Original Research Article

Association between urinary albumin excretion and serum dehydroepiandrosterone sulfate concentrations with diabetic retinopathy in type 2 diabetic men at Eastern India

Amrito Biswas[1], Prithwijit Banerjee[2], Sisir Chakraborty[3], Ratneswar Bhattacharyya[4*],Sukanta Sen[5], A K Basu[6]

[1]RMO cum Clinical Tutor, Department of Medicine, College of Medicine & Sagore Dutta Hospital, Kamarhati, Kolkata, West Bengal, India

[2]Associate Professor, Department of Pharmacology, College of Medicine & Sagore Dutta Hospital, Kamarhati, Kolkata,West Bengal, India

[3]Assistant Professor, Department of Medicine, College of Medicine & Sagore Dutta Hospital, Kamarhati, Kolkata, West Bengal, India

[4]Associate Professor, Department of General Medicine, ICARE Institute of Medical Sciences and Research, PO-Balughata, Haldia, Purba Medinipur, West Bengal, India

[5]Professor & Head, Department of Pharmacology, ICARE Institute of Medical Sciences and Research, PO-Balughata, Haldia, Purba Medinipur, West Bengal, India

[6]Professor & Head, Department of Endocrinology and Metabolism, Medical College and Hospital, 88, College Street, Kolkata, West Bengal, India

Received: 07-07-2020 / Revised: 25-08-2020 / Accepted: 30-08-2020

Abstract

Background: Diabetic retinopathy is one of the leading causes of blindness in working-age individuals. The relationship between urinary albumin excretion (UAE) and serum dehydroepiandrosterone sulfate concentrations with diabetic complications like development of retinopathy in type 2 diabetes has not been studied in a Eastern part of India. **Materials & Methods:** In this cross-sectional study, 100 type 2 diabetic male patients aged between 40-70 years attending Medicine OPD, Endocrine OPD, or admitted in Medicine IPD, Medical College & Hospital, Kolkata who fulfilled inclusion and exclusion criteria were included. Ophthalmological examination like direct ophthalmoscopy, indirect ophthalmoscopy with 20 D lens and slit lamp bimicroscopy with 90 D lens Laboratory investigations like FBS, PPBS**,** HbA1c and serum DHEAS concentration were done**.** Spot morning urine sample 5ml for routine and microscopic examination, for culture sensitivity and albumin-creatinine ratio (ACR) were done. Serum DHEAS concentration was measured by taking 2 ml of blood from each patient and was measured by chemiluminescent microparticle immunoassay. **Results:** Serum DHEAS concentrations were lower in patients of microalbuminuric group (107.97 ± 6.68) compared to patients of normoalbuminuric group (125.74 ± 4.76). Serum DHEAS concentrations were also low in patients of macroalbuminuric group (89 ± 6.51) compared to patients in microalbuminuric and normoalbuminuric group. Among 100 patients of type 2 diabetes 45 patients (45%) were detected to have no/mild NPDR (non proliferative diabetic retinopathy), 31 patients (31%) were having moderate-severe NPDR and the rest 24 patients (24%) were having PDR (proliferative diabetic retinopathy). **Conclusion:** Our study provides insight for investigating effects of DHEA on the prevention of diabetic microangiopathy and macroangiopathy.

Keywords: Type 2 diabetes, microalbuminuria, diabetic retinopathy, urinary albumin excretion [UAE], serum dehydroepiandrosterone sulfate concentrations [DHEA]

**Correspondence*

Dr. Ratneswar Bhattacharyya

Associate Professor, Department of General Medicine, ICARE Institute of Medical Sciences and Research, PO-Balughata, Haldia, Purba Medinipur, West Bengal, India.

