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Pulse Pressure in Diabetic Microalbuminuric Adults: An Observation from a Single Centre in Eastern India

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The prevalence of diabetes and diabetic complications are increasing exponentially day by day. People developing one type of diabetic complication are prone to develop another type of diabetic complication as the basic pathophysiologic mechanisms behind their development remain the same. We aimed to study the pattern of pulse pressure and its associated factorsamong type 2 diabetic subjects with microalbuminuria. The study was conducted at a specialized diabetes care facility in Eastern India involving 260microalbuminuric diabetic adults aged between 18 to 70 years.Our findings showed a higher prevalence of wide pulse pressure in 84% of the participants. It suggested that wider pulse pressure was associated with male gender, elder participants and those with elevated HbA1c. Subjects in the upper half of microalbuminuria chart exhibited wider pulse pressure than those in the lower microalbuminuric range. Nosignificant correlation was found between pulse pressure and fasting blood in this study.

BACKGROUND & AIM:-

Diabetes has become a global health issue and the number is expected to rise further in the years to come1,2.It is a chronic health condition where the level of glucose in the circulation remains persistently high above an amount that has been permittedand this makes diabetes more of a vascular disorder. It is the most common cause of end stage renal disease3,4, reversible cause of blindness5,6and the second most common cause of below knee amputation.Diabetic patients are at higher risk of developing cardiovascular disease7and coronary artery disease is the main reason of premature death in diabetics8. Hypertension and dyslipidemia are the usual companions of hyperglycemia and obesity9. Cardiovascular disease, cerebrovascular disease and peripheral arterial diseases are the macrovascular complications of diabetes10. Similarly complications like diabetic neuropathy, nephropathy and retinopathy are the three microvascular complications that pose significant burden on the individual as well as on the health care system11. The deterious effects of hyperglycemia are modulated by several mechanisms including endothelial dysfunction,atherosclerosis, platelet aggregation and oxidative stress12,13leading to accelerated vascular ageing14. The existence of one type of diabetic complication invites another type ofcomplication due to the common pathophysiological mechanisms15. Presence of microvascular complications in diabetes multiplies risk of having CV mortality and morbidity16, 17. Renal damage can beseen in a higher proportion of long standing diabetics. Microalbuminuria is one the earliest indicators of diabetic nephropathy and has prognostic implications from renal point of view18.In addition to diabetes, kidney disease, hypertension anddyslipidemia, there are several other non-modifiable causes of CV diseases like age, race and gender19,20. Pulse pressureis considered to be one of the easiest means to access the vasculature stiffness status of an individual21,22. Widened pulse pressure is a risk factor for cardiovascular diseases23. Pulse pressure is calculated by deducting the diastolic blood pressure from the systolic blood pressure and is expressed in millimeter of mercury24.As pulse pressure is a function of systolic and diastolic pressure, conditions that can influence either of them can change pulse pressure.So the above listed situations have the potential to alter the vascular endothelium and finally the pulse pressure of a person25. Pulse pressure increases gradually with age till the 6th decade after which it slowly starts to decline26. Nevertheless microalbuminuriais a potential risk factor for microvascularcomplication27;pulse pressure is a sign of impending macrovascular complication.The uniqueness of the renal microvasculature is that the afferent arteriolar resistance is low28,29. With this background, we looked into the pulse pressure profile of patients with type 2 diabetes and microalbuminuria.

METHODOLOGY:-

The study was conducted involving adults having type 2 diabetes who visited Sevayan Diabetes Centre, a diabetes specialty facility in an urban area located 60 kilometers away from Bhubaneswar, the state capital of Odisha. The study period was from November 2019 to March 2020. The participants were older than 18 years, but less than 70 years of age in order to be enrolled. Those with type 1 diabetes, gestational diabetes, type 2 diabetes with pregnancy or lactating mothers were excluded from the study. Subjects with normal renal function as evident by normoalbuminuria and those with macroalbuminuria were also excluded.It was only those with microalbuminuria status were recruited. Similarly subjects who had a history of any degree of kidney disease, whether acute or chronic were also barred from participation. Patients unwilling to participate were also excluded.Consecutive diabetic patients were asked to give their consent before entry into the study.Anthropometric measurements were taken. Thorough medical and surgical history was recorded. All subjects underwent fasting blood glucose, HbA1c measurement and urine microalbumin testing in early morning samples.After a rest for 5 minutes blood pressure was recorded in the dominant arm in a calm environment with a gap of at least one minute between two successive readings. The average of three BP recordings was taken. HbA1c was estimated as per National Glycohemoglobin Standardization Program recommendation and was measured by therecognized boron affinity method from the venous blood sample. Glucose was estimated by GOD-POD method from the blood collected in the fasting state.Diabetes was defined in accordance with the American Diabetes Association guidelines30 as a fasting glucose concentration of 126 mg/dL or higher, HbA1c 6.5% or higher, or self-reported use of antihyperglycemic drugs. Early morning urine sample was used to check the urinary albumin status of the participants and was expressed as mg/g. Urinary albumin creatinine ratio (ACR) ≥30 mg/g to <300 mg/g was used to describe microalbuminuria as per KIDGO classification31.

