ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume IX Issue VIII August 2024

Evaluation of Some Renal Biomakers in Patients with Benign Prostatic Hyperplasia/Prostate Cancer Attending Nnamdi Azikiwe University Teaching Hospital Nnewi

Anthonia Chinenye Ogueze, Nancy Amara Mbachu, Augustine Chinedu Ihim, Ejike Christian Onah, Nkiruka Chinenye Nwoka, Stellamaris Chinenye Okeke, Juliet Chinonso Akaeme, Chiazoka Frances Nduka

Department of Clinical Chemistry, Faculty of Medical Laboratory Science, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria.

DOI: https://doi.org/10.51584/IJRIAS.2024.908036

Received: 24 July 2024; Accepted: 02 August 2024; Published: 10 September 2024

ABSTRACT

Benign prostatic hyperplasia (BPH) and prostate cancer (PCa) are among the urological conditions that affect aging men. Patients with this pathology could develop renal impairment. Renal biomarkers like beta-2-microglobulin (BMG), urea, urine creatinine, microalbumin (MALB), and albumin to creatinine ratio (ACR) were assessed with total (tPSA) and free prostate specific antigen (fPSA), systolic blood pressure (SBP), diastolic blood pressure (DBP), height, weight and BMI. This cross sectional study recruited 120 men using convenient sampling technique which comprised 40 BPH, 40 PCa and 40 control attending Urology Clinic of NAUTH Nnewi, Anambra State. Five (5) milliliters of blood/ urine samples were collected from the patients and the necessary data were obtained from clinical records of the patients. The weight (kg) and height (m) were measured using standard beam balance scale and a stadiometer respectively and the BMI calculated. Blood pressure was measured using sphygmomanometer and stethoscope. PSA (ng/ml) was estimated by Enzyme immunoassay technique, BMG (mg/l) and MALB (mg/l) by immunoturbidimetric method, urea and creatinine were determined spectrophotometrically using modified Urease-Berthelot method and Jaffe slot alkaline picrate method respectively. Data analysis was conducted using SPSS version 21.0. The results were presented as median. Kruskal Wallis was used to determine significant differences between the mean values. $P<0.05$ was considered to be statistically significant. The results showed a significantly higher median values of tPSA, fPSA BMG and MALB in patients with BPH /PCa when compared with the control. MALB had a strong correlation with ACR in all the groups. Despite the significant increase in BMG and MALB in this study, routine indices of renal function remained normal. The increase in the sensitive markers in patients with BPH/PCa is an indication of early renal impairment.

Keywords: Benign Prostatic Hyperplasia, Prostate Cancer, Acute Kidney Injury, Prostate Specific Antigen, Beta-2-microglobulin, microalbumin

INTRODUCTION

Benign prostatic hyperplasia (BPH) or benign prostate enlargement (BPE) and prostate cancer (PCa) are two common urological conditions in western society. BPH is a noncancerous increase in size of the prostate gland while prostate cancer is malignant tumor of the prostate gland. The symptoms are similar, ranging from mild to severe as in the case of prostate cancer [1]. The symptoms include frequent urination, trouble starting to urinate, weak stream urine, urinary retention, loss of bladder control or inability to urinate, hematospermia, haematouria, erectile dysfunction. Metastatic symptoms of prostate cancer include weight loss, loss of appetite, lower extremity pain, bone pain with or without pathologic fracture, edema, uraemic symptoms. Complications can include urinary tract infections, bladder stones, and chronic kidney problems [2]. Globally, the odds of developing PCa are 1 in 18 and the odds range from 1 in 52 for low sociodemographic index (SDI) countries to 1 in 9 in high SDI countries [3]. An estimated 14,334 deaths in the year 2020 were as a result of prostate cancer [4]. Prostate cancer represents the second most common cancer in men worldwide and accounting for 4% of cancer –associated death [1].

