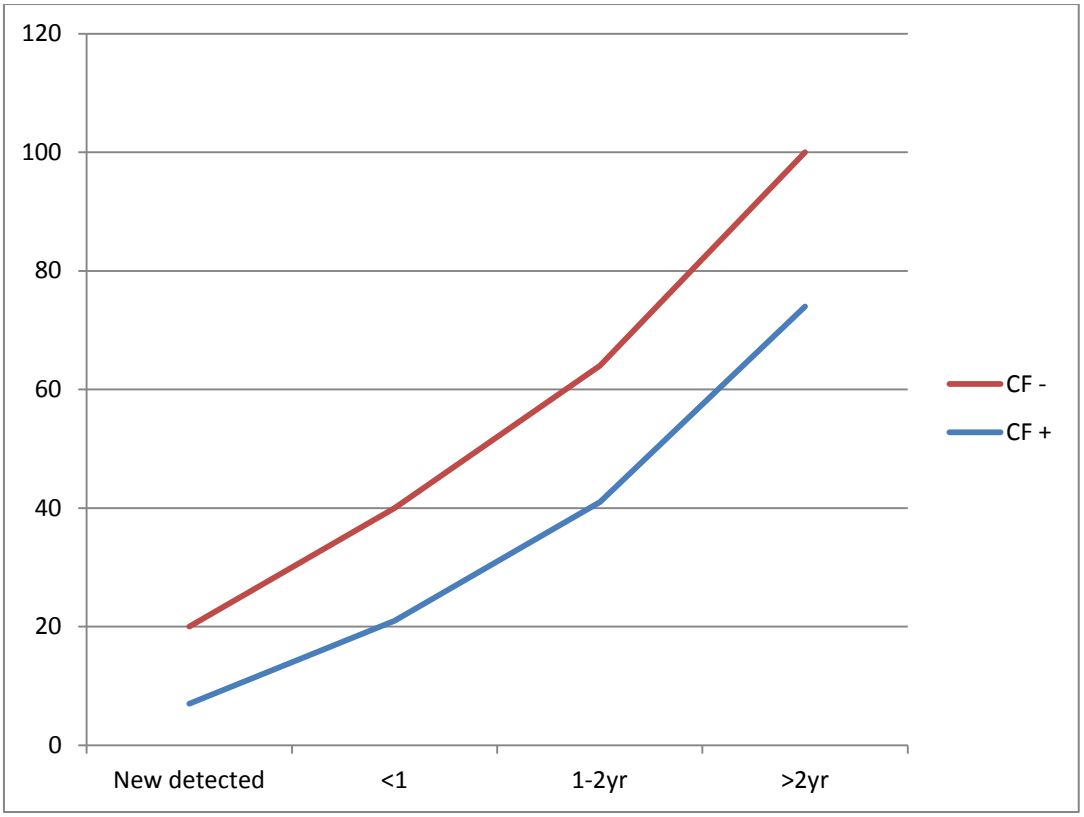
Results suggesting no of hospital stay in more in patient with MA positive than MA negative, which is matched with the study done by Gardner LI, Klein RS, Szczech LA, Hoover DR, et al showed MA associated with increase the risk of hospitalization compare to MA negative patients.

Table. 8.

DURATION	+	-	CF +	CF -		DOF	3
New detected	7	13	7	13		CHI SQUARE	22.90367
<1	14	6	21	19		p-Value	4.23E-05
1-2yr	20	4	41	23		Alpha	0.05
>2yr	33	3	74	26		Result	Reject
TOTAL	74	26					

Graph. 7.



