Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2024.257905.3067 Volume 30, Issue 5, August 2024
Manuscript ID ZUMJ-2312-3067 (R2)
DOI 10.21608/ZUMJ.2024.257905.3067

ORIGINAL ARTICLE

Serum Aldosterone Level in Different Stages of Diabetic Kidney Disease in Type 2 Diabetes Mellitus

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Submit Date 2023-12-24
Revise Date 2024-01-16
Accept Date 2024-01-21

ABSTRACT

Background: New evidence links elevated blood aldosterone levels to endothelial dysfunction which causes insulin resistance and kidney damage in diabetics. In this study, we aimed to measure serum aldosterone levels and assess the severity of renal injury in different stages of diabetic nephropathy.

Methods: The 52 participants in this case-control study were classified according to albuminuria and ACR, and they all had type 2 diabetes mellitus (T2DM): Group (A): 13 healthy individuals as control, Group (B): 13 controlled patients with T2DM with normoalbuminuria and normal albumin/create ratio ≤30mg/gm, Group (C): 13 patients with T2DM with microalbuminuria and albumin/create ratio 30-300mg/g, and Group (D): 13 patients with T2DM with macroalbuminuria and albumin/create ratio ≥300mg/g. Serum aldosterone and serum renin were assessed.

Results: Serum aldosterone and renin differed significantly between the four groups (p<0.001). In the microalbuminuria diabetic group, a statistically significant strong negative correlation was found between s. aldosterone and high-density lipoprotein (HDL) (p= 0.025), and a statistically significant strong positive correlation was found between s. aldosterone and Alb/Cr ratio & s. renin (p=.0.037, 0.007 respectively). In the macroalbuminuria diabetic group, a statistically significant strong negative correlation was found between s. aldosterone and all of the Alb/Cr ratios, as well as total leucocytic count (TLC) (p=0.009, 0.029 respectively), and a statistically significant strong positive correlation was found between s. aldosterone, HDL, and K (p=0.042, 0.013, respectively). Post hoc analysis of S. Aldosterone showed that there was a statistically significant difference between the four studied groups (P<0.001), and as regards S. renin there was a statistically significant difference between Group A vs Group D (p= P3,0.015), Group B vs Group D (p=0.001), and Group C vs Group D (p<00.001).

Conclusion: serum aldosterone level could have a significant role in the progression of diabetic kidney disease.

Keywords: Aldosterone, Diabetic Kidney Disease, Type 2 Diabetes Mellitus.

INTRODUCTION

A typical consequence of diabetes, diabetic kidney disease (DKD) increases the risk of cardiovascular morbidity and death and often progresses to end-stage kidney disease. Over time, hyperglycemia causes a gradual decline in kidney function, which in turn causes changes in renal structure and function, ultimately leading to diabetic kidney disease (DKD). Around 40% of the estimated 35 million people with diabetes will acquire chronic kidney disease and eventually develop diabetic kidney disease (DKD) by the year 2035 [1]. Proliferation and growth of mesangial cells and their matrix, proteinuria (microalbuminuria), and

glomerular and tubulointerstitial fibrosis are the hallmarks of diabetic nephropathy (DN) [2].

An essential component of diabetic kidney damage that is not dependent on the angiotensin II (Ang II) pathway is the increased synthesis of extracellular matrix (ECM) proteins by aldosterone. A recent study found that increased levels of aldosterone in the blood are associated with endothelial dysfunction and insulin-signaling pathway defects, which in turn cause insulin resistance and kidney damage [3]. Over the past few decades, our knowledge of the physiological and pathological roles of mineralocorticoids and mineralocorticoid receptors (MR) has undergone a dramatic change [4].

Endothelin 1, microRNA-21, and neutrophil gelatinase-associated lipocalin (NGAL) are downstream targets of the aldosterone-mineralocorticoid receptor, and it has been suggested that local damage, oxidative stress, or cell death contribute to mineralocorticoid receptor-mediated inflammation. In particular, in dendritic cells, macrophages, and peripheral blood mononuclear cells, NGAL expression rises after aldosterone-mineralocorticoid receptor activation [5].

To find out why Mineralocorticoid receptor antagonists (MRAs) enhance nephroprotection when used in conjunction with RAS blockade, we need to examine the possible mechanisms by which these drugs exert their nephroprotective effects. In particular, we need to understand how finerenon works in conjunction with the RAS blockade. One possible hemodynamic effect and one direct action on tissue inflammation and fibrosis are the two primary nephroprotective strategies that may be accomplished by renin-angiotensin system (RAS) blockage [6].

Therefore, we did this work to measure serum aldosterone levels and assess the severity of renal injury in different stages of diabetic nephropathy.

PATIENTS AND METHODS

Between March and August of 2023, 52 participants who were checked at the outpatient clinics of the Endocrinology Unit of the Internal Medicine Department at Zagazig University hospitals as part of this case-control study.

