The Inflammatory Role of the Neutrophil Platelet Ratio in Health, Hypertension and Chronic Kidney Disease

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ABSTRACT

Introduction: Inflammation is a known associate and accelerator of kidney disease. Both are associated with changes in the hemogram, particularly elevated neutrophils and platelets counts, in association with reductions in the lymphocyte count.We assessed the neutrophil platelet ratio (NPR) and its association with demographic, urinary and serum indices of kidney function in health, hypertension and CKD.

Methods: In this prospective study, history and other relevant clinical data was obtained from the participants using a structured proforma.Blood samples were collected for full blood count, serum electrolytes, urea, creatinine, uric acid, albuminand fasting lipids. Urine samples were collected for albumin creatinine ratio.Student t-test and Chi square was used to identify the association between NPR and the demographic, urinary(urine albumin creatinine ratio)and serum indices (glomerular filtration rate) of kidney function in health, hypertension and CKD while multiple regression analysis was used to obtain the determinants of elevated NPR.

Results: Of the 298 participants studied, the healthy cohorts, the hypertensives, and CKD cohorts were 146, 94 and 58 respectively. The participants mean age was 54.91±64 years; the CKD cohorts were older, $p<0.001$. The urine albumin creatinine ratio (UACR) were higher in the elderly. The mean urine albumin creatinine ratio (UACR) was higher in CKD than hypertension (36.66±6.89 versus 26.36±12.04), $p<0.001$. The absolute neutrophil count was higher in hypertension (5456.79±6.90) than CKD (5216.53±9.29), $p<0.001$ whilethe platelet count was higher in CKD (411,456.99±45.43) than hypertension (329,704.58±66.90), $p<0.001$. The mean neutrophil platelet ratio (NPR) was significantly higher in hypertension (1.58±1.03) than CKD (1.32±0.83), $p=0.02$, and in males(1.81±0.25) than females

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(1.58±0.16), p=0.001. The NPR and the UACR were positively correlated in participants less than 40 years (r=0.259, p=0.068), negatively correlated in participants 40-64 years (r=-0.120, p=0.219), and had a strong negative correlation inparticipants ≥65 years (r=-0.41, p=0.016).The NPR had a stronger negative correlation with the UACR in hypertension (r=—0.276, p=0.060) than CKD (r=0.047, p=0.810) Elevated NPR was associated with advancing age (p<0.001), female gender (p<0.001), hypertension (p<0.001), elevated absolute neutrophil count (ANC) (p<0.001), elevated UACR (p=0.01), higher GFR (p<0.001) and reduced kidney volume (p=0.02). Only hypertension (OR-2.93, 95% CI-2.15-9.48) and ANC (OR-2.14, 95% CI-1.96-5.07) were independent associates of elevated NPR.

Conclusion: The mean NPR was highest in hypertension, and higher in health than CKD, it tends to be an inflammatory marker in hypertension but as an anti-inflammatory marker in CKD and in health. Future studies involving multi-racial populations are needed to ascertain the definitive inflammatory (or otherwise) role of the NPR in kidney disease.

Keywords: *Microalbuminuria, neutrophil-platelet count, inflammatory marker, kidney function, chronic kidney disease.*

INTRODUCTION

Inflammation is recognized as a cause, associate, and accelerator of kidney disease, being a mediator of the progression from acute kidney injury (AKI), through chronic kidney disease (CKD) to end-stage renal disease (ESRD) [1]. The hallmark ofrenalfunctional derangement is the alteration in serum concentrations of glomerular-filtered, tubule-reabsorbed substances,or urinary concentration of tubules-secretedsubstances [2]. Kidney diseases are associated with changes in the leucocyte population and these changes are reflected in the widely reportedhigher neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR) in CKD [3,4,5]. Whileneutrophilia and thrombocytosistypifies inflammationand stress, lymphopenia is indicative of physiologic stress associated with chronic ill –health [3].

A positive relationship exist between the absolute neutrophil count (ANC) and cardiovascular risk profile. This is similar to thepositive relationship between a faster CKD progression and higher mortality rate, (using elevated NLR as an inflammatory marker) in patients on maintenance hemodialysis (MHD) [1,4]. Neutrophils stimulates plateletsactivation and migration to site of vascular injury, while platelet stimulates tissue neutrophilinfiltration that can lead to disruptions in cell adhesion molecules (CAMs). This in the brain can lead to disruption of the blood brain barrier (BBB) during stroke, resulting in fluid extravasation into the brain parenchyma and cerebral edema [6].

A chronic inflammatory process in the renal bed, particularly if immunologic and affecting the glomerulus, can progress to podocytes capping, effacementand, structural and electrochemical alterationsof the filtration apparatus with loss of its size, shape and charge selectivity [7]. This is complicated by increasedalbumin trafficking across the filtration barrier evidenced by a higher urinary albumin creatinine ratio (UACR). Albuminuria can induce endothelial damage,and chronic remodeling seen in the kidneys, heart, brain parenchyma and blood vessels [8].