E- mail: drsukant@gmail.com

Introduction

Diabetic retinopathy is one of the leading causes of blindness in the world that increases the chance of losing the sight about 25 times higher compared to normal individuals[1]. Decrease in visual acuity in diabetic retinopathy is either associated with maculopathy or proliferative complications of it. Many studies have been undergone to find out the precipitated factors of retinopathy such as duration and type of diabetes, hyperglycemia, pregnancy, change in hormonal level, genetics and microalbuminuria[2,3]. Using new surgical and medical techniques, the incidence of blindness can be reduced up to 90%[4].The more advanced the DR, the greater the risk of visual loss. Furthermore, patients with DR are at higher risk for coronary heart disease, stroke, diabetic nephropathy, limb amputations, and death[5]. The main risk factors for the development or progression of DR are duration of diabetes mellitus[6], poor glycemic control[7,8] and hypertension[9].Microalbuminuria, which is defined as a urinary albumin to creatinine ratio (UACR) between 30 to 300 mg/g, is a known predictive marker of cardiovascular disease (CVD) and mortality in individuals with and without diabetes[10]. Elevated urinary albumin excretion is also associated with increased risk of cardiovascular mortality, but the pathophysiologic mechanism underlying this association is poorly understood. Dysfunction of the vascular endothelium and chronic low-grade inflammation may be key features of the pathophysiology of both atherosclerosis and microalbuminuria[11]Dehydroepiandrosterone(DHEA) and its sulfate ester DHEA sulfate (DHEA-S) together represent the most abundant adrenally produced steroid. DHEA-S, which is converted to active DHEA in a linear manner, is a good marker for DHEA availability. DHEA is a weak androgen that contributes to androgenicity mainly after peripheral conversion to more potent androgens, such as testosterone and dihydrotestosterone[12,13].

Decreased serum concentrations of DHEA may contribute to insulin resistance, while DHEA supplementation appears to improve insulin sensitivity and may slow the progression of type 2 diabetes[14,15]. Decreased serum concentrations of DHEA are associated with dysfunction of the vascular endothelium and chronic low-grade inflammation[16].

The considerations above raise the possibility of DHEA as a causal intermediate linking urinary albumin excretion to CVD and diabetic angiopathy. We therefore investigated the relationship between degree of urinary albumin excretion and serum DHEA-S concentrations in male patients with type 2 diabetes.

Materials & methods

In this cross-sectional study, 100 type 2 diabetic male patients aged between 40-70 years attending Medicine OPD, Endocrine OPD, or admitted in Medicine IPD, Medical College & Hospital, Kolkata who fulfilled inclusion and exclusion criteria were included. Study period was between March 2013 – June 2014. Clinical examinations findings, history taking data of study participants were captured. Ophthalmological examination like direct ophthalmoscopy, indirect ophthalmoscopy with 20 D lens and slit lamp bimicroscopy with 90 D lens Laboratory investigations like fasting blood sugar (FBS), post prandial blood sugar, serum creatinine, glycemic control (HbA1c) and serum DHEAS concentration were done. Spot morning urine sample 5ml for routine and microscopic examination, for culture sensitivity and albumin-creatinine ratio (ACR) were done. They were asked for any history suggestive of IHD and diabetic retinopathy. Systolic and diastolic pressure of each patient was measured by sphygmomanometer. The patients were sent to the Department of Ophthalmology for assessment of diabetic retinopathy by slit lamp biomicroscopy, direct ophthalmoscopy, indirect ophthalmoscopy. Patients were divided in 3 categories: (1) no/mild NPDR, (2) moderate to severe NPDR, (3) PDR (diabatic retinopathy was classified according to International Clinical Diabetic Retinopathy Disease Severity scale).17 All the relevant examinations were completed by an ophthalmologist and the patients were categorized according to the degree of their retinopathy.Spot urine sample was collected from each patient in aseptic manner. Urinary albumin was measured by immunoturbidimetric method and expressed as µg/dl. Urinary creatinine was measured by modified kinetic Jaffe reaction and expressed as gram per dl. ACR (albumin is to creatinine ratio was expressed as mg /gram). According to definition normoalbuminuria is urinary albumin excretion <30mg/gram of cretinine, microalbuminuria 30-300mg/gram of creatinine and macroalbuminuria >300 mg/gram of creatinine. Serum DHEAS concentration was measured by taking 2 ml of blood from each patient and was measured by chemiluminescent microparticle immunoassay. HbA1C was measured by taking 3 ml of blood in EDTA tube and was measured by high performance liquid chromatography.

Continuous variables are expressed as mean ± Standard Deviation and compared across the groups using one-way ANOVA test. The dependence of between log ACR on duration, SBP, BMI, HB1AC & serum DHEAS (µg/dL) have been separately analyzed using simple regression while the collective impact of all the variables on log ACR have been captured using multiple regression. The statistical software SPSS version 20 was used for the analysis. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

Results

Clinical characteristics of the 100 male patients with type 2 Diabetes enrolled in this study are shown in table 1. The mean and standard deviation of theprincipal characteristics of the 3 groups (normo-albuminuric, microalbuminuric,macroalbuminuric) were calculated and were compared using one way ANOVA test.