Verbal and written informed consent was obtained from all participants after an explanation of the procedure and medical research. The research was conducted under the World Medical Association's Code of Ethics (Helsinki Declaration) for human research. This study was carried out after the approval of the Institutional Review Board (IRB) (#9524).

Patients were divided according to albuminuria and ACR: Group (A): 13 healthy individual matched age and sex serves as control group, Group (B): 13 controlled patients with T2DM with normoalbuminuria and normal albumin/create ratio ≤30mg/g, Group (C): 13 patients with T2DM with microalbuminuria and albumin/create ratio 30-300mg/g, Group (D): 13 patients with T2DM with macroalbuminuria and albumin/create ratio ≥300mg/g.

Cases with the following criteria were included: aged 18 or older who had type 2 diabetes mellitus and had diabetic nephropathy in different stages.

Cases with the following characteristics were excluded: Patients with type 1 DM, any patient with nephropathy due to other causes than diabetes as (hypertension – autoimmune – glomerulonephritis – drugs – amyloidosis - etc.), patients who received drugs that affect aldosterone level (Angiotensin-converting enzyme inhibitor-angiotensin receptor blockers-spironolactone antagonist-etc), and patients who had any kidney disease than nephropathy that was diagnosed by ultrasound.

All subjects of this study were subjected to full history, clinical, and laboratory assessment. Laboratory investigations: The following tests were performed following the protocols used in the clinical pathology department and laboratories of the hospitals affiliated with Zagazig University: kidney function test, serum sodium, and potassium, albumin, hemoglobin A1c, estimated glomerular filtration rate (eGFR), albumin creatinine ratio (ACR), lipid profile, serum aldosterone, and serum renin.

Serum aldosterone and Serum Renin were evaluated using enzyme-linked immune sorbent assay (ELISA) using human aldosterone ELISA kit Catalog No. 201-12-1238 and No. 201-12-1017 by Shanghai Sunred Biological Technology Co., Ltd. No.128 Lane 628, Jufengyuan Road, Baoshan, China. Normal aldosterone level was 3.1-35.4 ng\dl, and normal serum renin level was 0.6-4.3 ng/ml/hr.

STATISTICAL ANALYSIS

Using SPSS 24.0 for Windows, we gathered, tabulated, and statistically analyzed all of the data (SPSS Inc., Chicago, IL, USA). The qualitative data was shown using relative percentages and frequencies. The stated difference between qualitative variables was calculated using the chi-square test ($\chi 2$) and Fisher exact. For parametric data, the quantitative information was presented as the mean plus or minus the standard deviation, while for non-parametric data, the median and range were

used. For comparisons involving more than two dependent groups of normally distributed variables, the one-way ANOVA test (F) was utilized in conjunction with the LSD post hoc test. The Kruskal-Wallis test was employed for variables that did not follow a normal distribution. For normal variables, we utilized Pearson's correlation coefficient; for non-parametric variables, we utilized Spearman's correlation coefficient.

RESULTS

Concerning comorbidities, there was a highly statistically significant difference among the four groups that were analyzed ($p \leq 0.001$), as patients with macroalbuminuria have a significantly higher incidence of comorbidities (mainly HTN) compared to the other diabetic groups (Table 1).

There was a highly statistically significant difference between the four studied groups as regards HbA1C ($P<0.001$), cholesterol, HDL, and TG ($p<0.005$ for each), as diabetic groups have significantly higher HbA1C, cholesterol, and TG compared to the non-diabetic group. There was a highly statistically significant difference between the four studied groups as regards creatinine, eGFR, and Alb/Cr ratio ($p \leq 0.001$), as the DM patients in the macroalbuminuria group have higher kidney injury (higher creatinine, low eGFR, and higher Alb/Cr ratio) followed by microalbuminuria group (Table 2).

Results revealed that S. Aldosterone differed significantly between the four groups ($p \leq 0.001$). Also, S. renin showed a high statistically significant difference between the four groups ($p \leq 0.001$); Post hoc analysis of S. Aldosterone showed that there was statistically significant difference between the four studied groups ($P<0.001$), and as regards S. renin there was statistically significant difference between Group A vs Group D (p= P3,0.015), Group B vs Group D ($p=0.001$), and Group C vs Group D ($p<00.001$). (Table 3).

In normo- albuminuria diabetic group, a statistically significant strong positive correlation was found between s. aldosterone and Alb/Cr ratio ($p<0.05$). (Table 4 and Figure 1 A).

In the microalbuminuria diabetic group, a statistically significant strong negative correlation was found between s. aldosterone and HDL, while a statistically significant strong positive correlation was found between s. aldosterone and Alb/Cr ratio & s. renin ($p<0.05$). (Table 4, Figure 1 B, C, and D).

In the macroalbuminuria diabetic group, a statistically significant strong negative correlation was found between s. aldosterone and Alb/Cr ratio & TLC while a statistically significant strong positive correlation was found between s. aldosterone and HDL & K ($p<0.05$). (Table 4, Figure 1 E, F, G and H).

