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# Relationship of Changes in Blood-Glucose Level with Albuminuria in Diabetic Patients Reporting in Civil Hospital-Karachi

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\* this is joint team work, each investigator worked by heart for the improvement of study

**UNDERTAKING:**

The whole manuscript is reviewed and approved by all investigators and there is not any conflict of interest between us. This whole study or any part of manuscript never sent for any publication.

Our study also includes three table and we are going to bear the cost of its publication if any. This study has been ethically approved by the office of the director research (DUHS).

**IMPORTANCE OF ARTICLE:**

Our study focuses on multiple ideas like the impact of duration of diabetes on the level of Random Blood Sugar, or the relationship of the duration of the diabetes diagnosed on the urine albumin level.

Most importantly our study shows the impact of RBS level on the level of urinary albumin level.

The International Journal of Research (IJR) is well-known for its high standard and authenticity, which attracts people involved in all lines of medical profession to submit their research articles to it.

Furthermore, publication in a recognized journal is both a source of honor, dignity and produces positive results in professional future.

**WORD COUNT:**

ABSTRACT: 314 words including Mesh words.

MAIN ARTICLE: 3804 Words

**UNDERTAKING**

I, ABUBAKAR TAUSEEF, and my below mentioned colleagues are submitting our original *research titled "RELATIONSHIP OF CHANGES IN BLOOD-GLUCOSE LEVEL WITH ALBUMINURIA IN DIABETIC PATIENTS REPORTING IN CIVIL HOSPITAL-KARACHI"* to the International Journal of Research for publication.

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We also attest that any human and /or animal studies undertaken as part of the research from which this manuscript was derived are in compliance with regulation of our institution and with generally accepted guidelines governing such work.

We further attest that we have herein disclosed any and all financial or other relationships which could be construed as a conflict of interest and that all sources of financial support for this study have been disclosed and are indicated in the acknowledgement.

Yours' sincerely,

ABUBAKAR TAUSEEF and the co-authors.

## **ABSTRACT:**

**Objective:** *RELATIONSHIP OF CHANGES IN BLOOD-GLUCOSE LEVEL WITH ALBUMINURIA IN DIABETIC PATIENTS REPORTING IN CIVIL HOSPITAL-KARACHI*

**Participants and Method:** *It was a questionnaire based study conducted during the period of September 2015 till February 2016. In this study all data was collected by the co-investigators during a period of 1<sup>st</sup> September 2015 to 29<sup>th</sup> February 2016, 300 patients were selected on the basis of internationally used equations used to calculate the sample size, and in the end data was analyzed by using SPSS 20.0 version.*

**Results:** *This study shows that as the duration of diagnosed diabetes increases the rate of RBS becoming uncontrolled increases directly like, 62.8% of individuals with duration of 20 years or more have a Random Blood Glucose level(RBS) of 301-400 mg/dl as compared to 22.1% of individuals with duration of Less than 5 years. Also it shows that as the duration of diabetes increases the level of urine albumin increases like, 3.9% of individuals with diagnosis of diabetes for less than 5 years have urinary albumin level of >300mcg/mg of Creatinine, which reaches up to 82% in case when duration reaches 20 years or more, Also this study shows that as the level of RBS increases the level of urine creatinine increases exponentially, showing that as the duration of Diabetes increases the chances of nephropathy increases greatly*

**Conclusion:** *This study shows that as the duration of diabetes and level of RBS increases the chances for nephropathy increases exponentially so in order to reduce the risk of Diabetic Nephropathy (which is very much common in our society) doctors has to counsel their patients about the diabetes, its risk, and most importantly its complications as by doing this we can control the complications of diabetes like nephropathy, ultimately reducing the ratio of mortalities and morbidities caused by the silent killer of the society, 'THE DIABETES'*

**MesH words:** Relationship; Diabetes; Nephropathy; Glucose level; Karachi.

## **INTRODUCTION:-**

Diabetes mellitus is a set of metabolic diseases of carbohydrate metabolism defined by increase blood sugar levels due to defect in insulin secretion, insulin action or both. The universal prevalence of diabetes is expected to rise from 4% in 1995 to 5.4% by the year 2025[1]. Glucose processing uses a variety of diverse metabolic pathways; hence, chronic hyperglycemia can induce multiple cellular changes. The longstanding hyperglycemia of diabetes is related to long term damage and failure of various organ especially the eyes, kidneys, nerves, heart and blood vessels and these long term complications of diabetes determine the mortality and morbidity . Diabetes is the most renown cause of renal failure, responsible for nearly 44% of new cases[2].