Inflammation-associated changes in the leucocytespopulation can be correlated with increasesin UACR (both surrogate markers of kidney damage) [9]. There is vast literature on the positive relationship between the inflammatory process and the differential leucocyte population blood cell counts, particularly with neutrophil, platelets and lymphocyte. However, studies assessing the relationship between the neutrophil platelet ratio with inflammatory indices of kidney function, particularly in CKD, have not been reported. We assessed the NPR and its association with demographic, urinary (albumin creatinine ratio) and serum indices (glomerular filtration rate) of kidney function in health, hypertension and CKD.

Materials and Methods: This was a hospital based cross sectional study conducted at Babcock University Teaching Hospital (BUTH), Ilishan-Remo, Ogun State, Nigeria.

Study population: Participants were 18 years of age or older and were grouped into three cohorts: healthy, those with hypertension and, those with CKD. Consecutive sampling was used in recruiting

participants till the desired sample size was attained. The healthy participants were hospital staffs. Those with hypertension were newly diagnosed or receiving treatment for hypertension. The CKD patients were recruited using the KDOQI2012 Clinical Practice Guideline for Diabetes and CKD [10]. Participants had an abdominal ultrasound scan to determine the kidney volume, to rule out obstructive kidney diseases, and for proper placement into a cohort group [11].

Sample size: This was determined using the prevalence of elevated NPR of 65%, power of 80% and margin of error of 6%, thisgave a sample size of 222 [12].

We excluded participants who smoked, had acute diseases, infections, cancers, connective tissue diseases, heart failure, liver disease, hematologic diseases, had current use of antibiotics, anti-inflammatory agents use, pregnancy and hormonal contraceptives use within the preceding six months and those with ultrasound-detected intra-abdominal lesions. Women of reproductive age were instructed to refrain from providing urine samples collected from the day before their menstrual flow until the first day after it ended.

We obtained data on socio-demographics and drug history from the medical records, measured the height, weight and blood pressure according to standardized protocols), and documented the results (full blood count, renal biochemical parameters, and urine albumin creatinine ratio) from analysed samples. Standardized protocols had been followed in the quantitative testing for UACR with the Micra Albustix test strip.

A strip was taken from the micra albustix container which was immediately closed. The strip-end with pad was completely immersed in the urine for 50 seconds and removed bygently rolling it against the bottle edge, this removes excess urine. The color of the strip pad was matched with that inscribed on the strip container, and results were entered. Venous blood was collected between 8 am ad 8:30 am at room temperature from a peripheral vein (with participants in the sitting position) into an ethylenediaminetetraacetic acid (EDTA) bottle for analysis of the complete blood count (CBC) and, into a Lithium heparin bottle for renal biochemistry (electrolytes, urea, creatinine, and uric acid) using an autoanalyzer (Roche Diagnostics GmbH, Mannheim Germany). Creatinine-based glomerular filtration rate (GFR) was calculated using the CKD-EPI formula [13].

Definitions of Cases and Variables

Healthy participants were those with no history of hypertension, diabetes, sickle cell anemia or any other chronic no-communicable disease, with normal BP, fasting blood glucose (FBG), and had normal echogenicity pattern on RUS.

Hypertensives were defined as those with history of hypertension, or using BP lowering drugs [14].

Chronic kidney disease: <60 mL/min

Elevated NPR: any value greater than 4.2 [15]

Microalbuminuria was UACR greater than 30mg/g [16].

Anaemia was haematocrit of less than 39% in males or 36% in females [17].

Hypoalbuminemia was a serum albumin less than 35 g/L [18].

Hyperuricemia was greater than0.42 mmol/L in males and greater than 0.36mmol/L in females [19]

The SPSS version 22 was used for data analysis. Means with standard deviation, as continuous variables were compared using student's t-test between 2 groups while a one-way ANOVA was used for means comparison in more than 2 groups. Proportions and frequencies, as categorical variables were compared using the Chi-square or fisher's exact test. Variables from the univariate analysis with $p<0.025$ were adjustment variables for the multivariate analysis to determine independent associates of elevated NPR in the studied population. Pearsons correlation was used in measuring the correlation between variables. The P-value <0.05, was considered statistically significant.

This study was approved by the Babcock University Human Research Ethics Committee (NHREC/24/01/2018 and BUHREC501/19).

RESULTS

Two hundred and twenty two participants were studied, of which 146 (71 males and 75 females) were healthy, 47 (20 males, 27 females) had hypertension and, 29 (12 males and 17 females) had CKD (Table

1). The mean age of the population was 62.48±9.43 years, healthy (47.14±5.83 years), hypertensives (52.56±3.78 years) and CKD (68.73±11.15 years). A greater proportion of the healthy and hypertensive cohorts were middle aged (56.2% and 42.6%) while majority (58.6%) of the CKD cohorts were elderly. There was a significant gender difference in the age representation among the CKD cohort unlike the hypertensives, p=0.01 versus p=0.07 (Table 2). The mean NPR of the males was significantly higher than females (2.03±0.04 versus 1.82±0.05), p=0.02 and in hypertensives than CKD (1.45±0.04 versus 1.20±0.02), p=0.02