Multivariate logistic regression for the prediction of DKD among diabetic groups showed that HbA1c, duration of diabetes, hyperlipidemia, albuminuria, serum aldosterone, hypertension, GFR & Creatinine were significant predictors for DKD (p=0.018, 0.001, 0.007, 0,.003, 0.006, 0.007, 0.23, and <0.001 respectively).

Table 1: Baseline data among the studied groups

Variable	**Group A (N=13)**		**Group B (N=13)**		**Group C (N=13)**		**Group D (N=13)**		**F-test**	**P-value**
Age (years): ***Mean ± SD Range***	54.3 ± 10.2 39-64		50.1 ±11.5 33-62		48.9 ± 9.1 33-60		58.4 ± 8.7 40-74		2.5	0.074
Variable	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**χ 2**	**P-value**
Sex: ***Males*** ***Females***	4 9	30.8 69.2	2 11	15.4 84.6	5 8	38.5 61.5	6 7	46.2 53.8	3.1	0.383
Comorbidities: ***No*** ***DM*** ***DM-HTN*** ***DM-HTN-IHD***	13 0 0 0	100 0 0 0	0 5 7 1	0 38.5 53.8 7.7	0 6 7 0	0 46.2 53.8 0	0 1 11 1	0 7.7 84.6 7.7	59.7	**<0.001 (HS)**

DM: Diabetes mellitus, DM-HTN: Diabetes mellitus and Hypertension, DM-HTN-IHD: Diabetes mellitus, Hypertension and Ischemic heart disease Data is shown as mean ± standard deviation, prevalence was represented as percentage. Anova (F- test) and chi square (χ 2) tests were used. *HS: Highly significant*

Bold values are statistically significant at p<0.05.

Table 2: HbA1C, Lipid profile, Kidney function and electrolytes among the studied groups

Variable	Group A (N=13)	Group B (N=13)	Group C (N=13)	Group D (N=13)	F-test	P-value	LSD
HbA1C (%): ***Mean ± SD*** ***Range***	5.2± 0.2 5-5.5	8.7 ±1.9 6.1-12.6	8.4 ± 2 5.5-13	8.9 ± 1.2 7.4-11	17.7	**<0.001 (HS)**	**P1<0.001** **P2<0.001** **P3<0.001** P4,0.642 P5,0.633 P6,0.347
Cholesterol (mg/dl): ***Mean ± SD*** ***Median*** ***Range***	142.8± 46.8 130 95-220	187.5 ±66 192 118-372	177.5 ± 40.2 162 121-258	194.6 ± 39.5 201 97-240	2.8 (k)	**0.049 (S)**	**P1,0.025** **P2,0.079** **P3,0.010** P4,0.607 P5,0.715 P6,0.381
LDL (mg/dl): ***Mean ± SD*** ***Median*** ***Range***	101.5± 29.5 95 45.3-153	116.8±47.7 115 54.8-242	104.9 ± 41.5 89 57-187	103.9 ± 33.9 104 14.2-153	0.407 (k)	0.749	------
HDL (mg/dl): ***Mean ± SD*** ***Range***	69.1± 18.9 45-114	53.1 ±6.6 39.7-64	52.9 ± 15.4 29-85	79.8 ± 26.1 36-130	6.8	**0.001 (HS)**	**P1,0.030** **P2,0.027** P3,0.137 P4,0.973 **P5<0.001** **P6 <0.001**
TG (mg/dl): ***Mean ± SD*** ***Range***	67.2± 15.6 45-88	105.3 ±33.7 61-163	106.3 ± 35.7 54-167	95.9 ± 31.9 55-160	4.8	**0.005 (S)**	**P1,0.002** **P2,0.002** **P3,0.018** P4,0.933 P5,0.429 P6,0.382
S. creatinine (mg/dl): ***Mean ± SD*** ***Median*** ***Range***	0.53± 0.12 0.5 0.4-0.7	0.85 ±0.16 0.9 0.4-1.1	0.99 ± 0.6 0.8 0.6-2.8	1.2 ± 0.79 0.9 0.7-3.7	3.7 (k)	**0.017 (S)**	P1,0.113 **P2,0.028** **P3,0.002** P4,0.518 P5,0.107 P6,0.326
eGFR: ***Mean ± SD*** ***Median*** ***Range***	120.5± 12.9 127 95-131	86.3 ±13.8 83.6 68.7-116	88.6 ± 27.7 95.1 19.6-120.1	68.2 ± 29.3 65.4 15-120.1	12.4	**<0.001 (HS)**	**P1<0.001** **P2,0.001** **P3<0.001** P4,0.795 **P5,0.044** **P6,0.024**
Alb/Cr ratio: ***Mean ± SD*** ***Median*** ***Range***	9.1± 2.3 9.1 6-14	18.2 ±6 16.7 7.6-29.6	102.7 ± 78 74.5 36-282	701 ± 430.8 360 324-1663.9	29.8 (k)	**<0.001 (HS)**	**P1,0.001** **P2<0.001** **P3<0.001** **P4<0.001** **P5<0.001** **P6<0.001**

HBA1c: Hemoglobin A1c, LDL: Low density lipoprotein, HDL: High density lipoprotein, TG: triglycerides, S. Creatinine: Serum creatinine, eGFR: estimated Glomerular filtration rate, Alb/Cr: Albumin/Creatinine
P1: Group A vs Group B P2: Group A vs Group C P3: Group A vs Group D P4: Group B vs Group C P5: Group B vs Group D P6: Group C vs Group D, LSD: Least significant difference.