RESULTS:-

A total of two hundred sixty persons met the inclusion criteria and were recruited after due consent. The sample included 164 males and 96 females with an averageage of53.3±18.2 years. The mean value for fasting plasma glucose was 157.8 ± 34.7 mg/dl whereas the mean HbA1c wasfound to be 8.3 ± 2.4 %. The quantitative albumin level in the urine samplesaveraged at 148.4±67.1mg/g. The mean systolic and diastolic blood pressure recorded were156.1±16.2mm Hg and 89.5±9.7 mm Hg respectively; whereas the mean pulse pressure was 69.3 ± 11.1 mm of Hg. Majority of the study sample exhibited higher pulse pressure. Only 41 subjects had a normal pulse pressure, whereas 219 (84.2%) had an elevated pulse pressure of >60 mm of Hg32.

		n =	%
Gender	Males	164	63.1
	Females	96	36.9
Marital status	Married	224	86.2
	Single / widow	36	13.8
BMI	<18.5	11	4.2
	18.5 to <23	173	66.6
	≥23	76	29.2
Education	No formal education	9	3.5
	Up to graduation	204	78.5
	Graduation & above	47	18

Table 1

Parameters	Mean ± SD
Age (years)	53.3 ± 18.2
HbA1c (%)	8.3 ± 2.4
Fasting blood glucose (mg/dl)	157.8 ± 34.7
Microalbuminuria (mg/g)	148.4 ± 67.1

Table 2

When wedivided the subjects into two groups based on their pulse pressure, it was seen that the group with higher pulse pressure exhibited more albumin in their urine (p≤ 0.05) than the other group. A similar trend of widened pulse pressure was also observed among subjects when they were categorized as per their albuminuria status (p ≤ 0.05). There was a direct correlation between microalbuminuria and pulse pressure. The higher the level of microalbumin in the urine, greater was the pulse pressure. Both of the above findings were statistically significant and pointed towards a possible and proportionate link between quantity of urinary albumin excretion and pulse pressure.

Variables	Pulse pressure (mm Hg)	p- value	
Gender	Males	73.8 ± 13.4	<0.05
	Females	63.7 ± 10.3	
Age	≤ 55 years	65.1 ± 11.7	<0.05
	> 55 years	73.3 ± 13.2	
Microalbuminuria	Upper half	74.2 ± 13.6	<0.05
	Lower half	64.8 ± 11.2	
HbA1c	≤ 8.5%	65.2 ± 12.4	<0.05
	>8.5%	74.2 ± 11.7	

Table 3

We also founda linear association between HbA1c and pulse pressure. The average pulse pressure of subjects with HbA1c above 8.5% was significantly higher than those whose HbA1c was ≤8.5% (65.2 ± 12.4 mm Hg and 74.2 ± 11.7 mm Hg respectively). Three fourth of the subjects with pulse pressure above the upper quadrant of pulse pressure had an HbA1c ≥8.5%, whereas only 11% of the participants in the lowest quadrant had an HbA1c above 8.5%. On the contrary, no relationship between pulse pressure and short term glycemic control in the form of fasting blood glucosecould be drawn (p < 0.05).The pulse pressure among the male and female participants varied greatly (73.8 ± 13.4 versus 63.7 ± 10.3 mm Hg) and was statistically significant. Our study found that the younger participants had a lower pulse pressure compared with their elder comparators.

DISCUSSION:-

Microalbuminuria is a powerful predictor of cardiovascular events33and may be useful as an early warning sign of diabetic nephropathy34. Hypertension is a common accompaniment in people with diabetes and is linked to end organ damage35. There are cross sectional studies conducted among hypertensive as well as general population showing the association between pulse pressure and microalbuminuria36. The pulse pressure has been linked to morbidity and mortality in people with diabetes, particularly from cardiovascular and renal point of view37. Studies in diabetics show higher pulse pressure38, which was also observed in the present study. Here we found more than 84% of the study participants to be having a hiked pulse pressure.In this study we demonstrated that higher was the microalbuminuria, wider was the pulse pressure. There are several other studies from India which have demonstrated a similar trend of a higher pulse pressure among albuminuric adults39.The gender difference in terms of pulse pressure variation seen in our study could be attributed to the protective effect of estrogen in females and the atherosclerosis promoting effect of testosterone in the males. Ahimastos et al has reported similar findings in their studies which involved pre and post pubertal males and

females40.In a meta-analysis, the decrease in eGFR and increase in ACR were associated with an increased risk for cardiovascular mortality independent of each other traditional risk factors41. Earlier studies have been inconclusive while describing the effects on pulse pressure on renal function, while some showed an increase in pulse pressure on worsening nephropathy42,43,44, while others showed no association between them45,46.We noticed an association between pulse pressure and albumin excretion in the urine. With an increase in the urinary albumin excretion among people with diabetes there as a rise in the pulse pressure as observed in some studies47.CKD and CVD are closely associated due to clustering of several cardiovascular risk factors, including hypertension, diabetes mellitus, and dyslipidemia in those patients48.We tried to measure blood pressure with accuracy. Single blood pressure reading can potentially overestimate the pulse pressure values49. To overcome this we have taken 3 blood pressure readings for each of the participants and considered the average of them.Our study was meant to find a causal relationship between pulse pressure and microalbuminuria in diabetic adults. Moreover this being a cross sectional study, we did not look into the impact of pulse pressure on the progression of diabetic nephropathy. The present study did not segregate the types of antihypertensive medications used by the participants and hence did not evaluate their impact on pulse pressure, which was narrated by some of the investigatorsin earlier studies50. We also did not compare patients based on the presence or absence of diabetic autonomic neuropathy. This was thought to be crucial by some authors as autonomic neuropathy can cause an increase in diastolic blood pressure and hence have the ability to narrow down the pulse pressure51.

CONCLUSION:-

Our observation concluded that majority of the patients (84%) had high pulse pressure. Data generated from the present study revealed a direct association between pulse pressure and albuminuria among people with diabetes independent of other factors. Wider pulse pressure was found to belinked to male gender and elevatedglycated hemoglobin. Our study did notshowanyrelationshipbetweenpulsepressureandfastingbloodglucose.

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