Diabetic nephropathy or diabetic kidney disease refers to structural and/or functional abnormalities in kidneys due to hyperglycemia [3]. It is one of the most serious complications of diabetes. Structural renal defects constitutes hypertrophy of kidney, increase thickness of glomerular basement membrane, glomerulosclerosis , tubular atrophy and interstitial fibrosis[4] . Functional abnormalities include increase in glomerular filtration rate with intraglomerular hypertension, proteinuria and eventual loss of renal function[5]. Diabetic nephropathy develops in 20 to 40% of diabetic patients[6]. It is responsible for 35% of ESRD in US and costs around \$50,000 per patient annually[7].Cardiovascular morbidity and mortality rate widely increases with the development of diabetic nephropathy[8].

Diabetic nephropathy is an extremely lethal complication in type 1 diabetes[9] . Diabetic kidney disease develops in more than 30% of

patients with type 1 diabetes mellitus[10]. However, due to preventive management , prevalence of ESRD is declining in type 1 diabetic victims[11].Approximately 80% of patients with type 1 diabetes mellitus who have developed sustained microalbuminuria progress to a stage of overt nephropathy at a rate of 10-20% per year over a span of 10-15 years and 50% of type 1 diabetic individuals with overt nephropathy ends up in ESRD within a period of 10 years[12]. Formerly, type 2 diabetes was considered to be comparatively a benign condition having relatively little effect on renal functions however the incidence of renal complications is rising today in type 2 diabetes mellitus and it should be taken as seriously as type 1 diabetes[13].35% of subjects with type2 diabetes develop diabetic kidney disease[14].In previous studies , patients with type 2 diabetes have shown a link between the degree of hyperglycaemia and increased risk of microvascular complications[15].

The progression of diabetic nephropathy occurs in stages ; the first stage being feautered by microalbuminuria i.e. 30-300 mg urinary albumin per 24 hours progressing to macroalbuminuria i.e. >300 mg urinary albumin per 24 hour and ultimately culminating at renal insufficiency and ESRD[16].

Factors related to progression to persistent micro albuminuria are urinary albumin excretion rate(AER),hemoglobin A1c concentration, mean arterial blood pressure , being male and height[17]. Other accepted risk factors include smoking[18], dyslipidemia[19], dietary factors[20],inherited factors[21] and racial factors[22].

Microalbuminuria is considered to be the earliest indicator for diabetic nephropathy[23]. The level

of proteinuria has proved to be the foremost risk for progressive nephropathy in diabetic patients[24] yet the level of serum albumin, serum creatinine and hemoglobin further reinforces the prognosis of ESRD[25]. The extent of proteinuria corresponds with the progression of glomerulosclerosis and tubulointerstitial fibrosis[26]. The onset of proteinuria is influenced not only by the level of exposure to hyperglycemia but environmental and genetic factor also seems to play its role[27]. Decreasing the extent of urinary albumin excretion is an important objective in the management of diabetic nephropathy.

Hemoglobin A1c higher than 7.5% and postprandial blood glucose more than 200 mg/dl boost up the risk for declining glomerular function[28]. Diabetic patient with long term poor glycemic control has 3.6 times likelihood of micro albuminuria than those with good glycemic control[29]. In Diabetes Control and Complication Trial, intensive glucose control in type 1 diabetic subjects reduced the incidence of micro albuminuria by 39% and decreased the progression to macro-albuminuria by 54%[30]. In subjects with diabetes mellitus who are susceptible to the development of renal impairment, there is a link between long-term glycemic control and the rate at which the nephropathy process occurs[31]. Therefore, glycemic control remains critical in maintaining and decelerating progression of established nephropathy. Furthermore, pancreatic transplantation has shown to reverse the renal damage in type 1 diabetic subject[32].

When compared to general population, hypertension is twice more common in diabetic patients[33]. It results in a sevenfold increase in mortality[34]. The prevalence of hypertension at

each stage of CKD rises, approaching 90% for ESRD subjects[35]. The etiology of hypertension in diabetic nephropathy includes mechanisms with various inter-related mediators that leads to increase renal sodium reabsorption and peripheral vasoconstriction. Blood pressure is generally normal in diabetic subjects with minor degree of microalbuminuria but tends to be elevated in diabetic subjects with more pronounced microalbuminuria[36]. The combination of hypertension and diabetes is a serious clinical condition and treatment of hypertension dramatically decreases the risk of microvascular defects in diabetic patients. Blood pressure targets for patients with diabetes are lower relative to patients without diabetes[37]. Effective management of simultaneous hypertension reduces renal mortality among patients with albuminuria[38].

Dyslipidemia has also been linked with the evolution and progression of nephropathy and other vascular complications[39] and lipid lowering drug may retard the renal progression[40]. Furthermore, intensive diabetes managements associated with better glycemic control and also with significantly lower triglycerides, LDL cholesterol, and ApoB[41].