Table 3: S. Aldosterone and S. renin among the studied groups:

Variable	Group A (N=13)	Group B (N=13)	Group C (N=13)	Group D (N=13)	F-test	P-value	LSD
S. Aldosterone (Nmg/dl): ***Mean ± SD*** ***Median*** ***Range***	22.3± 14.4 20.1 4.3-42.1	118.2 ±155.1 54.5 30.9-608.9	213.7 ± 379.9 133.1 3.3-1460.2	644.5 ±395.3 870.4 5.3-1002.1	12.1	**<0.001 (HS)**	**P1<0.001** **P2<0.001** **P3<0.001** **P4<0.001** **P5<0.001** **P6<0.001**
S. renin (Nmg/dl): ***Mean ± SD*** ***Median*** ***Range***	0.59± 0.25 0.62 0.11-0.96	0.399±0.28 0.42 0.06-1.03	0.24 ± 0.17 0.19 0.02-0.62	1.1 ± 1 0.73 0.04-2.8	6.6	**0.001 (HS)**	P1,0.375 P2,0.107 **P3,0.015** P4,0.459 **P5,0.001** **P6<0.001**

S. Aldosterone: serum aldosterone, S. renin: Serum renin
P1: Group A vs Group B P2: Group A vs Group C P3: Group A vs Group D
P4: Group B vs Group C P5: Group B vs Group D P6: Group C vs Group D

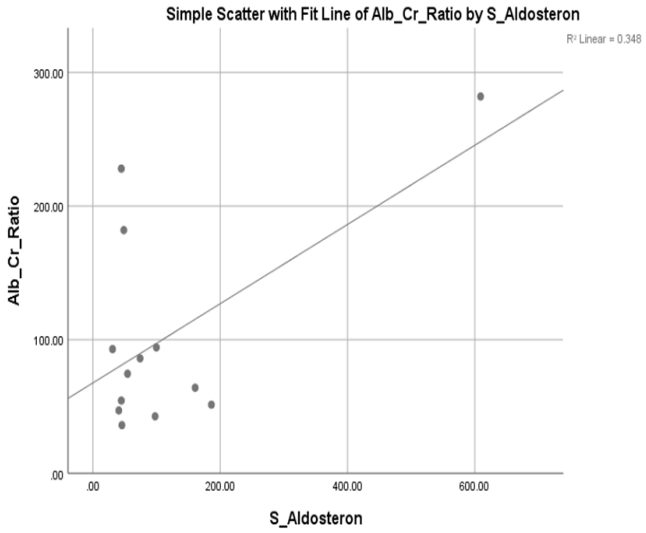
Table 4: Correlations between S. Aldosterone and other laboratory measures among groups A, B, C, and D
HBA1c: Hemoglobin A1c, LDL: Low density lipoprotein, HDL: High density lipoprotein, TG: triglycerides, S. Creatinine

Variable	S. Aldosterone Group A		S. Aldosterone Group B		S. Aldosterone Group C		S. Aldosterone Group D	
	r	p-value	r	p-value	r	p-value	r	p-value
HbA1C	0.162	0.597	-0.083	0.788	0.046	0.882	-0.354	0.456
Cholesterol	0.383	0.197	-0.344	0.250	-0.297	0.325	-0.307	0.307
LDL	0.480	0.097	-0.289	0.388	-0.269	0.232	-0.085	0.782
HDL	0.249	0.411	-0.048	0.881	**-0.615**	**0.025**	**0.570**	**0.042**
TG	-0.226	0.459	-0.023	0.941	-0.415	0.155	0.511	0.074
Alb/Cr ratio	0.278	0.357	**0.590**	**0.034**	**0.581**	**0.037**	**-0.687**	**0.009**
S. creatinine	0.165	0.590	0.079	0.798	0.182	0.551	-0.342	0.252
Na	0.333	0.266	0.291	0.344	-0.242	0.425	0.232	0.446
K	0.277	0.359	-0.297	0.360	-0.180	0.556	**0.664**	**0.013**
eGFR	-0.194	0.252	0.051	0.868	-0.354	0.235	-0.179	0.558
Hgb	-0.204	0.503	0.917	0.519	0.103	0.737	0.422	0.151
TLC	0.221	0.469	-0.242	0.426	-0.232	0.445	**-0.603**	**0.029**
S. Renin	-0.09	0.756	-0.137	0.655	**0.705**	**0.007**	0.167	0.108