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume IX Issue VIII August 2024

In Africa, prostate cancer is the most common cancer among men [5]. Nigeria had the highest number of deaths from prostate cancer (among men 0-84 years) with 8,382 (58.5%) deaths out of 14,334 [4]. Benign prostate hyperplasia (BPH) accounts for 78.3% of all prostate-related diagnoses and increases from 20% to 90% in men who are 40–80 years of age, whereas prostatic adenocarcinoma accounts for 92.4%–96.7% of all malignant tumors in the prostate [6], [7]. The underlying mechanism for BPH involves the prostate pressing on the urethra thereby making it difficult to pass urine out of the bladder. Diagnosis is typically based on symptoms and examination after ruling out other possible causes [2]. The current screening method for benign prostate hyperplasia and prostate cancer relies on a combination of Prostate specific antigen (PSA) assay and a Digital Rectal Examination (DRE) while biopsy is done to confirm if there is suspicion of cancer.

Kidney injury starts by inducing biological and molecular changes that, over time, evolve into cellular damage [8]. Therefore, the discovery and validation of a reliable biomarker for AKI prediction and early diagnosis seems provident, as it would allow early diagnosis and inform on the progression of AKI, thereby improving treatment strategies [9]. Benign prostatic hyperplasia (BPH) and Prostrate Cancer (PCa) are among the risk factors of kidney disease. The enlargement of the prostate can produce voiding symptoms, which can lead to pathological changes in the urinary bladder and the kidney. Early diagnosis prevents progression to CKD and other complications [9].

Previous studies in NAUTH have not been able to evaluate the renal status in these two pathological conditions of the prostate and have not assessed the levels of BMG and MALB in both conditions. In the work done by [10] on the assessment of serum prostate specific antigen and some renal indices and uric acid levels in subjects with benign prostatic hyperplasia at Lokoja, Nigeria, only urea, creatinine, total protein and uric acid were the renal indices that were measured. They did not include sensitive biomarkers that can detect early renal tubular or glomerular damage. Therefore, the levels of BMG, MALB, urea and creatinine in patients with BPH and PCa were measured in this study and their ratios and correlations were determined. This study intends to discover early kidney disease in patients with BPH and PCa thereby reducing renal disease complications in these patients. Hence this study aimed at evaluating beta-2-microglobulin (BMG), urea, urine creatinine (uCr) and microalbumin (MALB) as well as tPSA and fPSA in BPH and PCa.

MATERIALS AND METHODS

A total of 120 subjects were recruited for this cross-sectional study which comprised 40 BPH, 40 PCa and 40 control subjects. Patients with benign prostatic hyperplasia/prostate cancer and apparently healthy age matched subjects as control were recruited for the study using convenient sampling technique. Patients with known history of diabetes, renal diseases and patients on drugs were excluded from the study.

Necessary data of the patients were obtained from their clinical records. Five (5) milliliters of blood/urine samples were collected from patients with benign prostatic hyperplasia (BPH) and prostate cancer (PCa) attending Urology clinic of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State, Nigeria and dispensed in plain containers and sterile universal container respectively. The blood samples were centrifuged at 4000rpm for 10 minutes after clotting to obtain the serum for the determination of prostate specific antigen, beta-2-microglobulin and urea while the urine samples were for the determination of urinary creatinine and microalbumin. Samples were stored at -20°C prior to analysis.

Total PSA and free PSA were determined by sandwich Enzyme immunoassay technique as described by [11]. Determination of β-2-microglobulin (BMG) was by latex immunoturbidimetric method as described by [12]. Determination of microalbumin was by immunoturbidimetrc method. Urea and creatinine were determined by modified Urease–Berthelot method and Jaffe-Slot alkaline picrate method respectively as described by [13]. Body mass index (BMI) was calculated as weight in kilogram divided by height squared in meters. BMI (Kg/m^2) = Weight (Kg)/Height (m^2).

Ethical approval to carry out this study was sought and obtained from the Ethics Committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi. Written informed consent was obtained from all participants before recruiting them into the study.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume IX Issue VIII August 2024

Data analysis was conducted using SPSS version 21.0 (IBMInc, Chicago, IL). Values were assessed for normality by checking for skewness. The results were presented as median. Kruskal Wallis was used to determine significant differences between the mean values. P<0.05 was considered to be statistically significant. Relationship or strength of the association between parameters was assessed using Pearson's correlation.