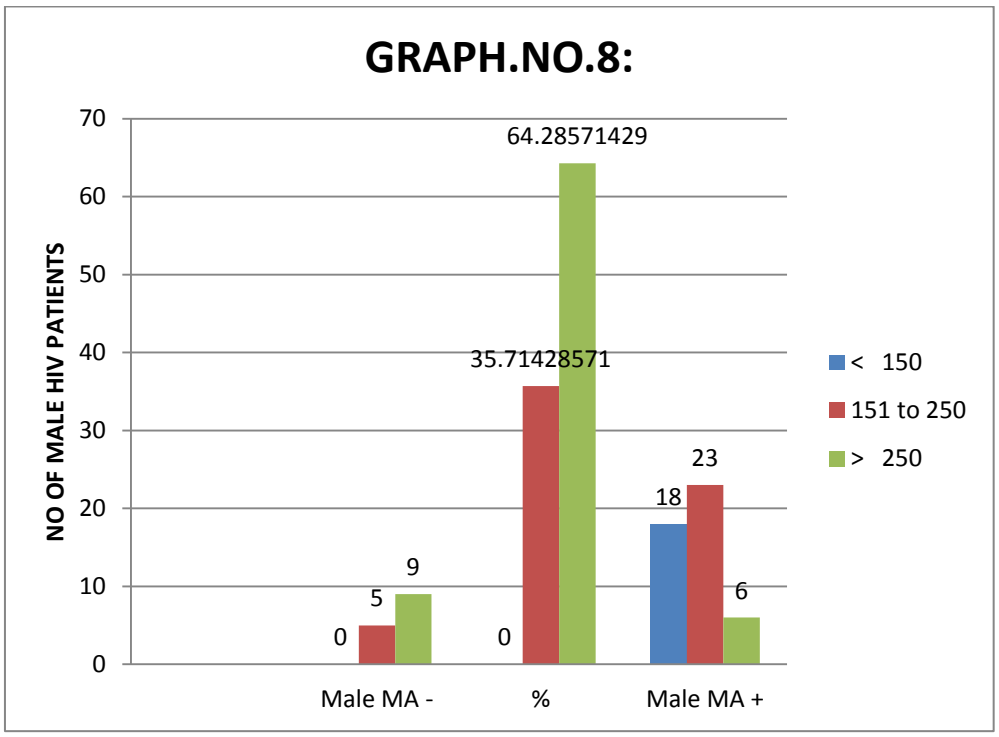


Suggesting presence of MA associated with duration of HIV also showing presence of MA increases with HIV duration.

Table. 9.

CD4 COUNTS	Male MA -	%	Male MA +	%	CF	CF
< 150	0	0	18	38.29787	0	18
151 to 250	5	35.71429	23	48.93617	5	41
> 250	9	64.28571	6	12.76596	14	47
TOTAL	14	100	47	100		

Graph. 8.]