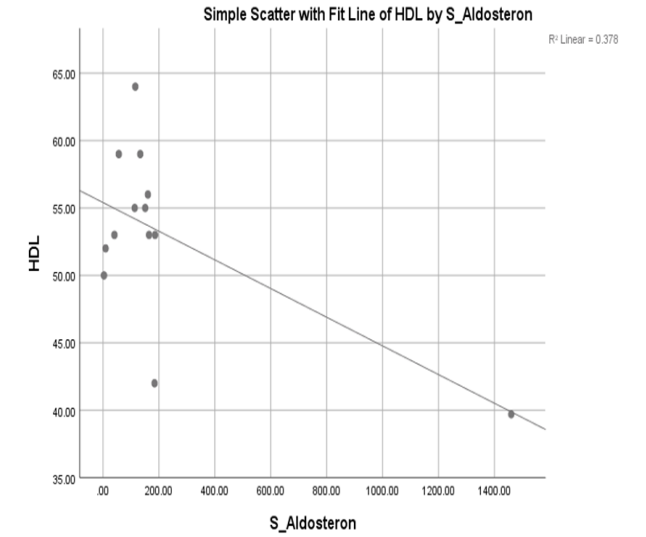
Table 5: Multivariate logistic regression for prediction of DKD among diabetic groups

Variable	B	S.E	Wald	O.R (95%C.I)	P-value
HbA1c	0.62	0.26	5.63	1.86 (1.11-3.12)	**0.018**
Duration of DM	0.15	0.04	13.8	1.07 (1.07-1.26)	**0.001**
Hyperlipidemia	0.17	0.25	7.6	1.99 (1.17-1.27)	**0.007**
Albuminuria	1.03	0.35	8.67	2.8 (1.41-5.57)	**0.003**
Serum aldosterone	0.13	0.04	7.6	1.14(1.03-1.25)	**0.006**
HTN	0.08	0.03	7.7	1.09 (1.02-1.15)	**0.007**
GFR	0.61	0.30	5.08	1.82 (1.11-3.4)	**0.23**
Serum Creatinine	0.65	0.81	12.2	1.92 (1.15-4.3)	**<0.001**

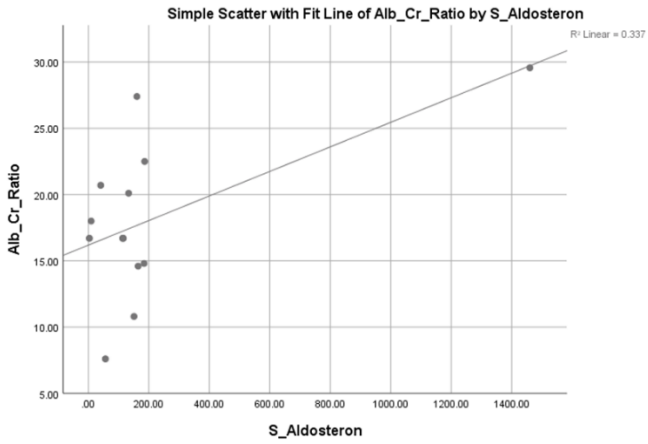
HbA1c: Hemoglobin A1c,DM: Diabetes mellitus, GFR: Glomerular filtration rate, HTN: Hypertension



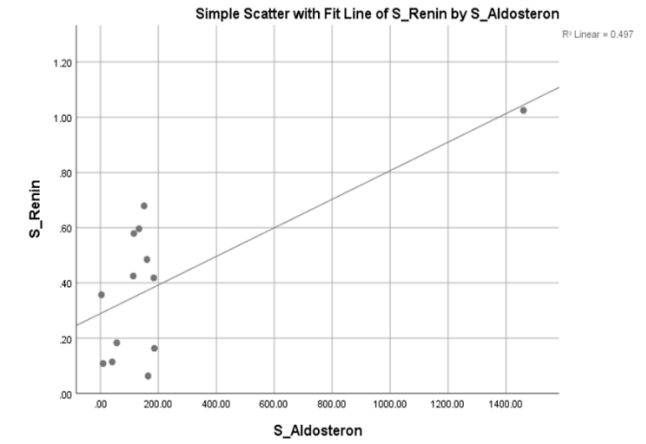
(A) Positive correlation between s. aldosterone and Alb/Cr ratio among group B



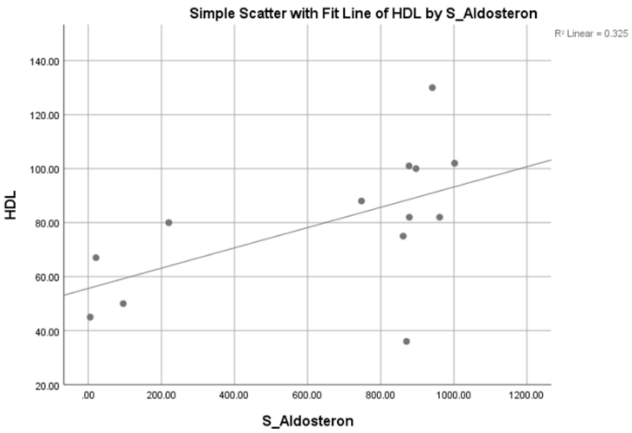
(B) Negative correlation between s. aldosterone and HDL among group C