Table 1: Clinical characteristics of male patients with type 2 Diabetes [n=100]

	Category			P Value		
	Normo albuminuria	Microalbuminuria	Macroalbuminuria			
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Normo Vs Micro	Normo Vs Macro	Micro Vs Macro
Age	61.9 ± 1.4	62.1 ± 2.82	62 ± 2.64	0.674	0.837	0.900
Age of Onset	51.5 ± 2.14	50.33 ± 2.9	47.4 ± 3.69	0.043	<0.001	0.003
Duration	10.08 ± 1.61	11.77 ± 1.74	14.5 ± 3.05	<0.001	<0.001	<0.001
BMI (kg/m^2)	22.3 ± 1.13	24.19 ± 0.89	27.3 ± 1.63	<0.001	<0.001	<0.001
SBP	120.52 ± 4.04	136.27 ± 3.27	148.1 ± 3.46	<0.001	<0.001	<0.001
DBP	78.12 ± 4.54	84.4 ± 4.05	87.9 ± 2.71	<0.001	<0.001	0.001
HbA_1C (%)	7.02 ± 0.12	7.32 ± 0.09	7.77 ± 0.19	<0.001	<0.001	<0.001
Creatinine (mg/dl)	1.04 ± 0.1	1.35 ± 0.1	1.83 ± 0.21	<0.001	<0.001	<0.001
Urine ACR (mg/gm)	19.92 ± 7.14	185.53 ± 87.11	704 ± 202.13	<0.001	<0.001	<0.001

Among the 100 patients included in this study 50 patients were in normoalbuminuric group, 30 patients were in microalbuminuric group, the rest 20 were in macroalbuminuric group [Table 1].

Table 2: Age distribution among study participants

	Category			P Value		
	Normoalbuminuria	Microalbuminuria	Macroalbuminuria			
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Normo Vs Micro	Normo Vs Macro	Micro Vs Macro
Age	61.9 ± 1.4	62.1 ± 2.82	62 ± 2.64	0.674	0.837	0.900

The mean age in the normoalbuminuric group was 61.9 ± 1.4, in the microalbuminuric group was 62.1 ± 2.82 and 62 ± 2.64 in the macroalbuminuric group. Using one way ANOVA test, there was no significant difference in age distribution among the three groups [Table 2].

Table 3: Age of onset and duration of diabetes among study participants [n=100]

	Category			P Value		
	Normoalbuminuria	Microalbuminuria	Macroalbuminuria			
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Normo Vs Micro	Normo Vs Macro	Micro Vs Macro
Age of Onset	51.5 ± 2.14	50.33 ± 2.9	47.4 ± 3.69	0.043	<0.001	0.003
Duration	10.08 ± 1.61	11.77 ± 1.74	14.5 ± 3.05	<0.001	<0.001	<0.001

There were significant differences in age of onset and duration of diabetes in 3 groups. Age of onset was significantly earlier in microalbuminuric group as compared to normoalbuminuric group and also for macroalbuminuric group as compared to normoalbuminuric and microalbuminuric group. Similarly duration of diabetes was significantly higher in microalbuminuric and macroalbuminuric group as compared to normoalbuminuric group [Table 3].

Table 4: Systolic and diastolic blood pressure among study participants [n=100]

	Category			P Value		
	Normoalbuminuria	Microalbuminuria	Macroalbuminuria			
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Normo Vs Micro	Normo Vs Macro	Micro Vs Macro
SBP	120.52 ± 4.04	136.27 ± 3.27	148.1 ± 3.46	<0.001	<0.001	<0.001
DBP	78.12 ± 4.54	84.4 ± 4.05	87.9 ± 2.71	<0.001	<0.001	0.001

Systolic blood pressure were significantly higher in microalbuminuric (136.27 ± 3.27) group compared to normoalbuminuric (120.52 ± 4.04) group and in macroalbuminuric(148.1 ± 3.46) group compared to microalbuminuric and normoalbuminuric group. Diastolic blood pressure were also significantly higher in microalbuminuric (84.4 ± 4.05) group compared to normoalbuminuric (78.12 ± 4.54) group and in macroalbuminuric (87.9 ± 2.71) group compared to microalbuminuric and normoalbuminuric group [Table 4].