RESULTS

A significant difference was observed in the ages of the test groups when compared with the control group (P = 0.013). There were no significant differences in the median ages of patients with BPH when compared with control subjects (P=0.138). Similarly, no significant difference was observed in the median ages of patients with PCa when compared with control subjects (P=0.090). The median age value was significantly higher in PCa (75.00) when compared with BPH (68.00) (P=0.005). There was significantly higher median level of SBP in BPH (130.00) and PCa (140.00) when compared with the control subjects (122.50)(P<0.001). The DBP remained the same throughout the group. There was no significant difference in the median values of weight in BPH (69.500) and PCa (76.000) when compared with the control subjects (73.500)(P=0.093).There was no significant difference in the median value of height in patients with BPH (1.750) and PCa (1.790) when compared with the control subjects (1.775)(P=0.282). Also there was no significant difference in BMI of patients with BPH (23.441) and PCa (24.100) when compared with the control subjects (23.790)(P=0.316) (Table 1).

Table 1: Median values of Age, weight, height, BMI, SBP, and DBP in BPH, PCa and control group.

Group	Age (years)	Weight (Kg)	Height (m)	BMI (kg/m^2)	SBP (mmHg)	DBP (mmHg)
BPH (A)	68.00	69.500	1.750	23.441	130.00	80.00
PCa (B)	75.00	76.000	1.790	24.100	140.00	80.00
Control (C)	70.00	73.500	1.775	23.790	122.50	80.00
Kruskal Wallis	8.653	4.748	2.528	2.307	16.676	8.551
p-value	0.013*	0.093	0.282	0.316	<0.001**	0.014*
A vs B	0.005*	0.037*	0.152	0.118	0.271	0.139
A vs C	0.138	0.153	0.232	0.603	0.005*	0.005*
B vs C	0.090	0.405	0.557	0.386	<0.001**	0.106

Keys: **p<0.001 = significant, *p<0.05 = significant, p>0.05 = not significant, BMI = body mass index, SBP = systolic blood pressure, DBP = Diastolic blood pressure, PCa = prostate cancer, BPH = benign prostatic hyperplasia

There was a significantly higher median level of tPSA in patients with BPH (10.349) and PCa (6.286) when compared with the control subjects (2.487) (P<0.001). Similarly, the median fPSA level in BPH (0.154) and PCa (0.163) was significantly higher when compared with the control subject (0.147)(P = 0.039). There was significantly higher median level of BMG in BPH (1.685) and PCa (1.604) when compared with the control group (1.448)(p<0.001). There was significantly higher median level of MALB in BPH (35.455) and PCa

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume IX Issue VIII August 2024

(33.360) when compared with the control group (21.308)(P = 0.003). There was no significant difference in the median urea level in BPH (4.742) and PCa (5.716) when compared with the control subjects (5.123)(P = 0.145). Similarly, there was no significant difference in the median urine creatinine (uCr) level in BPH (2.286) and PCa (2.193) when compared with the control subjects (2.527)(P = 0.197). Finally the median level of ACR was significantly higher in BPH (14.453) and PCa (13.519) when compared with the control subjects (8.533; P<0.001) (Table 2).

Table 2: Levels of tPSA, fPSA, BMG, urine MALB, urea, urine creatinine and ACR in BPH, PCa and control group (median).

Group	tPSA (ng/ml)	fPSA (ng/ml)	BMG (mg/l)	MALB (mg/l)	Urea (mmol/l)	uCr (g/l)	ACR (mg/g)
BPH (A)	10.349	0.154	1.685	35.455	4.742	2.286	14.453
PCa (B)	6.286	0.163	1.604	33.360	5.716	2.193	13.519
Control (C)	2.487	0.147	1.448	21.308	5.123	2.527	8.533
Kruskal Wallis	24.682	6.476	28.244	11.903	3.866	3.249	15.990
P-value	<0.001**	0.039*	<0.001**	0.003*	0.145	0.197	<0.001**
A vs B	0.052	0.135	0.159	0.186	0.062	0.870	0.240
A vs C	0.032*	0.062	<0.001**	0.001*	0.279	0.107	<0.001**
B vs C	0.048*	0.045*	<0.001**	0.014*	0.340	0.121	0.005*