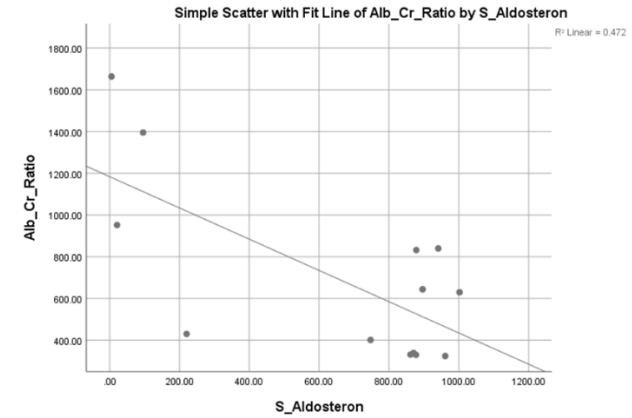
(C) Positive correlation between s. aldosterone and Alb/Cr ratio among group C



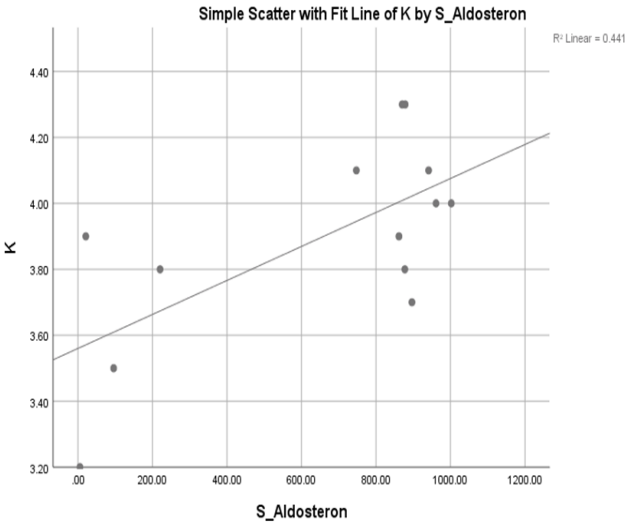
(D) Positive correlation between s. aldosterone and s. renin among group C.



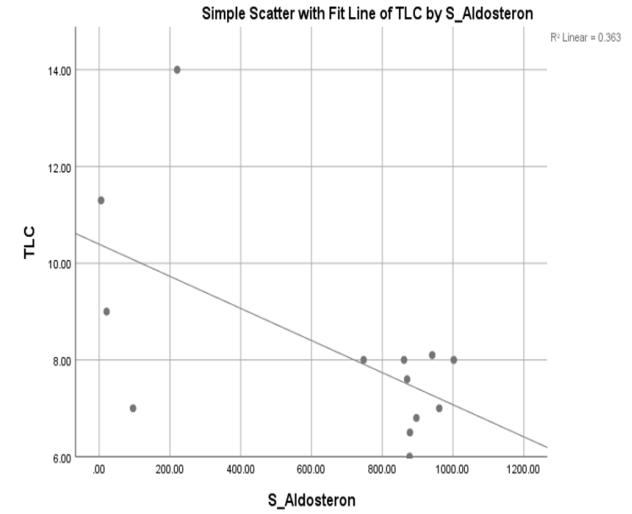
(E) Positive correlation between s. aldosterone and HDL among group D



(F) Negative correlation between s. aldosterone and Alb/Cr ratio among group D



(G) Positive correlation between s. aldosterone and K among group D.



(H) Negative correlation between s. aldosterone and TLC among group D

Figure 1: Correlations between s. aldosterone other laboratory measures among groups B, C, and D

DISCUSSION

Hyperglycemia, lipid abnormalities, and hypertension are some of the many variables that lead to diabetic nephropathy [7]. Constriction of blood vessels, hypertension, and an increase in sodium reabsorption—all of which contribute to the gradual deterioration of renal function—are all well-documented effects of the renin-angiotensin-aldosterone system [8]. One in ten people with hypertension have primary aldosteronism (PA), an endocrine disease that causes the blood pressure to rise. People with PA have low plasma renin activity (PRA) and high plasma aldosterone (PAC) [9,10].

Proteinuria and the progression of renal injury are strongly associated with aldosterone's promotion of sodium (Na) reabsorption through the mineral corticoid receptor (MR) on renal tubular epithelial cells, leading to an increase in fluid volume and blood pressure. It is known that MR induces vascular damage by a mechanism that is not dependent on high pressure; it is present in renal tubular epithelial cells, vascular endothelial cells, mesangial cells, and other types of cells [5,11]. Few studies have examined aldosterone's role in diabetic nephropathy patients' kidney damage progression.