From the univariate analysis on the combined hypertension and CKD population (Table 3), theNPR was negatively associated with age (p<0.001), female gender (p<0.001), hypertension (p<0.001), elevated ANC (p<0.001), elevated UACR (p=0.01), higher GFR (p<0.001) and reduced kidney volume (p=0.02). The multivariate model (Table 4) however showed hypertension (OR-2.93, 95% CI-2.15-9.48) and elevated ANC (OR-2.14, 95% CI- 1.96-5.07) as the independent associates of elevated NPR. The NPR had a significant negative relationship with the UACR in females (Figure 1). The NPR was positively correlated with the UACR in hypertension but had a

Table 1: Socio-demographic, Clinical and Laboratory characteristics of the study participants

Variables	Healthy (n=146) (Mean ± SD) (%)	Hypertensives (n=94) (Mean ± SD) (%)	CKD (n=58) (Mean ± SD) (%)	p-value
Sex				
Male	71 (48.63)	40 (42.55)	24 (41.38)	0.001
Females	75 (51.37)	54 (57.45)	34 (58.62)	
Age, years				
18-39	54 (36.99)	22 (23.41)	0 (0.00)	<0.001
40-64	82 (56.16)	40 (42.55)	24 (41.38)	
≥65	10 (6.85)	32 (34.04)	34 (58.62)	
WHR	0.99 ± 0.22	1.02 ± 0.24	1.06 ± 0.31	0.04
Systolic BP, mmHg	118.32±12.85	145.06±8.11	145.28±10.93	<0.001
Diastolic BP, mmHg	75.56±7.33	90.32±4.19	88.83±6.60	<0.001
ANC, $x10^9$	4396.46±38.03	5456.79±6.90	5216.53±9.29	<0.001
ALC, $x10^9$	2382.59±8.28	1932.17±7.48	1128.38±4.30	<0.001
Platelet, $x10^9$	304,871.26±60.44	329,704.58±66.90	411,456.99±45.43	<0.001
NPR	1.44±1.04	1.58±1.03	1.32±0.83	0.03
NLR	1.52±1.02	2.69±1.13	5.28±2.37	<0.001
PLR	1.28±0.10	1.71±0.43	3.65±1.31	<0.001
UACR, mg/g	13.02±5.76	26.36±12.04	36.66±6.89	<0.001
GFR, ml/min/1.73m^2	97.36±14.74	81.55±8.93	33.12±6.46	<0.001
Hematocrit, %	40.63±1.38	36.45±1.36	35.28±1.09	0.01
Albumin, mg/dL	44.75±12.58	40.81±12.58	35.89±10.23	0.001
Elevated TC, mg/dL		19 (20.21)	22 (37.93)	0.001
Low HDL, mg/dL		22 (23.40)	18 (31.03)	0.04
Elevated LDL, mg/dL		28 (29.79)	24 (41.37)	0.03
Elevated TG, mg/dL		32 (34.04)	25 (43.10)	0.01
Reduced KV, cm^3		10 (10.63)	33 (56.89)	<0.001

CKD-chronic kidney disease, WHR-waist hip ratio, BP-blood pressure, ANC-absolute neutrophil count, ALC-absolute lymphocyte count, NPR-neutrophil platelet ratio, NLR-neutrophil lymphocyte ratio, PLR-platelet lymphocyte ratio, UACR-urine albumin creatinine ratio, GFR-glomerular filtration rate, TC-total cholesterol, HDL-high density lipoprotein, LDL-low density lipoprotein, TG-triglyceride, KV-kidney volume.

Table 2: Gender correlates in participants with hypertension and chronic kidney disease

Variables	**Hypertensives**		**P-value**	**Chronic kidney disease**		**P-vale**
	Males n=40(%) Mean ± SD	**Females n=54 (%) Mean ± SD**		**Males n=24 (%) Mean ± SD**	**Females n=34 (%) Mean ± SD**	
Age						
Mean, years	59.56±6.62	58.35±6.44	0.06	67.74±8.93	70.89±8.99	0.04
18-39	10 (25.00)	12 (22.22)	0.07	0 (0.00)	(0.00)	0.01
40-64	16 (40.00)	24 (44.45)		12 (50.00)	12 (35.29)	
>65	14 (35.00)	18 (33.33)		12 (50.00)	22 (64.71)	
WHR	1.03±0.24	1.01±0.22	0.07	1.03±0.24	1.08±0.31	0.05
SBP, mmHg	146.17±14.28	144.95±11.28	0.06	145.87±13.33	144.88±12.64	0.08
DBP, mmHg	90.07±5.46	90.47±6.36	0.09	87.52±4.43	89.92± 6.02	0.04
UACR, mg/g	28.01±9.03	27.56±8.07	0.05	36.04±6.27	37.09±6.63	0.03
Hematocrit, %	36.61±1.18	36.32±1.19	0.06	35.31±1.09	35.26±1.09	0.07
GFR, ml/min	87.25±12.34	76.87±10.36	<0.001	34.69±7.83	32.09±6.88	0.02
Albumin, g/L	42.92±13.30	39.25±9.57	0.02	36.18±9.14	35.68±7.46	0.06
ANC	5916.53±49.29	6484.83±56.33	0.03	5256.79±46.90	5335.84±49.110.08	
PC	2918.51±25.37	3552.31±31.34	0.01	3625.38±28.16	4431.53±42.71	<0.001
NPR	2.03±0.04 (n=28)	1.82±0.05 (n=22)	0.02	1.45±0.04 (n=12)	1.20±0.02 (n=17)	0.02
	Mean ± SD	Mean ± SD	P-value	Mean ± SD	Mean ± SD	P-value
PCwCLOP	322.86±51.63	363.44±92.48	<0.001	349.61±49.42	481.63±96.17	0.001
PCwASA	318.15±72.37	360.38±66.28	<0.001	351.54±38.18	387.88±78.23	<0.001