Keys: **P<0.001 = significant, *p<0.05 = significant, p>0.05 = not significant, tPSA = total prostate specific antigen, fPSA = free prostate specific antigen, BMG = β-2-microglobulin, MALB = microalbumin, uCr = urine creatinine, ACR = albumin to creatinine ratio, BPH = benign prostatic hyperplasia, PCa = prostate cancer

There was strong positive correlation between MALB and ACR in patients with BPH (r = 0.891, P<0.001). There was no correlation between BMG and ACR (r = 128; P = 0.431), BMG and MALB (r = -0.073, P= 0.118), tPSA and ACR (r = -0.073, P=0.652) in patients with BPH (Table 3).

Table 3: Correlation of various biochemical variables in BPH

Parameters	r-value	p-value
MALB vs ACR	0.891	<0.001**
BMG vs ACR	0.128	0.431
BMG vs MALB	0.251	0.118
tPSA vs ACR	-0.073	0.652

Keys: **p<0.001 = significant, p>0.05 = not significant, MALB = microalbumin, ACR = albubin to creatinine ratio, BMG = β-2-microglobulin, tPSA = total prostate specific antigen.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume IX Issue VIII August 2024

There was strong positive correlation between MALB and ACR (r = 0.932, P<0.001). A weak positive correlation existed between BMG and ACR (r = 0.420, P = 0.007), BMG and MALB (r = 0.321, P = 0.043) as well as tPSA and ACR (r = -0.371, p = 0.018) in patients with PCa (Table 4).

Table 4: Correlation of various biochemical variables in PCa

Parameters	r-value	p-value
MALB vs ACR	0.932	<0.001**
BMG vs ACR	0.420	0.007*
BMG vs MALB	0.321	0.043*
tPSA vs ACR	-0.371	0.018*

Keys: **p<0.001 = significant, *P<0.05 = significant, P>0.05 = not significant, MALB = microalbumin. ACR = albumin to creatinine ratio, BMG = β-2-microglobulin, tPSA = total prostate specific antigen

There was a strong positive correlation between MALB and ACR (r = 0.921, P = <0.001) in the control group. A strong negative correlation was also observed between tPSA and BMG (r= -0.842, P = 0.002) in the control group (Table 5).

Table 5: Correlation of various biochemical variables in control

Parameters	r-value	p-value
MALB vs ACR	0.921	<0.001**
BMG vs ACR	0.281	0.164
BMG vs MALB	0.311	0.122
tPSA vs ACR	-0.309	0.385
tPSA vs BMG	-0.842	0.002*

Keys: **p<0.001 = significant, *P<0.05 = significant, P>0.05 = not significant, MALB = microalbumin. ACR = albumin to creatinine ratio, BMG = β-2-microglobulin, tPSA = total prostate specific antigen

DISCUSSION

The findings of this study revealed a significant difference in the ages of the test group when compared with the control group. This is in agreement with a previous epidemiological study which reported that BPH affects 70% of men aged 60–69 years old and 80% of those ≥70 years old [14]. Although, age is a risk factor for the development of BPH and prostate cancer but other factors like family history also contributes to the development of BPH and PCa. According to [15], the greatest prevalence occurs among men ages 70 to 79 years. There was an association between BPH and increased age: decreased male hormone levels, especially testosterone, leading to a significant reduction in kidney function [16]. There was no significant increase in the weight, height and BMI of patients with benign prostatic hyperplasia and prostate cancer when compared with the control group. In contrast, studies have reported association between obesity and many cancers including PCa [17] – [19]. Obesity is associated with increased free or bioactive Insulin-Like Growth Factor (IGF-1). IGF-1 plays a portal role in stimulating cell proliferation, regulating differentiation and reducing apoptosis.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume IX Issue VIII August 2024