The current study revealed a statistically significant difference in age between the groups analyzed, with the oldest participants having macroalbuminuria ($p \leq 0.001$). In concordance with the current study, Salman et al. [12] revealed that type II diabetic patients with macroalbuminuria were significantly older than those with microalbuminuria and no

albuminuria. Still, there was no significant difference as regards sex. However, Mohamed et al. [13] showed that there was no significant difference between the normoalbuminuric DM, microalbuminuric DM, macroalbuminuria DM, and control groups as regards age and sex. This could be attributed due to different inclusion criteria, as in the present study the older age and longer duration of the disease could be predictive factors for diabetic complications.

Concerning comorbidities, there was a highly statistically significant difference among the four groups that were analyzed ($p \leq 0.001$), as patients with macroalbuminuria have a significantly higher incidence of comorbidities (mainly HTN) compared to the other diabetic groups. In concordance with the current study, Thi et al. [14] revealed that the patients with macroalbuminuria have significant SBP &DBP compared to those with microalbuminuria, normoalbuminuric, and control groups. Also, Tsai et al. [15] showed that the patients with macroalbuminuria and microalbuminuria have significantly higher SBP& DBP compared to normoalbuminuric group

There was a highly statistically significant difference between the four studied groups as regards HbA1C ($P<0.001$), cholesterol, HDL, and TG ($p<0.005$ for each), as diabetic groups have significantly higher HbA1C, cholesterol, and TG compared to the non-diabetic group. In line with the current study, Thi et al. [14] revealed that there was a highly significant difference between the normoalbuminuric DM, microalbuminuria DM, macroalbuminuria DM, and control groups as regards HbA1C. However, the macroalbuminuria DM group has significantly higher HbA1C, followed by the microalbuminuria group and then normo-albuminuria.

Also, Mohamed et al. [13] revealed that there was a highly significant difference between the normoalbuminuric DM, microalbuminuria DM, macroalbuminuria DM, and control groups as regards HbA1C.

The current study results were in line with Mohamed et al. [13], who showed that there was a significant difference between the normoalbuminuric DM, microalbuminuria DM, macroalbuminuria DM, and control groups as regards lipid profile as there was higher LDL, TC, and TG in macroalbuminuria group followed by microalbuminuria group compared to the other groups.

Regarding renal functions, the current study showed that there was a highly statistically significant difference between the four studied groups as regards creatinine, eGFR, and Alb/Cr ratio ($p \leq 0.001$), as the DM patients in macroalbuminuria group have higher kidney injury (higher creatinine, low eGFR, and higher Alb/Cr ratio) followed by microalbuminuria group. Also, in concordance with the present study, Rabie et al. [16] revealed that there was a highly significant difference in Creatinine, e-GFR, and Urea among the microalbuminuria DM, macroalbuminuria DM, and control groups.

Regarding S. Aldosterone among the studied groups, it was revealed that that there was highly statistically significant difference between the four studied groups ad regard S. Aldosterone ($p \leq 0.001$); there was highly statistically significant difference between each group and another. The highest mean S. Aldosterone was found in macroalbuminuria patients, followed by microalbuminuria, then normoalbuminuria groups, and the lowest level was found in the control group.

There was a highly statistically significant difference between the four studied groups as regards S. renin ($p \leq 0.001$); there was a statistically significant difference between the control group and macroalbuminuria group ($p \leq 0.05$) and a highly statistically significant difference between the normo-albuminuria group vs macroalbuminuria group & microalbuminuria group vs macroalbuminuria group ($p \leq 0.001$).

The metabolic and other pathophysiological changes, inflammation, oxidative stress, and fibrotic effects in the cardiovascular system, kidneys, and heart can all be caused by an excess of aldosterone. Interconnected changes in these processes lead to metabolic abnormalities, CAD, and renal failure [17].

Katsuragawa et al. [18] Our findings on the role of S. aldosterone in diabetic nephropathy are supported by multiple regression analysis, which showed that elevated S. aldosterone was associated with a decreased estimated glomerular filtration rate among patients with type 2 diabetes, regardless of age, sex, glycated hemoglobin, diuretic use, or hypertension ($P = 0.025$). As well, Frimodt-Møller et al. [19] concluded that an essential factor in the establishment of renal and cardiovascular problems, aldosterone promotes inflammation and fibrosis.

In concordance with the current study, Dart et al. [20] concluded that Higher serum aldosterone is associated with albuminuria in youth with type 2 diabetes. Also, Catena et al. [21] Microalbuminuria was found to be associated with higher plasma aldosterone levels in a logistic regression model. This association was found to be true regardless of

glomerular filtration or other demographic, anthropometric, or metabolic factors. Moreover, Deo et al. [22] revealed that there was a significant association between elevated aldosterone levels and impaired renal functions (lower eGFR) and elevated albumin levels. Also, Minakuchi et al. [23], in their linear regression analysis, demonstrated a strong correlation between the yearly change in eGFR and the concentration of plasma aldosterone.