WHR-waist hip ratio, SBP-systolic blood pressure, DBP-diastolic blood pressure, UACR-urine albumin creatinine ratio, GFR-glomerular filtration rate, ANC-absolute neutrophil count, PC-platelet count, PCwCLOP-platelet count with clopidogrel, PCwASA- platelet count with aspirin, NPR-neutrophil platelet ratio.

Table 3: Univariate analysis showingfactors associated with elevated Neutrophil Platelet Ratio in a combinedhypertensive and chronic kidney disease population

Variables	Normal NPR (n=113)	Elevated NPR (n=39)	P-value
Age, (years) mean	65.75±9.21	54.83±7.49	<0.001
Sex			
Males (n, %)	36 (56.25)	28 (43.75)	<0.001
Females (n, %)	77 (87.50)	9 (12.50)	
Study cohort			
Hypertensives (n, %)	63 (67.02)	31 (32.92)	<0.001
CKD cohorts, (n, %)	50 (86.20)	8 (13.80)	
Elevated WHR (n, %)	64 (56.67)	18 (46.15)	0.1
Elevated SBP, mmHg (n, %)	59 (52.21)	20 (51.28)	0.9
Elevated DBP, mmHg (n, %)	55 (48.67)	22 (56.41)	0.3
Elevated ANC (n, %)	54 (47.79)	29 (74.36)	<0.001
Elevated PC, (n, %)	69 (61.06)	11 (28.20)	<0.001
Low lymphocyte count, (n, %)	36 (31.86)	7 (17.95)	0.07
Elevated UACR, mg/g (n, %)	66 (58.41)	13 (33.3)	0.01
eGFR mean (range)	49.85±6.37 (19.23-63.2)	100.90±9.37 (52.59-119.74)	<0.001
Anemia, % (n, %)	31 (27.43)	6 (15.38)	0.06
Hypoalbuminaemia g/L (n, %)	33 (29.20)	6 (15.38)	0.05
Elevated TC, mg/dL (n, %)	33 (29.20)	8 (20.51)	0.08
Low HDL, mg/dL (n, %)	30 (26.55)	10 (25.64)	0.9
Elevated LDL mg/dL (n, %)	44 (38.94)	8 (20.51)	0.05
Elevated TG, mg/dL (n, %)	46 (40.71)	11 (28.21)	0.06
Reduced Kidney vol, cm^3 (n, %)	38 (33.63)	5 (12.82)	0.02

NPR- neutrophil platelet ratio, CKD-chronic kidney disease, WHR-waist hip ratio, SBP-systolic blood pressure, DBP-diastolic blood pressure, ANC-absolute neutrophil count, PC- platelet count, UACR-urine albumin creatinine ratio, GFR-glomerular filtration rate, TC-total cholesterol, HDL-C-high density lipoprotein cholesterol, LDL-C-low density lipoprotein protein, TG-triglyceride.

Table 4: Independent associates of elevated neutrophil platelet ratio

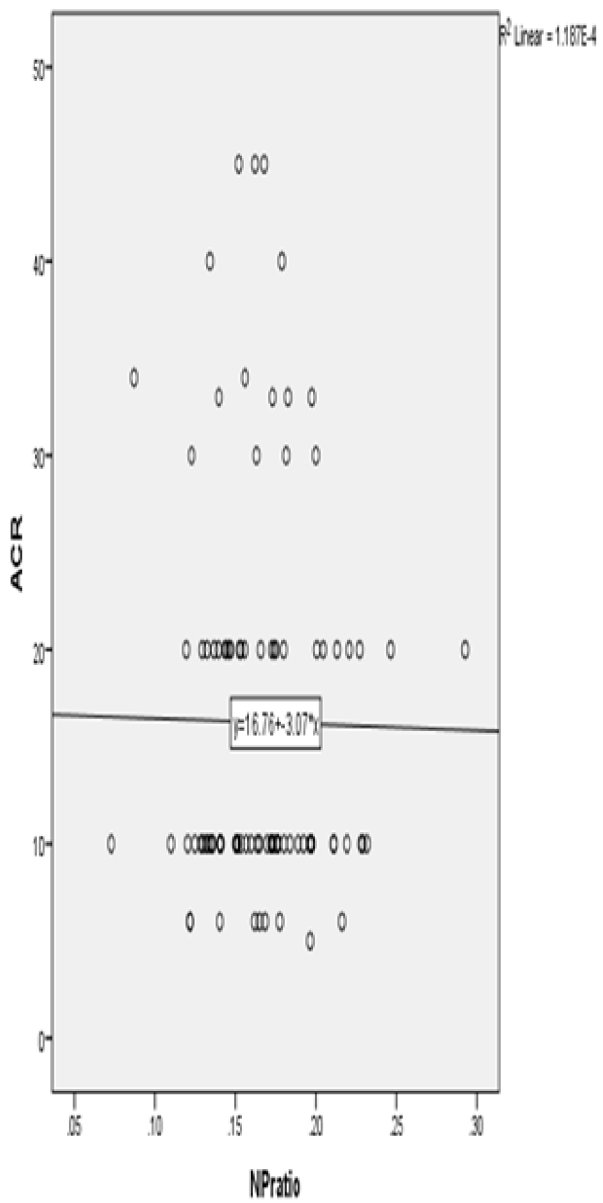
Variables	Odd ratio	95% CI	p-value
Hypertension	2.93	2.15-9.48	<0.001
Absolute neutrophil count	2.14	1.96-5.07	0.001