Tissue levels of IGF-1 appear to be critically important factor during initiation and progression of Prostate Cancer. Also the systolic and diastolic blood pressure was statistical significant in all the group. There was significant increase in the SBP of patients with BPH and PCa when compared with the control but no significant difference was observed in their diastolic blood pressure. The systolic blood pressure (SBP) is the maximum blood pressure during contraction of the ventricles. Studies have shown a positive correlation between SBP and all storage symptoms. It has been shown that bladder dysfunction may occur in the presence of endothelial dysfunction in pelvic vascular system. The mechanism is based on increased sympathetic activity especially α-1-adrenoreceptor activity. Other studies have demonstrated that there is an association between BPH and hypertension via activation of insulin-like growth factor and increased sympathetic nervous system activity [20]. [21] showed that there was a positive correlation between hypertension and lower urinary tract symptoms. On the other hand, [22] in Norway stated that among the MetS components, only high blood pressure had a significant correlation with the mortality of prostate cancer.

The study revealed a significantly higher median level of tPSA and fPSA in patients with BPH and PCa when compared with the control group. The elevated tPSA is in accordance with the study of [23] who reported that elevated serum tPSA can be detected in either benign prostatic hyperplasia or prostate cancer. Also, the elevated PSA in BPH is also in conformity with the work done by [10] who reported an elevated tPSA and fPSA in patients with BPH. The significant increase in f PSA could indicate its valuability in the prediction of prostate cancer. The free to total PSA is one of such parameters used to improve the sensitivity of cancer detection when total PSA is in the normal range (<4ng/mL) and to increase the specificity of cancer detection when total PSA is in the "gray zone" (4.1 to 10 ng/mL) [24]. In addition, it was reported that patients with a PSA level ≤ 4 ng/mL still have the risk of PCa, and the detection rate may reach up to 20% [3].

This study also revealed a significantly higher median serum beta-2-microglobulin (BMG) and urine microalbumin (MALB) in patients with benign prostate hyperplasia (BPH) and prostate cancer (PCa) when compared with the control group. The significant increase in BMG is in agreement with the finding of [25] who reported an increase in BMG in patients with acute kidney injury. Also, Increase in urinary BMG indicates tubular dysfunction, and measurement of BMG in urine is a sensitive and reliable assay for detecting tubular injury [26]. BMG has also been evaluated as a marker of tubular injury. Some population-based studies have shown that urinary BMG levels can be used to detect tubular injury due to various toxins. BMG has been used as a marker of tubular dysfunction in subjects exposed to heavy metals such as cadmium with urinary BMG levels strongly correlating with serum cadmium levels [27]. Serum BMG has been proposed as an independent marker of severity of AKI and its outcomes in children and individuals with intracerebral bleeds [28], [29]. Urine BMG has been reported to remain elevated in almost half of the patients who recover from AKI resulting from snake envenomation [30]. Urine concentration of BMG is mainly associated with the development and function of renal tubules. When there is obstruction of renal tubular re-absorption function, obviously increase in the concentration of urine BMG and tubular proteinuria occurs. The significant increase in microalbumin (MALB) in the test subjects is in line with the finding of [31] who reported a significant increase in MALB among diabetic patients. Microalbuminuria has been assumed to result from alterations in glomerular filtration secondary to changes in intra glomerular pressure and/or structural changes of the podocyte or glomerular basement membrane. Further, it is associated with renal injury in children due to variety of causes such as diabetes, hypertension, cardiovascular diseases, structural renal diseases, urinary tract infections and sickle cell disease [32] – [34]. The significant increase in MALB observed in the test group when compared with the control group is also in agreement with the study of [35] who observed that MALB and serum creatinine levels were consistently higher and positively correlated in participant with kidney disease.

The study revealed no significant differences in the median level of serum urea and urine creatinine in patients with BPH and PCa when compared with the control group. Serum urea and creatinine has been shown not to be sensitive markers in early detection of renal injury. This is in accordance with the report of [36] that serum urea and creatinine has been shown to lack high predictive value in the early detection of renal injury.

The ratio of albumin to creatinine was significantly increased in patients with BPH and PCa when compared with the control group. Albumin/protein: creatinine ratios have themselves been shown to be powerful predictors of adverse cardiovascular [37] and renal outcomes [38], [39]. In particular, ACR has been used to

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume IX Issue VIII August 2024

demonstrate an association of even low (submicroalbuminuria) levels of albuminuria with renal and cardiovascular event [40].