Table 5: Serum DHEAS concentration among study participants [n=100]

	Category			P Value		
	Normoalbuminuria	Microalbuminuria	Macroalbuminuria			
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Normo Vs Micro	Normo Vs Macro	Micro Vs Macro
Serum DHEAS (ug/dl)	125.74 ± 4.76	107.97 ± 6.68	89 ± 6.51	<0.001	<0.001	<0.001

Serum DHEAS concentrations were lower in patients of microalbuminuric group (107.97 ± 6.68) compared to patients of normoalbuminuric group (125.74 ± 4.76). Serum DHEAS concentrations were also low in patients of macroalbuminuric group (89 ± 6.51) compared to patients in microalbuminuric and normoalbuminuric group [Table 5].

Table 6: Distribution of patients according to severity of diabetic retinopathy [n=100]

Degree of Retinopathy	Frequency	Percent
No/mild NPDR	45	45.0
Moderate-severe NPDR	31	31.0
PDR	24	24.0
Total	100	100.0

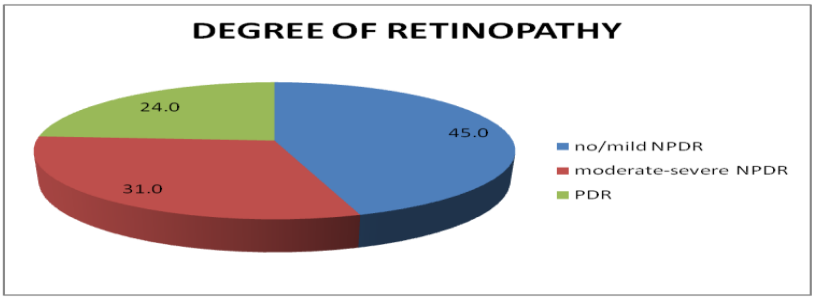

Fig 1: Distribution of patients according to severity of diabetic retinopathy [n=100]

Among 100 patients of type 2 diabetes 45 patients (45%) were detected to have no/mild NPDR (non proliferative diabetic retinopathy), 31 patients (31%) were having moderate-severe NPDR and the rest 24 patients (24%) were having PDR (proliferative diabetic retinopathy) [Table 6/Fig. 1].

Table 7: Correlation between urine ACR and degree of retinopathy in male patients with type 2 diabetes [n=100]

	Degree of retinopathy			P Value		
	No/mild NPDR (1)	Moderate-severe NPDR (2)	PDR (3)			
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	1 vs 2	1 vs 3	2 vs 3
Urine ACR	124.13 ± 209.55	272.23 ± 306.09	275.71 ± 323.42	0.01	0.02	0.96

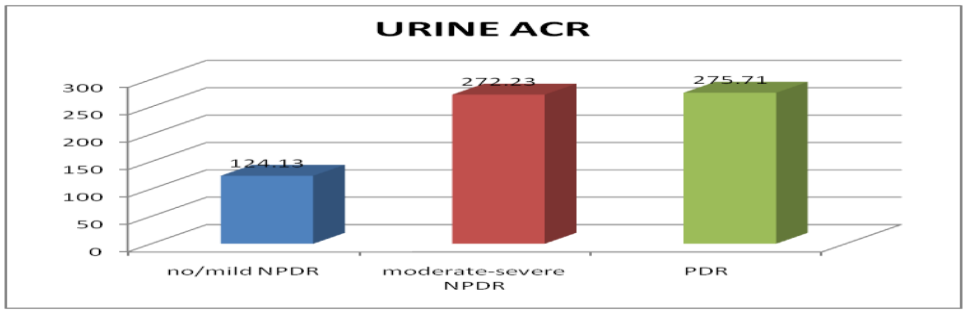

Fig 2: Correlation between urine ACR and degree of retinopathy in male patients with type 2 diabetes

The values of urine ACR in patients having moderate-severe diabetic retinopathy (272.23 ± 306.09) were significantly higher than patients having no features of retinopathy or having mild features of retinopathy (124.13 ± 209.55); p value 0.01. The values of urine ACR in patients having PDR (proliferative diabetic retinopathy) were also significantly (275.71 ± 323.42) higher than patients having no-mild NPDR (124.13 ± 209.55); p value 0.02. But there were no significant difference in urine ACR values in patients having moderate-severe NPDR (272.23 ± 306.09) and patients

having PDR (275.71 ± 323.42); p value 0.96 [Table 7/Fig. 2].