CI-confidence interval

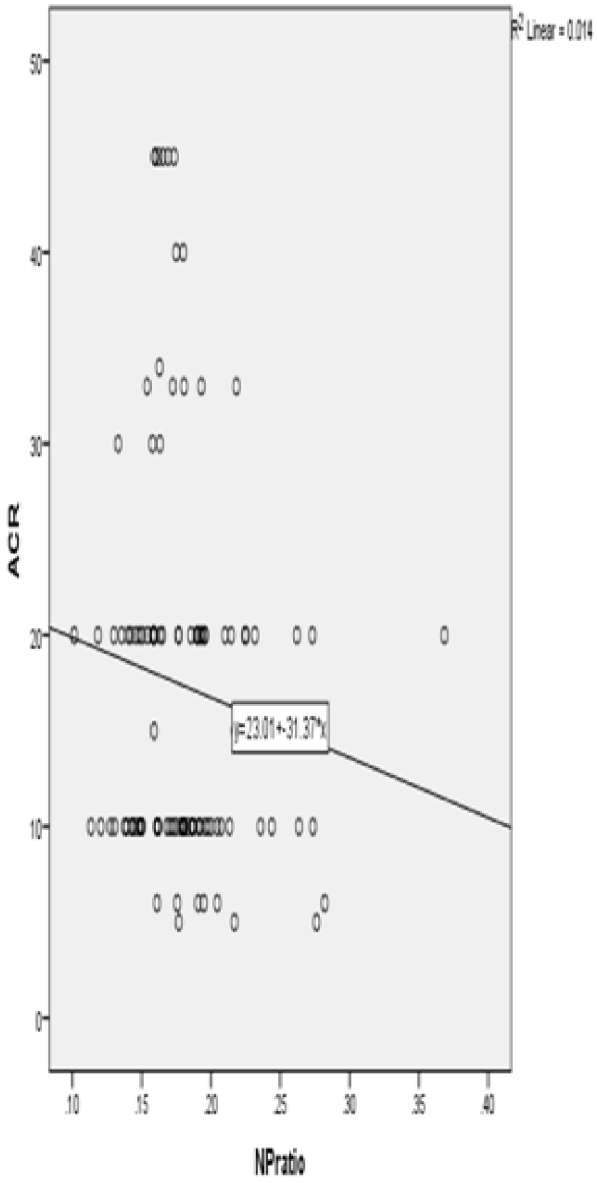
From the multivariate model (Table 4), independent associates of elevated NPR were hypertension (OR-2.93, 95% CI-2.15-948) and higher ANC (OR-2.14, 95% CI-1.96-5.07)).

The NPR and the UACR had a very weak negative correlation in males (figure 1) and a strong negative correlation in females.hypertension, and a strong negative correlation in CKD.