Of all the various biochemical parameters analyzed, MALB had a strong correlation with ACR in all the groups. [41] reported a very strong relationship between creatinine, MALB, and ACR in smokers. BMG correlated strongly with ACR, and weakly with MALB in PCa. ACR correlated weakly with tPSA in patients with PCa. Also BMG had a very strong negative correlation with tPSA in the control group. The correlation of BMG with PSA is in agreement with the findings of [42] who reported correlation of serum BMG Levels with prostate-specific antigen, Gleason score, clinical stage, tumor metastasis and therapy efficacy in prostate cancer.

CONCLUSION AND RECOMMENDATIONS

From the findings of this research, there was increase in the serum level of total PSA and free PSA in patients with prostate cancer and benign prostatic hyperplasia. There was an increase in the serum level of BMG and urine microalbumin with strong positive correlation of MALB and ACR in patients with BPH and PCa. There was also a strong positive correlation of BMG and ACR in patients with prostate cancer. Despite the significant increase in BMG and MALB in this study, routine indices of renal function like urea and urine creatinine remained normal. The increase in the sensitive markers of renal function in patients with benign prostatic hyperplasia and prostate cancer is an indication of early renal impairment.

More comprehensive and comparative studies on sensitive renal biomarkers similar to this study should be conducted and the potentials of these markers in early detection of renal injury should be evaluated.

CONFLICT OF INTEREST

No conflicts of interests exist

REFERENCES

1. Rawla, P. (2019). Epidemiology of prostate cancer. World Journal of Oncology.**10**:63-89.
2. Kim, S.R., Lee, Y.H., Lee, S.G. (2017). The renal tubular damage marker urinary N-acetyl-β-d-glucosaminidase may be more closely associated with early detection of atherosclerosis than the glomerular damage marker albuminuria in patients with type 2 diabetes. Cardiovascular Diabetology. **16**(16).
3. Fitzmaurice, C., Akinyemiju, T.F., A.l., Lami, F.H., Alam, T., Alizadeh-Navaei, R., Allen, C. (2018). Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2016: A systematic analysis for the global burden of disease study. JAMA Oncol.**4**:1553-1568.
4. Hyuna, S., Jacques, F., Rebecca, L, Mathieu, L., Isabelle, S., Ahmedin, J., and Freddie, B. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. Journal of American Chemical Society. **71**(3): 209-249.
5. Jernal, A., Siegel, R., Xu, J. (2010). Cancer statistics. Cancer Journal for Clinicians. **60**: 277-300.
6. Garget, M., Kaur, G., Malhotra, V., Garg, R. (2013). Histopathological spectrum of 364 prostatic specimens including immunohistochemistry with special reference to grey zone lesions. Prostate International. **1**:146-151.
7. Farooq, S., Bilai, S., Khaliq, B.I., Sidieq, F., Aslam, H., Shah, I. (2019). The spectrum of histopathological patterns observed in prostate specimens in a tertiary care hospital in Kashmir. International Journal of Contemplating Medical Research. **6:**1-3.
8. Beker, B.M., Corleto, M.G., Fieiras, C., Musso, C.G. (2018). Novel acute kidney injury biomarkers: Their characteristics, utility and concerns. International journal of Urology and Nephrology. **50**:705–713.
9. Gobe, G.C., Coombes, J.S., Fassett, R.G., Endre, Z.H. (2015). Biomarkers of drug-induced acute kidney injury in the adult. Expert Opinion on Drug Metabolism & Toxicology. **11**:1683–1694.