The present study showed that there was a highly significant difference in S. renin levels among the four groups: the control group compared to the macroalbuminuria group ($p \leq 0.05$), the normo-albuminuria group compared to the macroalbuminuria group ($p \leq 0.001$), and the microalbuminuria group compared to the macroalbuminuria group ($p \leq 0.001$). This was in line with Qiao et al. [24], who concluded that the Prescription of renin-angiotensin system blockage was more likely to occur in patients with higher albuminuria levels.

Also, Akbariromani et al. [25], in their meta-analysis, confirmed the association between renin level and Alb/Cr ratio level. They concluded that direct renin inhibitors slow down the progression of diabetic kidney disease.

In the normo-albuminuria diabetic group, a statistically significant strong positive correlation was found between s. aldosterone and Alb/Cr ratio ($p<0.05$). In the microalbuminuria diabetic group, a statistically significant strong negative correlation was found between s. aldosterone and HDL, while a statistically significant strong positive correlation was found between s. aldosterone and Alb/Cr ratio & s. renin ($p<0.05$). In the macroalbuminuria diabetic group, a statistically significant strong negative correlation was found between s. aldosterone and Alb/Cr ratio & TLC while a statistically significant strong positive correlation was found between s. aldosterone and HDL & K ($p<0.05$)

The results mentioned above established the significant role of s. aldosterone in the progression of diabetic kidney disease among DM patients with normal-, micro-, and macro-albuminuria, but these primary results need to be confirmed with larger studies.

Interestingly s. aldosterone and Alb/Cr ratio were positively correlated in normal- and micro-albuminuria groups, but the correlation reversed to a negative correlation among the macro-albuminuria group the presence of other contributors in s may explain this. Aldosterone level among the macro-albuminuria group, such as the presence of a negative correlation between s. aldosterone and TLC. High blood lymphocyte count may play a causal role in the development of hypertension [26], which was the main reason for albuminuria. Also, the current study showed a strong positive correlation between s. aldosterone and HDL&K, HDL was significantly positively associated with hypertension [27], while serum potassium was negatively correlated with blood pressure [28].

Li et al. [29] demonstrated a positive correlation between serum aldosterone and Alb/Cr ratio ($r=0.135$, $P<0.001$), which is in line with the present investigation. A higher probability of macro-albuminuria was linked to higher quintiles of blood aldosterone levels, according to multivariate logistic regression ($P<0.001$). Our results were supported by Deo et al. [22], who revealed that Higher levels of aldosterone were found to be independently linked to the development of end-stage renal disease in individuals with chronic kidney disease.

An essential process in the onset and advancement of chronic kidney disease (CKD) and cardiovascular disease is the activation of the renin-angiotensin-aldosterone system. Although the effects of RAAS blocking on type 1 and people with type 2 diabetes vary with CKD stage, randomized trials show that it is helpful in lowering cardiovascular events and preventing or slowing the progression of CKD [30].

Blood pressure (BP) and urine protein levels can be efficiently managed with drugs that block the renin-angiotensin-aldosterone pathway. This can slow down the evolution of renal disease and avoid the development of cardiovascular disease (CVD). As a result, the current therapy guidelines mostly advocate RAAS inhibitors, which include ACEIs and ARBs or angiotensin-converting enzyme inhibitors [31].

LIMITATIONS

The current study was done in one center on a relatively small sample size, it is required to do additional research, including longer follow-up and multicenter practice. Additional research is required to determine if the comparatively high aldosterone levels are the result of elevated aldosterone release or elevated aldosterone production by the kidneys. To better understand our findings and to find factors that contribute to the worsening of renal illness, more randomized controlled trials with bigger samples and longer follow-up periods are required. To determine whether ACE/ARB with aldosterone antagonists can alleviate the renal disease load in this high-risk group of patients, more research is required.

Author contribution: All authors contributed to the study. MK was responsible for selecting the subject, NAS was responsible for laboratory revisions and analysis, NWE was responsible for data collection, statistical analysis, and initial writing, and KAE was responsible for collecting the data of the studied cases, and all shared for the formulation of the study design, editing, revision, and preparation of the final manuscript.

CONCLUSION

A high serum aldosterone level was found to be associated with worsening diabetic kidney disease, according to the present research. Independently linked with DKD development and incident of ESRD, serum aldosterone concentrations were found to be inversely correlated with the estimated glomerular filtration rate (eGFR). So, serum aldosterone levels could have a significant role in the progression of diabetic kidney disease.

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To Cite:

Kamar, M., Sabbah, N., EL Sayed, N., El-Banna, K. Serum Aldosterone Level in Different Stages of Diabetic Kidney Disease in Type 2 Diabetes Mellitus. *Zagazig University Medical Journal*, 2024; (1879-1889): -. doi: 10.21608/zumj.2024.257905.3067