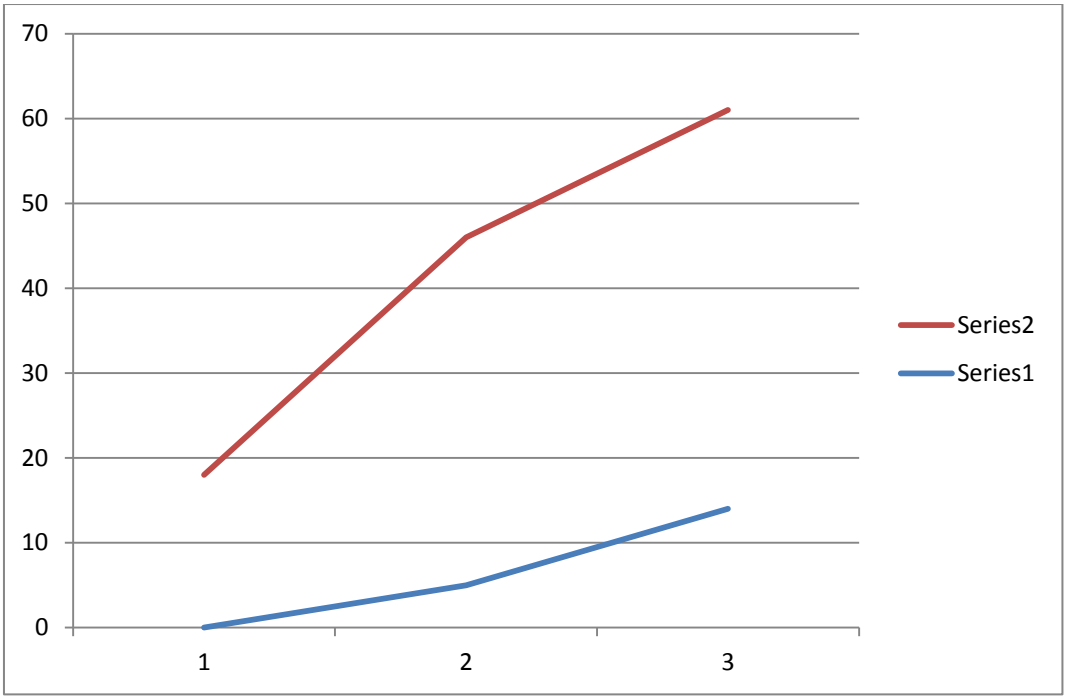
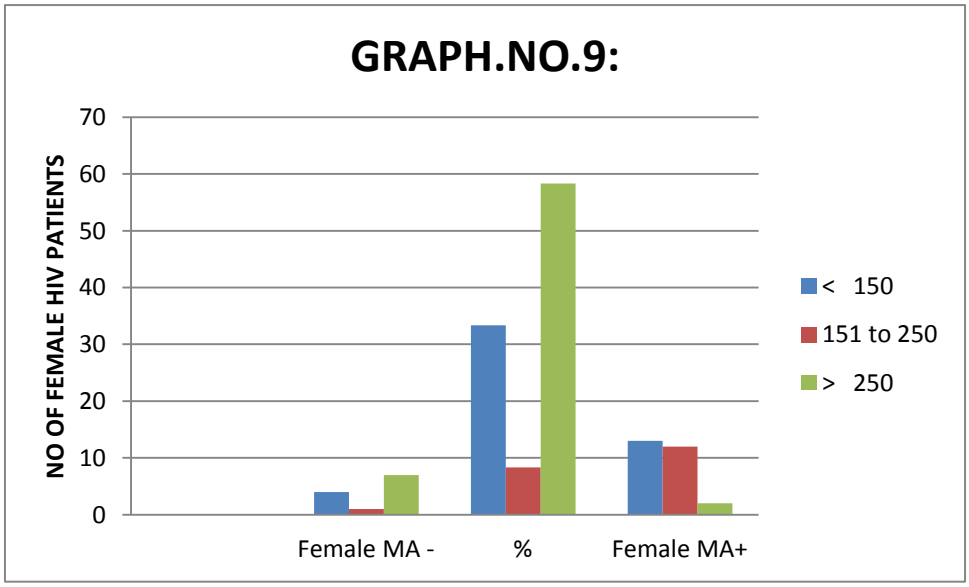
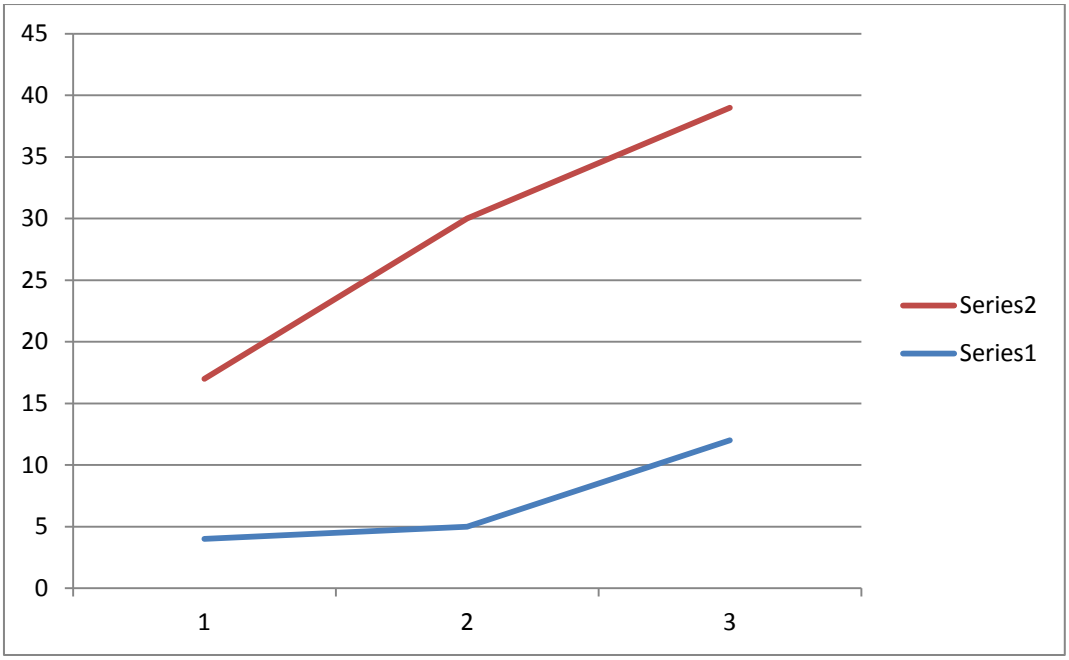