10. Emeje, I.P., Ukibe, N.R., Onyenekwe, C.C., Nnamah, N.K. (2017).Assessment of Serum Prostate Specific Antigen, Some Renal Indices and Uric Acid Levels in Subjects with Benign Prostatic Hyperplasia at Lokoja, Nigeria. Journal of Bioanalysis and Biomedicine**. 9**(5): 256-262.
11. Shah, K., Maghsoudlou, P. (2016). Enzyme-linked immunosorbent assay (ELISA). British Journal of Hospital Medicine. **77**(7): 98-101.
12. Mingsie, H., Chuannei, X., Dandan,Y., Le, G., Haw, Z. (2024).Optimization of immunoturbidimetric assay system enhanced by B2-microglobution latex. Bio web of Conferences. Dio:10.1051/ bioconference/2024.11102013.
13. Ihim, A., C., Ogbodo, E., C., Obi, P., C., Nosakhare, O., Ozuruoke, D., Francis, N., Oguaka, V., N. (2017). Effect of Short-Term Exposure to Formalin on Kidney Function Tests of Students in Nnewi. European Journal of Biomedical and Pharmaceutical Sciences. **4**(12): 122-125.
14. Wei, J.T., Calhoun, E., Jacobsen, S.J. (2005). Urologic diseases in America project: Benign prostatic hyperplasia. Journal of urology. **173**(4): 1256-1261.
15. Wasung, M.E., Chawla, L.S., Madero, M. (2015). Biomarkers of renal function, which and when? International Journal of Clinical Chemistry. **438**:350–357.
16. Thomas, R., J**.,** Bilal, C., Steven A.K. (2015). Testosterone and Benign Prostatic Hyperplasia. Asian Journal of Andrology. **2:** 212-216.
17. Vucenik, I., Stains, J.P. (2012). Obesity and cancer risk: evidence, mechanisms, and recommendations. Annals of the New York Academy of Sciences. **127**1:37–43.
18. De Pergola, G., Silvestris, F. (2013). Obesity as a major risk factor for cancer. European Journal of Epidemiology. **2013**: 2915.
19. Song, X., Pukkala, E., Dyba, T., Tuomilehto, J., Moltchanov, V., Mannisto, S. (2014). Body mass index and cancer incidence: the FINRISK study. European Journal of Epidemiology. **29**:477–487.
20. Kopp, W. (2018). Diet-Induced Hyperinsulinemia as a Key Factor in the Etiology of Both Benign Prostatic Hyperplasia and Essential Hypertension? 11:1178638818773072.
21. Rohrmann, S., Smit, E., Giovannucci, E.,and Platz, E.,A.(2005). Association between markers of the metabolic syndrome and lower urinary tract symptoms in the Third National Health and Nutrition Examination Survey (NHANES III). International Journal of Obesity. **29**:310–316.
22. Martin, R.M., Vatten, L., Gunnell, D., Romundstad, P., Nilsen T.I. (2009).Components of the metabolic syndrome and risk of prostate cancer: the HUNT 2 cohort, Norway. Cancer Causes Control. **20**:1181–1192.
23. Okuja, M., Ameda, F., Dabanja, H. (2021). Relationship between serum prostate-specific antigen and transrectal prostate sonographic findings in asymptomatic Ugandan males. African Journal of Urology. **27**:584
24. Adhyam, M., Gupta, A., K. (2012). A Review on the clinical utility of PSA in cancer prostate. Indian Journal of surgical Oncology. **3**(2): 120-129.
25. Puthiyottil, D., Priyamvada, P. S., Kumar, M. N., Chellappan, A., Zachariah, B. Parameswaran, S. (2021). Role of Urinary Beta 2 Microglobulin and Kidney Injury Molecule-1 in Predicting Kidney Function at One Year Following Acute Kidney Injury. International Journal of Nephrology and Renovascular Disease.**14:** 225–234.
26. Zeng, X., Hossain, D., Bostwick, D., Herrera, G., Ballester, B., Zhang, P.L. (2014). Urinary B2-microglobulin is a good indicator of proximal tubular injury: a correlation study with renal biopsies. Journal of Biomark. **1**(1): 103-108.
27. Ichinose, K., Ushigusa, T., Nishino, A., Nakashima, Y., Suzuki, T., Horai, Y. (2016). Lupus nephritis IgG induction of calcium/calmodulin-dependent protein kinase IV expression in podocytes and alteration of their function. Arthritis Rheumatology. **68**:944–952.
28. Barton, K.T., Kakajiwala, A., Dietzen, D.J., Goss, C.W., Gu, H., Dharnidharka, V.R. (2018).Using the newer kidney disease: improving global outcomes criteria, beta-2- microglobulin levels associate with severity of acute kidney injury. Clinical Kidney Journal. **11**(6):797–802.
29. Wang, R., Hu, H., Hu, S., He, H., Shui, H., Bahous, S.A. (2020). β2-microglobulin is an independent indicator of acute kidney injury and outcomes in patients with intracerebral hemorrhage. Medicine. **99**(8).