Figure 1: Correlation between NPR and UACR in males and females



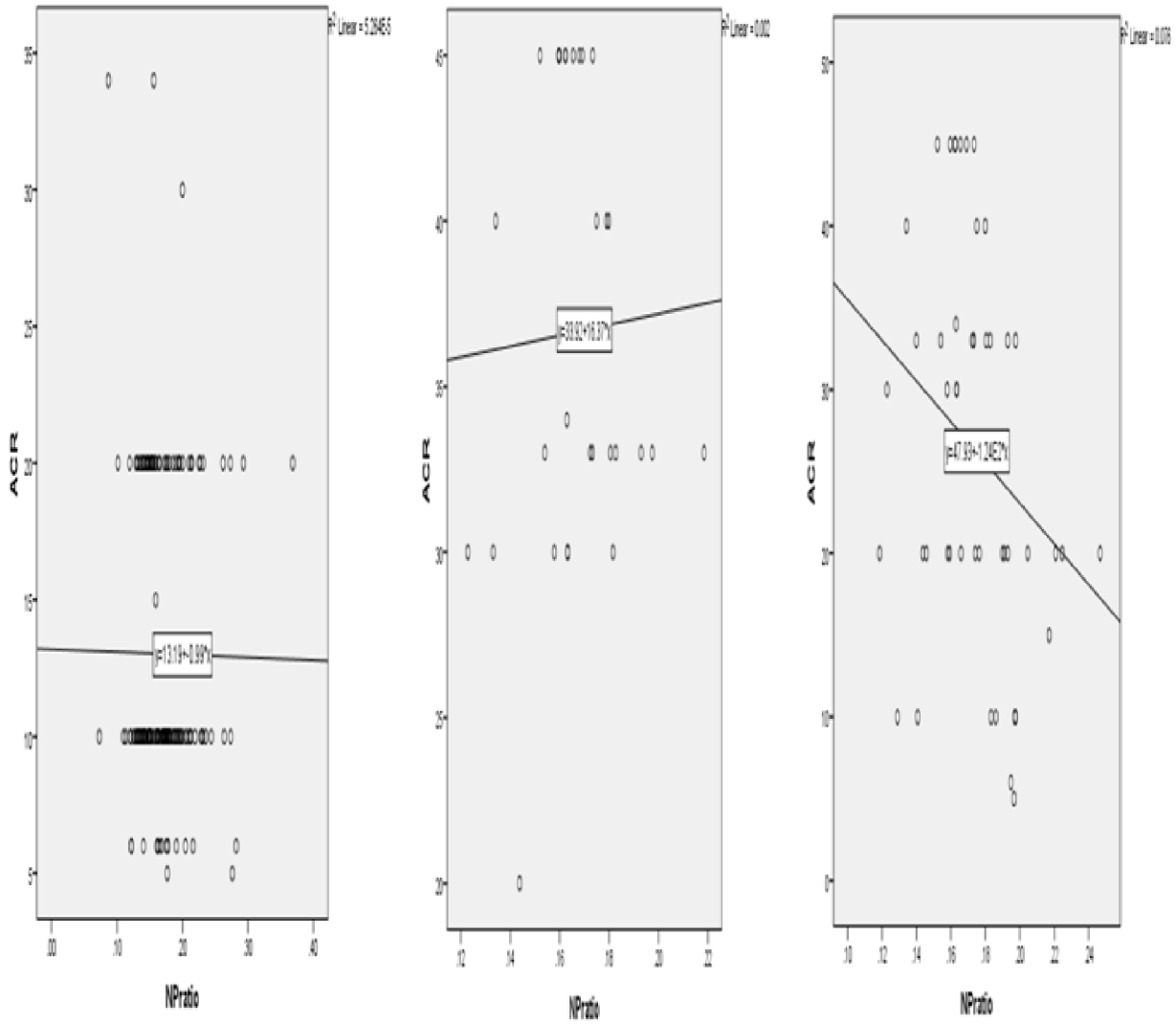
1a. Males (r=-0.011, p=0.917)



1b. Females (r=-0.120, p=0.219)

From figure 2, the NPR and the UACR had a very weak negative correlation in health, weak positive correlation in hypertension, and a strong negative correlation in CKD.

Figure 2: Correlation graphs between neutrophil platelet ratio and urine albumin creatinine ratio



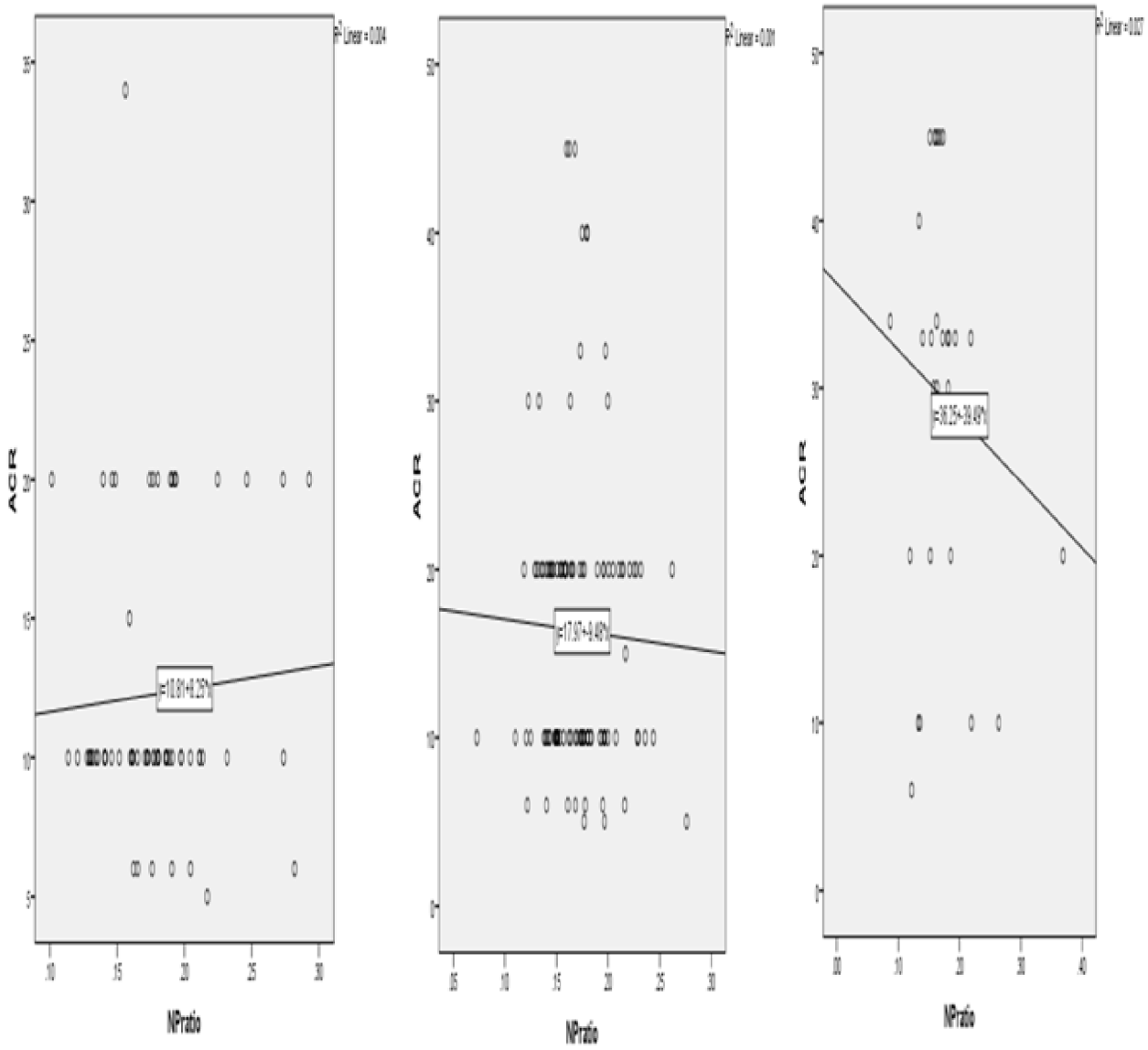
2a: Health (r=-0.007, p=0.931)