70
60
50
40
30
20
10
0
1
2
3
Series2
Series1

Table. 10.

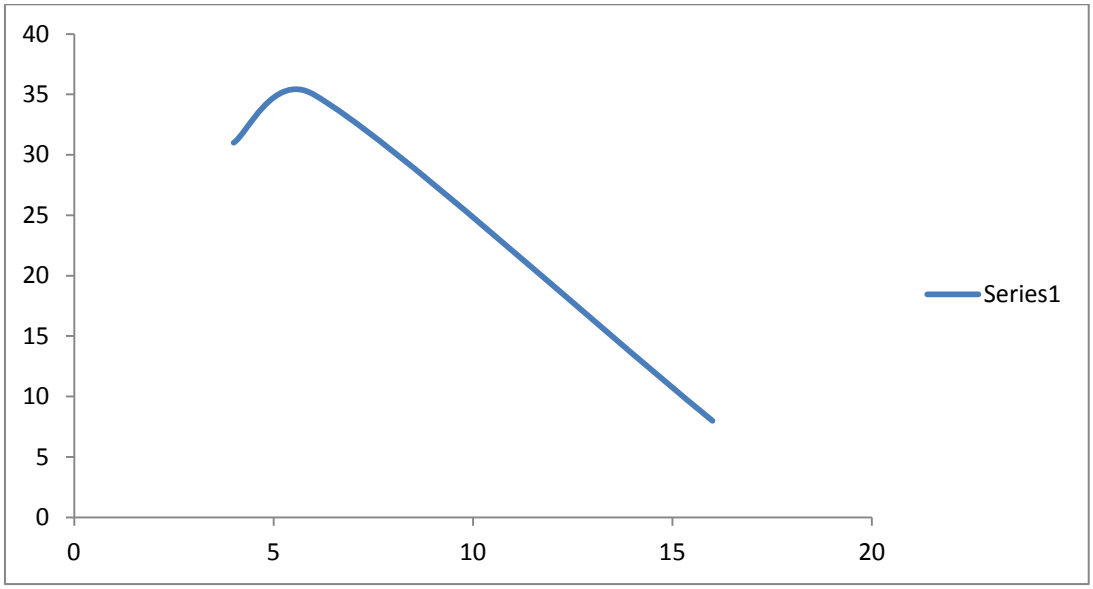
CD_4 COUNTS	Female MA -	%	Female MA+	%	CF	CF
< 150	4	33.33333	13	48.14815	4	13
151 to 250	1	8.333333	12	44.44444	5	25
> 250	7	58.33333	2	7.407407	12	27
TOTAL	12	100	27	100		

Graph. 9.





Graph. 10.



Above results are showing increasing the risk of MA with lower CD4 count, higher CD4 count is associated with less chances of MA and risk factors of MA include lower CD4 count which is matched the study done by Szczech LA, Gange SJ et al in 2002.