Table 8: Correlation between serum DHEAS concentration and degree of retinopathy in male patients with type 2 diabetes

	Degree of Retinopathy			P Value		
	No/mild NPDR (1)	Moderate-severe NPDR (2)	PDR (3)			
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	1 vs 2	1 vs 3	2 vs 3
Serum DHEAS(ug/dL)	118.33 ± 13.4	107.97 ± 15.46	109.75 ± 16.44	0.002	0.022	0.682

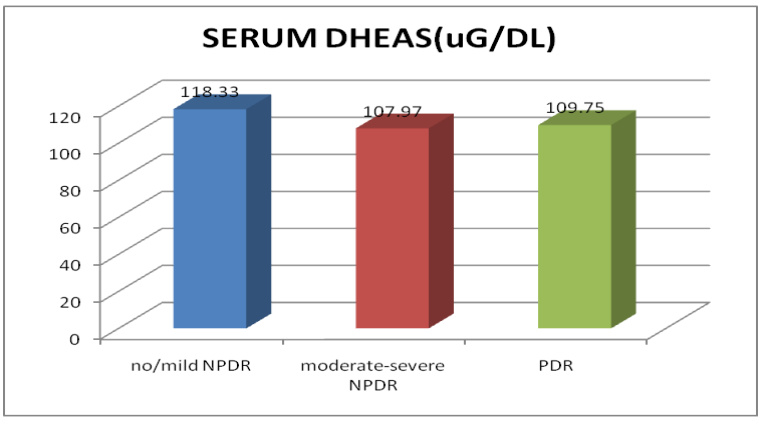

Fig 3: Correlation between serum DHEAS concentration and degree of retinopathy in male patients with type 2 diabetes

The values of serum DHEAS concentration in patients of moderate –severe NPDR (107.97 ± 15.46) were significantly lower than in patients of no- mild NPDR (118.33 ± 13.4); p value 0.002. The values of serum DHEAS concentration in patients of PDR (109.75 ± 16.44) were also significantly lower than in patients of no-mild NPDR (118.33 ± 13.4); p value 0.022. But the values of serum DHEAS concentration did not differ significantly in patients of moderate-severe NPDR (107.97 ± 15.46) and in patients of PDR (109.75 ± 16.44); p value 0.682 [Table 8/Fig. 3].

Discussion

The study titled "association between urinary albumin excretion and serum dehydroepiandrosterone sulfate concentration in male patients with type 2 Diabetes Mellitus" was done in Medical College and Hospital, Kolkata. The study comprised of 100 type 2 Diabetic male patients aged between 40 -70 years. Based on their urine ACR (urine albumin excretion) values 100 patients were subdivided in to 3 groups; normoalbuminuric group (ACR<30) / group 1, microalbuminuric group (ACR 30-300)/group 2, macroalbuminuric group (ACR>300)/group 3. Fifty patients were in normoalbuminuric group, 30 patients were in microalbuminuric group and 20 patients were in macroalbuminuric group.DHEA may also exert direct effects, **e.g.** via activation of the peroxisome proliferator-activated receptor-α and/or a yet-unidentified membrane receptor[18]. DHEA has been hypothesized to be of importance, **e.g.** for bone physiology, body composition and insulin sensitivity, immune functions and vascular physiology[19,20]. Pericyte loss is an early feature of diabetic retinopathy and represents a key step in the progression of this disease. Various pieces of evidence link the antioxidant properties of DHEA to its protective effect on glucose-induced toxicity in BRP[21]. The relationship to low-serum sex hormone-binding globulin suggests that increased androgenicity may be associated with the progression of retinopathy in male subjects with type I