2b: Hypertension (r=0.276, p=0.060)

2c: CKD (r=0.47, p=0.010)

As in figure 3, the NPR and the UACR were positively correlated in participants less than 40 years, were negatively correlated in participants 40-64 years, and strongly negative in the elderly population.

Figure 3: Correlation between NPR and ACR in age groups



2a. <40 years
(r=0.259, p=0.068)

2b. 40-64 years
(r=-0.120, p=0.219)

3c. ≥65 years
(r=-0.41, p=0.016)

strong negative correlation with the UACR in CKD (Figure 2). The NPR was positively correlated with age in the healthy cohort, had a weak negative correlation in hypertensives, but was strongly negatively correlatedin the CKD cohorts (Figure 3).

DISCUSSION

We conducted the first study to determine the relationship between the neutrophil platelet ratio and inflammation in hypertension and kidney disease. The hemogram in this study was found not only to be associated with inflammatory indicesin hypertension and CKD but also its severity evidence by elevated levels of neutrophils and platelets in both hypertensivess and CKD patients,with concurrent reductions in the ALC. Elevations in the neutrophil count were found to be higher in hypertension than CKD and also in females compared to males. These higher neutrophil counts compared to the platelet count gave the higher NPR in hypertension than CKD, and in females compared with males.

The greater increases in neutrophil count relative to platelet count in hypertension compared to CKD is similar to findings by Yamamoto et al [20] who found a positive relationship between the NPR and inflammatory indices in ulcerative colitis, a chronic inflammatory condition. Similarly, Klocperk *et al* [21] found fewer neutrophils, and neutrophil extracellular traps (NETs) in the serum of people at risk of type 1 diabetes mellitus (TIDM) and those just developing TIDM. The authors also reported a concurrent increase in pancreatic neutrophilic infiltration, associated with a heightened inflammatory destruction of the pancreas. The documented greater inflammatory response seen in CKD compared to hypertension could therefore be attributed to a more severe inflammation-induced neutrophilic tissue infiltration in CKD compared to hypertension. Moreover, platelets are known activators of neutrophil release from the bone marrow and their migration in response to injury. This platelet-stimulated neutrophil release seem more prominentin an acute inflammatory process as against the well reported stimulatory effects of neutrophils on platelet release, migration and aggregation via the formation and release of the NETs and neutrophil serine peptides, both, mediators ofchronic inflammatory injury and tissue damage [22]. This apparent lesser responsiveness of neutrophils in CKD compared to platelets could explain findings by some authors that NLR was a lesser inflammatory maker in CKD compared with the PLR [23-25].