30. Jaswanth, C., Priyamvada, P.S., Zachariah,B., Haridasan, S., Parameswaran, S., Swaminathan, R.P. (2019). Short-term changes in urine beta 2 microglobulin following recovery of acute kidney injury resulting from snake envenomation. Kidney International Reports. **4**(5):667–673.
31. Ritah, K.,Simon, P.R., Gertrude, N. K.(2019) .Microalbuminuria and Traditional Serum Biomarkers of Nephropathy among Diabetic Patients at Mbarara Regional Referral Hospital in South Western Uganda. Journal of Diabetes Research. **3**(53):42-60.
32. Becton, L.J., Kalpatthi, R.V., Rackoff, E., Disco, D., Orak, J.K., Jackson, S.M. (2010). Prevalence and clinical correlates of microalbuminuria in children with sickle cell disease. Pediatric Nephrology. **25**:1505–151.
33. Aloni, M.N., Mabidi, J.L., Ngiyulu, R.M., Ekulu, P.M., Mbutiwi, F.I., Makulo, J.R. (2017). Prevalence and determinants of microalbuminuria in children suffering from sickle cell anemia in steady state. Clinical Kidney Journal. **10**:479–486.
34. Cho, H., Kim, J.H. (2017). Prevalence of microalbuminuria and its associated cardiometabolic risk factors in Korean youth: Data from the Korea National Health and Nutrition Examination Survey. Public Library of Science. **12**(6): e0178716.
35. Mildred, Z.,Trevor, K., Timothy, K., Chisanga ,C., Panji, N., Musalula, S.(2016). Kidney injury molecular -1 and micoalbumin in levels in Zambian population: biomarkers of kidney injury. Pan African Medical Journals. **24**(54): 8759.
36. Steubl, D., Block, M., Herbst, V., Nockher, W.A., Schlumberger, W., Satanovskij, R., Angermann, S., Hasenau, A.L., Stecher, L., Heemann, U. (2016). Plasma uromodulin correlates with kidney function and identifies early stages in chronic kidney disease patients. Medicine. **95**:3011.
37. Matsushita, K., Vander, V. M., Astor, B.C., Woodward, M., Levey, A.S., De Jong, P.E., Coresh, J., Gansevoort, R.T. (2010).Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet. **375**: 2073–2081.
38. Hemmelgarn, B.R., Manns, B.J., Lloyd, A., James, M.T., Klarenbach, S., Quinn, R.R., Wiebe, N., Tonelli, M. (2010). Relation between kidney function, proteinuria and adverse outcomes. Journal of the American Medical Association. **303**:423–429.
39. Lambers, H.J., Gansevoort, R.T., Brenner, B.M., Cooper, M.E., Parving, H.H., Shahinfar, S., Zeeuw, D. (2010). Comparison of different measures of urinary protein excretion for prediction of renal events. Journal of the American Society of Nephrology. **21**:1355–1360.
40. Hallan, S.I., Ritz, E., Lydersen, S., Romundstad, S., Kvenild, K.,and Orth, S.R. (2009). Combining GFR and albuminuria to classify CKD improves prediction of ESRD. Journal of the American Society of Nephrology. **20**:1069–1077.
41. Abdallah, E.M., Gad, A., Modawe, N.M. (2016). Assessment of Creatinine and Microalbuminuria in Sudanese Smoker. School Bull. **2**(3):153-156.
42. Zhang, Y.X., Wang, l.I., Peng, S.Y., Zhao, G.G., Zhong, G., Wang, Z. (2013). Correlation of Serum β2-Microglobulin Levels with Prostate-specific Antigen, Gleason Score, Clinical Stage, Tumor Metastasis and Therapy Efficacy in Prostate Cancer. Archives of Medical Research. **44**: 100-103.