diabetes[22].Various studies have been conducted to find out the correlation between sex hormones and diabetic retinopathy. Some studies have shown that sex hormone receptors are found in the human eye. Hence if the derangement in the sex hormones can be detected beforehand there are chances that we can prevent the changes occurring in the retina of the patients suffering from long standing diabetes. Interaction of steroid-receptor complexes with responsive genes containing a consensus sequence for receptor binding can result in either induction or repression of transcription, depending on the target gene and tissue[23]. A study by Haffner et al[22], suggested that changes in sex hormones may influence the development of diabetic retinopathy. They measured serum testosterone, estradiol, DHEA-S and sex hormone binding globulin levels in men and women with type I diabetes from the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), a population-based study of diabetic complications. Serum testosterone concentrations were significantly higher in male diabetic subjects with proliferative retinopathy than in male diabetic subjects with minimal or no retinopathy[22].Systolic blood pressure was significantly higher in microalbuminuric (136.27 ± 3.27) group compared to normoalbuminuric (120.52 ± 4.04) group and in macroalbuminuric (148.1 ± 3.46) group compared to microalbuminuric and normoalbuminuric group. Diastolic blood pressure was also significantly higher in microalbuminuric (84.4 ± 4.05) group compared to normoalbuminuric (78.12 ± 4.54) group and in macroalbuminuric (87.9 ± 2.71) group compared to microalbuminuric and normoalbuminuric group. In our study the mean ACR in normoalbuminuric group was 19.92 ± 7.14, in microalbuminuric group was 185.53 ± 87.11 and in macroalbuminuric group was 704 ± 202.13. Using ANOVA test there was significant difference in mean ACR in the 3 groups.Our study found serum DHEAS concentrations were significantly lower in patients of microalbuminuric group (107.97 ± 6.68) compared to patients of normoalbuminuric group (125.74 ± 4.76). Serum DHEAS concentrations were also low in patients of macroalbuminuric group (89 ± 6.51) compared to patients in microalbuminuric and normoalbuminuric group. These results were in concordance with the previous studies done by Fukui *et al*. which showed significantly lower concentration of serum DHEAS in macroalbuminuric and microalbuminuric patients compared to normoalbuminuric patients [24,25].In the present study among 100 patients of type 2 diabetes 45 patients (45%) were detected to have no/mild NPDR (non proliferative diabetic retinopathy), 31 patients (31%) were having moderate–severe NPDR and the rest 24 patients (24%) were having PDR (proliferative diabetic retinopathy). The values of urine ACR in patients having moderate–severe diabetic retinopathy (272.23 ± 306.09) were significantly higher than patients having no features of retinopathy or having mild features of retinopathy (124.13 ± 209.55); p value 0.01. The values of urine ACR in patients having PDR (proliferative diabetic retinopathy) was also significantly (275.71 ± 323.42) higher than patients having no-mild NPDR (124.13 ± 209.55) with p value 0.02. But there were no significant difference in urine ACR values in patients having moderate-severe NPDR (272.23 ± 306.09) and patients having PDR (275.71 ± 323.42); p value 0.96. These results were concordant with the population based cross sectional study conducted in cohort of 1414 subjects with type 2 diabetes from Chennai metropolis in Sankara Netralaya, Chennai[26] that revealed individuals with macroalbuminuria in comparison to micro- or normoalbuminuria showed a greater prevalence of DR (60.5% vs. 31.0% vs. 14.1%, $p < 0.001$), and also a greater severity of the disease (60.9% vs. 21.4 vs. 9.9, $p < 0.001$). According to this study conducted in Chennai every sixth individual in the population of type 2 diabetes is likely to have albuminuria. Subjects with microalbuminuria were around 2 times as likely to have DR as those without microalbuminuria, and this risk became almost 6 times in the presence of macroalbuminuria[26].In the present study the values of serum DHEAS concentration in patients of moderate-severe NPDR (107.97 ± 15.46) were significantly lower than in patients of no- mild NPDR (118.33 ± 13.4); p value 0.002. The values of serum DHEAS concentration in patients of PDR (109.75 ± 16.44) were also significantly lower than in patients of no-mild NPDR (118.33 ± 13.4); p value 0.022. But the values of serum DHEAS concentration did not differ significantly in patients of moderate-severe NPDR (107.97 ± 15.46) and in patients of PDR (109.75 ± 16.44); p value 0.682.These results were different from the previous studies done by Fukui et al. which showed no relation of diabetic retinopathy with serum DHEAS concentration. In the study done by Fukui et al. Serum DHEA-S concentrations did not differ among patients with no diabetic retinopathy, those with simple diabetic retinopathy, and those with proliferative diabetic retinopathy[25,26]. In the present study conducted by us, by simple regression analysis we find a significant