The greater increase in NPR in hypertension compared with CKD in this study could also be attributed to the fact that people with hypertension-related complications like non-dipping and myocardial infarction (MI) are respectively associated with greater increases in platelets than in dippers and in hypertensives without MI [26]. This, coupled with the formation of NETs (which entails reductions in peripheral neutrophil count) in chronic tissue inflammation typified by CKD,further explains the higher NPR in hypertension than CKD. Poznyak *et al* [27] and, Chatzigeorgwu *et al* [28] had found an association between atherosclerosis (more common and severe in CKD than hypertension) and NETs, with low NETs associated with greater inflammation, respectively. Moreover, the lesser UACR in hypertension compared with CKD further attest to the higher inflammatory profile of CKD compared with HTN. Hypertension, a very common cause of CKD is associated with little or no podocyte cupping and effacement, this being a progressive occurrence induced by kidney damage from whatever cause [29]. Podocyte effacement, typical of CKD, more so in ESKD is associated with excess protein, particularly albumin trafficking across the glomerular filtration apparatus leading to proteinuria (albuminuria), for which the UACR is used clinically in diagnosis, therapeutics, prognosticating and monitoring response to treatment in clinical medicine [30,31].

The lesser mean NPR in females is supportive of earlier studies that foundthat greater inflammatory responses are mediated in females in acute settings, associated with higher neutrophil release and activation, compared to the chronic inflammatory processesin CKD. Connective tissue diseases are documented to benotable exceptions to this pattern [32]. This tend to partly explain the significantly higher NPR in males with CKD compared to hypertension in this study. Estrogen suppresses platelet activity and platelet reactivity (both surrogate markers of higher platelet counts), in addition to the fact that high on-treatment platelet reactivity (HTPR) is higher in females compare to males [33]. Hence, in this study with a predominant post-menopausal female CKD population, the lower NPR in females compared to males could also be attributed to the loss of the suppressive actions of

estrogens on the platelet count, reactivity and HTPR and this mirrors findings by Jastrszebka *et al* [34] who also reported further thatplatelet reactivity following double anti-platelet treatment (DAPT) was higher in females than males.

The role played by the higher fat deposits in females could also be contributory, as adipose tissue mediate greater release of inflammatory cytokines like interleukin 6 (IL-6), IL-1 ad TNF-á and these contribute to the higher platelets in females seeninthis study, evidencedby higher WHR in the female CKD population unlike the hypertensive cohorts where the men had higher WHR, thus heightening the inflammatory profile of CKD compared to hypertension [35].

The neutrophils-platelets (N-P) synergy as a mediator of the inflammatory process is well reported, as neutrophils in acute injury and infections stimulates the platelets which in turn activates further neutrophilic inflammatory involvement enhancing the phagocytic process and the formation of NETs [9,36]. The presence of IL-8 (a platelet component) as a potent neutrophil activator is known to be a major contributor to the inflammatory strength of the N-P synergy [37]. The formation of N-P complexes herald the generation of potent inflammatory and injurious compounds such as the intracellular adhesion molecules (ICAMs), NETs and the receptor for advanced glycation end products (RAGE). These compounds cause potent cellular and tissue damage on chronic bases and are commonly known risk factors and precipitants of chronic degenerative and malignant conditions [38].

The higher UACR and, the subunits of the haemogram in the study population underlines the synergism between, and its aftermath on cardiovascular function, events and deaths, known to be hinged on the role played by each in the pathogenesis of atherosclerosis [39]. The active interaction between the N-P, activated by neutrophil stimulation and migration eventually lead to widespread atherosclerosis, particularly in CKD. Proteinuria, by causing hypoalbuminemia, stimulates hepatic production of the pathologic (atherogenic) lipoproteins that augment atherogenesis, complimenting the immunologic pathway [39].

Bearing in mind, the positive association between inflammation and the neutrophils, and with the platelets, the relationship between the two blood lines in health and during inflammation entails accessing this relationship in strategic states and timings,taking cognizance of the fact that the neutrophil count tends to be low at about 8 am and rises as the day progresses just as the platelet count peaks at 2 pm from the lowest levels at 8 am [40]. This was the bases for the complete blood count sample collection from 8 am to 8:30 am. It must be borne in mind that ethnic and gender differences have been reported in the white blood cells (WBC) and differentials, in addition to reported differences based on the levels of urbanizations of the participants involved [40,41].

Study limitations

This included the retrospective design of the study, and the fact that repeated sampling at different times of the day were not conducted, considering the fact thatthe peripheral blood levels of the different blood cells particularly leucocytes vary with the time of the day. Though, smoking, alcohol use and hormonal contraception were exclusion criteria, the reliability of the information could be questioned based on cultural and psychological practices.

CONCLUSION

The mean NPR and ANC were higher in males than females, and in hypertension than CKD. The mean platelet count was higher in females than males and in CKD than hypertension. There was a positive association between NPR .and UACR in the young and in hypertension, but NPR was inversely related to UACR in CKD and in the elderly. Elevated NPR was associated with advancing age, males, hypertension, elevated ANC, elevated UACR, higher GFR, and reduced kidney volume. Only hypertension and ANC were independent associates of elevated NPR. Although the NPR was less predictive of inflammation in this study, the fact that it tended towards an anti-inflammatory marker, coupled with its elevation in hypertension, could be of significant clinical use (in conjunction with some other markers) in predicting the transition from hypertension to CKD. Being the very first study to assess the inflammatory status of NPR in hypertension and CKD, future studies involving multi-racial populations and across all ages are needed to ascertain the definitive inflammatory (or otherwise) role of the NPR in hypertension and kidney disease.

Conflicts of Interest: None declared.

Funding: None

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