DISCUSSION

This analysis demonstrated that HIV infection is a strong risk factor for presence of microalbuminuria, independent of other risk factors for presence of rebel disease like diabetes, hypertension and urinary tract infection.

Among HIV infected individuals risk factors for microalbuminuria included traditional HIV specific markers such as CD4 count. The association of HIV infection with albuminuria and proteinuria was reported in an earlier era of HIV epidemic in USA with a prevalence of between 19% and 34%.

Incidence of microalbuminuria is 20.1% among HIV in this study out of 100 HIV patients come 73 patients were found to be having microalbuminuria (30 mgldL out of 61 male, 47 (70%) were found to be having microalbuminuria and out of 39 female 27 (69%) were found to be having microalbuminuria though the prevalence microalbuminuria is found to be high in males, there is no statistical significant difference in risk of microalbuminuria between the two sex groups (p = 0.768). we found out that there is statistically significant difference between microalbuminuria and duration of HIV (P value – 4.23E-os), Longer the duration of HIV more possibility of microalbuminuria in urine. Also there is a statistically significant difference between microalbuminuria and CD4 count. Microalbuminuria is positive in 31 (41.8) patients out of 74, whose CD4 count is found to be <150 cells per cubic mm.

Study showing patients of microalbuminuria positive 62 patients (83.3%) are showing high systolic blood pressure (>140 mmHg) which is statistically significant (p= 3.566E), showing high mean systolic blood pressure (in microalbuminuria positive 145.33mmHg, microalbuminuria negative 133.2mmHg) as compare to microalbuminuria negative patients.

Our study is showing patients with microalbuminuria positive ,out of that 63 (84.2%) patients showing higher fasting blood sugar level. And there is statistically significant difference (P = 1.037E-14) of fasting blood sugar level in microalbuminuria positive HIV patients.

Our study is showing that patient's with microalbuminuria positive HIV patients have a higher number of hospital admissions as compared to microalbuminuria negative HIV patients which is statistically significant (mean no of hospital admission = 4.324 in microalbuminuria positive and 3.346 in microalbuminuria negative patients).

When our study parameters are compared to another study done by Szczech et al, found microalbuminuria is associated with duration of HIV infection, as well as lower CD4 count and microalbuminuria patients showed higher blood sugar level, and higher mean systolic blood pressure which is strongly associated with traditional renal and cardiovascular risk.

CONCLUSION

This study is conducted at BLDE University's Shri. B. M. Patil medical college hospital and research centre, Bijapur. This present study included 100 in patients of HIV infection. In the studied group 61% patients were male and 39% patients were female. We found significant association between microalbuminuria and duration of HIV infection (P valve = 4.23E-os).

Longer the duration of HIV more possibility of microalbuminuria in urine. Also there is a significant association between microalbuminuria and CD4 count. Patient's with microalbuminuria positive in 31 (41.8%) patients out of 74 whose CD4 count is found to be < 150 cell/mm^3 (P = 0.013) which is highly significant. Also found patient of microalbuminuria showing high systolic blood pressure (P = 3.566E) and higher fasting sugar level (P = 1.037E-14). Thus higher prevalence of microalbuminuria among the HIV infected could be at increased risk of both kidney and cardiovascular diseases in the future.

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PROFARMA

Name:	CASE NO:
Age:	IP NO:
Sex:	DOA:
Religion:	DOD:
Occupation:	DOD:
Residence:	

Presenting complaints with duration:

History of presenting complaints:

Past History:

History of hypertension

History of diabetes mellitus

Personal History:

Diet/appetite

Sleep

Bladder and bowel habits:

Smoking/Tobacco chewing/Snuff inhalation

Duration

Number of cigarettes/beedis pack year smoked

Amount of tobacco chewed/snuff inhaled

Alcohol

Duration Quantity/Frequency

Type

Family History:

History of Suggestive of Ischemic Heart Disease/hypertension diabetis mellitus

Treatment History:

General Physical Examination

Pallor: present/absent

Icterus: present/absent

Clubbing: present/absent

Generalized Lymphadenopathy: present/absent

Built: poor/middle/well

Nourishment: poor/middle/well

Vitals

PR:

BP:

RR:

Temp:

SYSTEMIC EXAMINATION

- Respiratory System

- Cardiovascular System

- Central Nervous System

- Per abdomen

INVESTIGATIONS

HAEMATOLOGY

Haemoglobin	Gm%
Total WBC counts	Cells.mm^3
Differentail counts	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	%
Basophils	%
ESR	mm after 1 hour

BIOCHEMISTRY

Random blood sugar	
Blood Urea	
Serum creatinine	
Urine for microalbumin	

URINE EXAMINATION

Albumin	
Sugar	
Microscopy	

CD4 Count

Final Diagonosis

ANNEXURES

B. L. D. E. U's

SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL &

RESEARCH CENTRE, BIJAPUR

RESEARCH INFORMED CONSENT FORM

TITLE OF THE PROJECT:

"STUDY OF MICROALBUMINURIA IN HIV PATIENTS"

GUIDE : DR. L.S.PATIL

INVESTIGATOR : DR. MANISH PATEL

PURPOSE OF RESEARCH:

I have been informed that the purpose of this study is to study the microalbuminuria in HIV patients.

PROCEDURE:

I understand that I will undergo detailed history and clinical examination, laboratory investigations.

RISKS AND DISCOMFORTS:

I understand that there is no risk involved and I may experience mild pain during the above-mentioned procedures.

BENEFITS:

I understand that my participation in this study will help to understand the importance of studying microalbuminuria in HIV patients & will provide a rationale for early management.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record & will be subjected to confidentiality and privacy regulations of hospital. If the data is used for publications, the identity of the patient will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw for study at any time.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me during the study I will get medical treatment but no further compensations.

(Signature of Guardian) **(Signature of Patient)**

Master chart Key words

ACR	Albumin creatinine Ratio
MSBP	Mean systolic blood pressure
GFBS	Fasting blood sugar
NOHO	Number of Hospital Admission

MASTER CHART

SNO	NAME	AGE	SEX	OCCUPATION	CHIEF COMPLAINT						HIV DURATION				PERSONAL HISTORY				MICROALBUMI		CD4 COUNT	ACR	MSBP	GFBS	NOOHS
					fever	loose stool	cough	sputum	altered sensor	other	New detected	<1	1-2yr	>2yr	Smoker	Tobacco chewar	alcoholic	drug abuser	prsent	absent					
1	RAVATAPPA	29	M	FARMER	+		+							+					+		145	>30	150	>126	4
2	MALLAYA	22	M	DRIVER	+						+				+		+		-		230	<30	132	<126	3
3	PARVATI	28	F	HW		+							+						+		185	>30	148	>126	3
4	KAMALA	27	F	HW			+							+					+		132	>30	152	>126	5
5	VISHNATH	29	M	FARMER		+						+							-		189	<30	142	<126	2
6	MALLANINR	31	F	HW	+		+						+						+		212	<30	146	>126	3
7	BALLUVAPPA	43	M	FARMER	+		+	+				+			+		+		+		242	<30	134	>126	2
8	GANGUBAI	31	F	HW	+									+					+		122	>30	152	<126	5
9	MALLIKARJUN	31	M	DRIVER		+						+							-		192	<30	136	<126	3
10	SEEMA	22	F	HW			+	+					+						+		185	>30	152	>126	4
11	SUBESH	41	M	FARMER		+								+		+			+		132	>30	150	>126	4
12	SAKINA	19	F	HW	+							+							+		212	>30	142	>126	3
13	RAJU	23	M	FARMER		+							+						+		190	>30	144	>126	4
14	PARUBAI	32	F	HW			+	+						+					-		142	<30	132	<126	5
15	RAJASAB	33	M	DRIVER			+	+				+			+				+		215	<30	142	>126	3
16	NAGAMMA	34	F	HW	+									+					+		148	>30	148	>126	5
17	SHARNNAPA	24	M	CLERCK		+						+				+			-		220	<30	130	<126	2
18	VINOD	18	M	FARMER	+							+							+		198	>30	146	>126	5
19	RUKMANIBAI	43	F	HW	+								+						+		134	>30	150	>126	4
20	INDUBAI	32	F	HW		+					+								-		225	<30	126	<126	2
21	SANKERAAPA	34	M	FARMER	+									+					+		135	>30	148	>126	5
22	SHOBHA	43	F	HW		+						+							-		180	>30	142	<126	4
23	ASHOK	19	M	LABOUR	+	+					+								+		224	<30	144	<126	3
24	JYOTI	9	F	LABOUR	+		+							+					-		132	>30	132	<126	3
25	VISHAWNATH	35	M	FARMER			+					+							+		210	<30	132	>126	3
26	NEELAMA	41	F	HW	+									+					+		140	>30	148	>126	5
27	MAHALING	29	M	FARMER		+						+							-		155	<30	124	<126	5
28	GIRIMALLA	32	F	HW			+							+					+		170	>30	146	>126	4
29	IRRAHHA	26	M	DRIVER	+						+								+		228	<30	132	>126	3
30	BHARTI	19	F	STUDENT	+		+				+								-		192	>30	130	<126	2
31	MAHESH	23	M	DRIVER	+									+			+		+		170	>30	142	>126	5
32	PREMA	29	F	HW		+			+				+						+		164	>30	144	>126	4
33	AMGARANDA	44	M	FARMER	+							+					+		+		190	>30	140	>126	4
34	SUDHA	18	F	HW			+				+				+				-		140	<30	136	<126	3
35	SACHIN	21	M	LABOUR	+	+								+		+			+		160	>30	144	>126	4
36	KARITA	31	F	HW	+								+						+		220	<30	122	>126	4