inverse correlation between serum DHEAS concentration and log ACR with r square value of 0.947 and p value of <0.001.Savage S et al study revealed that UAE was significantly associated with the presence of retinopathy ($P < 0.001$), neuropathy ($P < 0.001$), and cardiovascular disease ($P < 0.001$). In the multiple logistic regression analyses, UAE had strong independent associations with retinopathy, neuropathy, and cardiovascular disease[27]. Manaviat MR et al study showed that in addition to HbA1c, BMI, and length of illness, microalbuminuria is a contributing factor in the degree of retinopathy ($p = 0.001$) and this correlation can be explained by the common mechanism involved in tissue damage by all those factors[2].Fukui M et al study showed serum DHEA-S concentration, which correlated inversely with degree of urinary albumin excretion, may contribute to the link between elevated urinary albumin excretion and higher CVD mortality in male patients with type 2 diabetes[25]. They showed serum DHEA-S concentrations were lower in patients with macroalbuminuria (866.5 ± 523.8 ng/ml, $\mathbf{P} < 0.0001$) and in those with microalbuminuria (1,014.4 ± 525.3 ng/ml, $\mathbf{P} = 0.0006$) than in patients with normoalbuminuria (1,232.6 ± 542.4 ng/ml). Serum DHEA-S concentration correlated inversely with log (urinary albumin excretion) ($\mathbf{r} = -0.227$, $\mathbf{P} < 0.0001$). Multiple regression analysis demonstrated that duration of diabetes ($\beta = 0.147$, $\mathbf{P} = 0.0075$), HbA_{1c} ($\beta = 0.156$, $\mathbf{P} = 0.0048$), BMI ($\beta = 0.194$, $\mathbf{P} = 0.0007$), systolic blood pressure ($\beta = 0.195$, $\mathbf{P} = 0.0005$), and serum DHEA-S concentration ($\beta = -0.192$, $\mathbf{P} = 0.0010$) were independent determinants of log (urinary albumin excretion)**[24].**

Limitations of the Study

The nature of investigations involved was too costly to be carried out in a government hospital setup. This limited the study population to only 100 cases. There was no age matched controls without diabetes to compare for the serum DHEAS concentration levels. recall bias by the patient regarding the duration of diabetes and duration of treatment. The cross sectional nature of the study did not permit the determination of causality. Large longitudinal prospective trials and interventional studies are needed to better substantiate the relationship between degree of urinary albumin excretion and serum DHEA-S concentrations.

Conclusion

A significant correlation was found between albuminuria and low serum DHEAS concentration with severity of diabetic retinopathy in male patient with type 2 diabetes. Our study provides insight for investigating effects of DHEA on the prevention of diabetic microangiopathy and macroangiopathy. Thus, increasing UAE and low serum DHEAS in this type 2 diabetes was associated with an increased prevalence of diabetic retinopathy, neuropathy, and cardiovascular disease. This suggests that increase UAE and low serum DHEAS may be more than an indicator of renal disease in type 2 diabetes patients and, in fact, may reflect a state of generalized vascular damage occurring throughout the body. Large scale prospective studies in type 2 diabetes patients are needed to determine the predictive effect of UAE and serum DHEAS and the effect of decreasing UAE and increasing serum DHEAS on future diabetic micro- and macrovascular complications.

References

1. Taylor R, Williams R. Screening for Diabetic Retinopathy: An overview. Diabetic Medicine. 1994; 13: 946-952.
2. Manaviat MR, Afkhami M, Shoja MR. Retinopathy and microalbuminuria in type II diabetic patients. BMC Ophthalmol. 2004 1;4:9.
3. Marshall SM, Alberti KG. Comparison of the prevalence and associated features of abnormal albumin excretion in insulin-dependent and non-insulin-dependent diabetes. Q J Med 1989; 70: 61-71.
4. Fonseca V, Munshi M, Lawrence M, Bradford JD. Diabetic Retinopathy, a review for the primary care physician. Southern Medical Journal 1996; 89: 123-126.
5. Aiello LP, Gardner TW, King GL, Blankenship G, Cavallerano JD, Ferris FL III, et al. Diabetic retinopathy. Diabetes Care 1998; 21: 143-156.
6. Looker HC, Krakoff J, Knowler WC, Bennett PH, Klein R, Hanson RL. Longitudinal studies of incidence and progression of diabetic retinopathy assessed by retinal photography in Pima Indians. Diabetes Care 2003; 26: 320-326.
7. Stratton IM, Kohner EM, Aldington SJ, Turner RC, Holman RR, Manley SE, et al. UKPDS 50: risk factors for incidence and progression of retinopathy in type II diabetes over 6 years from diagnosis. Diabetologia 2001; 44: 156-163.
8. Adler AI, Stratton IM, Neil HA, Yudkin JS, Matthews DR, Cull CA, et al. Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes

(UKPDS 36): prospective observational study. BMJ 2000; 321: 412-419.
9. Cignarelli M, De Cicco ML, Damato A, Paternostro A, Pagliarini S, Santoro S, et al. High systolic blood pressure increases prevalence and severity of retinopathy in NIDDM patients. Diabetes Care 1992; 15: 1002-1008.
10. Ahn HJ, Moon DS, Kang DY, et al. Urinary Albumin Excretion Reflects Cardiovascular Risk in Postmenopausal Women without Diabetes: The 2011 to 2013 Korean National Health and Nutrition Examination Survey. Endocrinol Metab (Seoul). 2016;31(4):537–546.
11. Seliger SL, Salimi S, Pierre V, Giffuni J, Katzel L, Parsa A. Microvascular endothelial dysfunction is associated with albuminuria and CKD in older adults. BMC Nephrol. 2016;17(1):82.
12. Baulieu EE, Thomas G, Legrain S, et al. Dehydroepiandrosterone (DHEA), DHEA sulfate, and aging: contribution of the DHEAge Study to a sociobiomedical issue. Proc Natl Acad Sci USA. 2000; 97(8):4279-4284.
13. Lois K, Kassi E, Prokopiou M, et al. Adrenal Androgens and Aging. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279006/
14. Nestler JE, Usiskin KS, Barlascini CO, Welty DF, Clore JN, Blackard WG. Suppression of serum dehydroepiandrosterone sulfate levels by insulin: an evaluation of possible mechanisms. Journal of Clinical Endocrinology and Metabolism 1989; 69; 1040-1046.
15. Smith S, Ravnikar VA, Barbieri RL. Androgen and insulin response to an oral glucose challenge in hyperandrogenic women.Fertility and Sterility 1987; 48: 72-77.
16. Mannic T, Viguie J, Rossier MF. In vivo and in vitro evidences of dehydroepiandrosterone protective role on the cardiovascular system. Int J Endocrinol Metab. 2015;13(2):e24660.
17. Wilkinson CP, Ferris FL, 3rd, Klein RE, Lee PP, Agardh CA, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology. 2003; 110:1677–82.
18. Webb SJ, Geoghegan TE, Prough RA, Michael Miller KK. The biological actions of dehydroepiandrosterone involves multiple receptors. Drug Metab Rev. 2006; 38(1-2):89–116.
19. Tchernof A, Labrie F. Dehydroepiandrosterone, obesity and cardiovascular disease risk: a review of human studies. Eur J Endocrinol. 2004;151(1):1-14.
20. Dillon JS. Dehydroepiandrosterone, dehydro epiandrosterone sulfate and related steroids: their role in inflammatory, allergic and immunological disorders. Curr Drug Targets Inflamm Allergy. 2005;4(3):377-85.
21. Brignardello E, Beltramo E, Molinatti PA, Aragno M, Gatto V, Tamagno E, et al. Dehydroepiandrosterone protects bovine retinal capillary pericytes against glucose toxicity. J Endocrinol. 1998 ;158(1):21-6.
22. Haffner SM, Klein R, Moss SE, Klein BE. Sex hormones and the incidence of severe retinopathy in male subjects with type I diabetes. Ophthalmology. 1993;100(12):1782-6.
23. Anjum A, Waris A, Akhtar N, Ahmed A, Ahmed S. Diabetic Retinopathy and Sex Hormones. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 2017; 16(1):110-115.
24. Fukui M, Kitagawa Y, Nakamura N, Kadono M, Hasegawa G, Yoshikawa T. Association between urinary albumin excretion and serum dehydroepiandrosterone sulfate concentration in male patients with type 2 diabetes: a possible link between urinary albumin excretion and cardiovascular disease. Diabetes Care 2004; 27:2893–2897.
25. Fukui M, Kitagawa Y Kamiuchi K, Hasegawa G, Yoshikawa T, Nakamura N. Low serum dehydroepiandrosterone sulfate concentration is a predictor for deterioration of urinary albumin excretion in male patients with type 2 diabetes. Diabetes Res Clin Pract. 2006; 73(1):47-50.
26. Rani PK, Raman R, Gupta A, Pal SS, Kulothungan V, Sharma T. Albuminuria and Diabetic Retinopathy in Type 2 Diabetes Mellitus Sankara Nethralaya Diabetic Retinopathy Epidemiology And Molecular Genetic Study (SN-DREAMS, report 12). Diabetol Metab Syndr. 2011;3(1):9.
27. Savage S, Estacio RO, Jeffers B, Schrier RW. Urinary albumin excretion as a predictor of diabetic retinopathy, neuropathy, and cardiovascular disease in NIDDM. Diabetes Care. 1996;19(11):1243-8.

Source of Support:Nil
Conflict of Interest: Nil