37	VIJAY	22	M	LABOUR		+								+	+				+		162	>30	146	>126	5
38	LAKHSMI	24	F	HW	+								+						+		212	<30	124	>126	3
39	RAMGUDA	36	M	FARMER	+							+			+				+		235	<30	122	>126	4
40	SAHEBGUDA	28	M	DRIVER			+							+	+				+		170	>30	144	>126	5
41	SHANTI	19	F	HW		+					+								-		220	<30	132	<126	2
42	ASHOK PATIL	29	M	LABOUR	+							+					+		+		170	>30	144	>126	6
43	AJJU BAI	31	F	HW			+							+					+		140	>30	142	>126	5
44	ANNAD	28	M	FARMER	+							+				+			+		190	>30	142	>126	4
45	SAVUTA	27	F	HW		+							+						+		210	>30	144	>126	3
46	SUSMA	23	F	HW	+						+								-		212	<30	132	<126	2
47	RENUK RAJ	33	M	DRIVER	+									+		+			+		134	>30	150	<126	6
48	SHASIKALA	23	F	LABOUR			+	+					+		+				+		225	>30	148	<126	3
49	IBRAHIM	24	M	LABOUR		+						+			+				+		192	>30	146	>126	3
50	GANGUBAI	42	F	HW	+		+							+					+		144	>30	150	>126	5
51	MALKANGUDA	26	M	CLERCK	+		+				+					+			+		240	>30	142	>126	4
52	REKHABAI	27	F	HW		+	+						+						+		195	>30	144	<126	2
53	SHRISAIL	28	M	FARMER	+		+	+			+					+			-		245	<30	132	<126	2
54	RUPA	22	F	HW		+								+		+	+		+		137	>30	146	>126	6
55	NIJLINGPPA	34	M	FARMER	+		+						+						+		131	>30	148	>126	5
56	APPU	35	M	FARMER		+								+		+			+		142	>30	146	>126	6
57	CHANDAN	23	M	FARMER		+								+					+		129	>30	152	>126	6
58	JAYA	34	F	HW	+								+						-		123	<30	134	<126	5
59	ARJUN	26	M	DRIVER			+	+						+			+		+		210	>30	138	>126	3
60	APPASAB	36	M	LABOUR	+		+					+				0			+		217	>30	148	>126	3
61	UCCHAPAA	29	M	DRIVER	+									+	+		+		+		136	>30	152	>126	5
62	SANTOSH	37	M	FARMER		+							+				+		+		127	>30	152	>126	6
63	RAJANGUDA	31	M	LABOUR	+								+			+			-		212	<30	134	<126	4
64	DIVYA	29	F	HW			+	+	+		+								+		230	>30	134	>126	3
65	SHRIKANT	22	M	LABOUR		+	+				+					+			+		237	>30	132	>126	3
66	CHIRANJIVI	23	M	LABOUR	+		+							+	+				+		128	>30	146	>126	4
67	RANBHA	24	F	HW	+						+						+		-		220	<30	138	<126	3
68	FAIZAL	29	M	FARMER			+	+					+		+				+		180	>30	144	>126	5
69	FAUZIA	26	F	LABOUR	+									+		+			+		123	>30	148	>126	5
70	PARANAKAR	31	M	FARMER	+		+					+			+				+		189	>30	146	>126	5
71	SAVITRI	25	F	HW			+	+			+								+		227	>30	142	>126	6
72	SIDDU	26	M	DRIVER	+				+					+	+				+		133	>30	148	<126	6
73	SIDDAPA	9	M	STUDENT	+		+	+			+								-		247	<30	134	<126	5
74	JAYSREE	27	F	HW		+	+					+							+		214	>30	138	>126	3
75	SHIVANAD	36	M	FARMER	+	+							+		+				+		223	<30	136	>126	3
76	ROHIT	26	M	FARMER				+						+	+				+		147	>30	148	>126	5
77	VIJAY	23	M	LABOUR		+			+			+				+			+		197	>30	146	>126	5

78	JAYAPRADA	41	F	HW	+		+	+					+						-		225	<30	138	<126	3
79	GIRIMALLA	26	M	DRIVER		+							+			+			+		198	>30	142	<126	5
80	GOVIND	38	M	FARMER			+							+			+		+		125	>30	144	<126	6
81	SIDDHARTHA	29	M	LABOUR	+	+					+				+				+		239	>30	142	<126	6
82	VANDNA	29	F	HW	+		+	+				+							-		242	<30	134	<126	3
83	BHRAT	28	M	CLERCK		+								+	+				+		129	>30	152	<126	6
84	KISAN PATIL	19	M	LABOUR	+	+							+				+		-		217	<30	132	<126	5
85	ARUNABAI	26	F	HW			+						+						+		132	>30	148	<126	5
86	VINAYAK	32	M	FARMER		+	+				+						+		-		225	<30	132	<126	5
87	HARSHA	29	M	DRIVER	+									+	+				+		131	>30	144	>126	6
88	AJJU BAI PATIL	41	F	HW		+							+						+		144	>30	146	>126	6
89	M.V REDDY	22	F	LABOUR			+	+	+				+		+				+		127	>30	146	>126	5
90	SIVANADDA..	43	M	FARMER	+									+			+		+		145	>30	142	>126	4
91	MALIKARJUN R.	42	M	FARMER	+		+				+					+			-		241	<30	132	<126	2
92	CHETNA .Y	28	F	HW		+								+					+		129	>30	148	>126	6
93	RATNES	27	M	LABOUR	+		+				+						+		-		239	<30	132	<126	4
94	AKBAR	27	M	FARMER		+							+						+		143	>30	148	>126	3
95	N.NIJALLPAA	32	M	DRIVER				+	+					+		+			+		136	>30	150	>126	4
96	SHANKERAPPA.S	26	M	FARMER	+	+	+				+				+				-		241	<30	132	<126	5
97	TOSIF	29	M	LABOUR		+								+		+			+		124	>30	150	>126	2
98	MALLPA .B	36	M	FARMER	+		+							+		+			-		129	<30	132	<126	3
99	CHANDU	28	M	FARMER		+								+		+			+		135	>30	148	>126	4
100	KAVI	22	M	LABOUR	+				+					+	+		+		+		141	>30	150	>126	3