Diabetic siblings of patient with diabetes and renal diseases show five time more risk to develop nephropathy than diabetic siblings of patient with diabetes without renal involvement[42]. Hence, a group of patient may be at higher risk based on genetic factors[43].

Diabetic nephropathy is more prevalent among African Americans, Asians, and Native Americans than Caucasians[44]. Asian patients have demonstrated evidence of micro and macro vascular diseases at the time of diagnosis when related to Europeans[45].



Low birth weight defined as birth weight below the 10th percentile, known to be associated directly to adult height, presents with oligonephropathy i.e. reduced number of nephron which has been implied to increase the risk for systemic and glomerular hypertension in adult life and hence act as a risk factor for renal injuries[46].

Smoking is somewhat responsible for faster progression of nephropathy in diabetic subjects who smoke[47]. Likewise, deterioration in renal function occurs faster in smokers when compared to nonsmokers with type 2 diabetes mellitus undergoing treatment to improve blood pressure[48]. Risk of progression of diabetic kidney disease is directly proportional to the dose of smoking however ex-smokers carry similar risk as non-smokers[49].

Furthermore, electrolyte abnormalities such as dysnatremias, hyperkalemia, hypomagnesaemia, hypocalcemia, hypercalcemia and hypophosphatemia are far more prevalent in diabetic patient in the presence of renal impairment[50].

However, the morbidity and mortality caused by diabetes mellitus can be reduced by regular screening, early detection, and appropriate treatment of chronic complications. Sensitive tests are accessible to identify the patients with renal impairment early in the course of disease, when preventive measures may have greatest impact.

Blood tests for Blood urea nitrogen (BUN) and creatinine are the simplest way to monitor kidney function. There is strong affiliation of blood sugar level with blood urea level[51]. Urea level is increased whenever the kidneys are damaged or function improperly thus simultaneous rise in blood sugar level and blood urea level certainly

suggest that hyperglycemia leads to renal impairment.

#### METHOD AND METHODOLOGY:-

The study was carried out at Medical units of Civil Hospital Karachi; one of the most important and top notched facility providing enhanced health care to patients visiting the establishment. It is a questionnaire based statistical study conducted during the period of September 2015 till February 2016.

In the beginning the topic was decided and a Performa was outlined by our supervisor's help and joint collaboration of all the co-investigators. After all ifs and buts plus healthy arguments we finalized the Performa, which was divided into two components, first component includes demographic data containing name (as optional), age, gender, location, ethnic-group, Duration of diabetes and random blood sugar of the subjects of the study. Second component includes serum levels of blood urea nitrogen, Creatinine, Serum Sodium and serum potassium. This study is ethically and duly approved by Institute of Research Board (I.R.B) Subjects for this statistical study are selected randomly from all the Medical Units of Civil Hospital, Karachi. Sample size for this study equals 300 calculated by using the standard equations used internationally for calculating the sample size.

All those patients aged below 70 who are diagnosed previously with Diabetes Mellitus (on the basis of criteria of World Health Organization (W.H.O) are included, all those with at least two years of diagnosed diabetes are included, also all patients included in our study have a normal blood pressure, less than two years of diagnosed cases of diabetes are excluded from our study, all those who are outside the Civil hospital Karachi are also excluded from our study.

Performa of the respective study were to be filled by all the members of this study .After entire filling of the Performa, data is entered and statistically analyzed by using SPSS 20.0 version software and results were extracted through it as per given below in results.

### **RESULTS:-**

A total of 300 individuals are included in this study out of which 172(57.3%) are males and 128 (42.7%) are females. This study shows that as the duration of diagnosed diabetes is increasing, the level of control over Random Blood Sugar is decreasing ; like 62.8% of individuals with duration of 20 years or more have a Random Blood Glucose level(RBS) of 301-400 mg/dl in contrast to 22.1% of individuals with duration of Less than 5years **(TABLE I).**

Also it was found that as the duration of diabetes increases level of albumin in urine also increases exponentially, like 3.9% of individuals with diagnosis of diabetes for less than 5 years have urinary albumin level of >300mcg/mg of Creatinine but the same level was found in 4.7% of cases with diagnosed diabetes for up to 5-10 years which increases dramatically up to 56.44% of individuals when the duration of diabetes reaches 10-15 years, which extends to 82% in case when duration reaches 20 years or more. **(TABLE II)**

Most importantly, it was found that as the Level of Random Blood Sugar increases the urine level of albumin increases exponentially, 25.65% of individuals having Random Blood Glucose level of 140-200mg/dl found to have a urine albumin level >300mcg/mg of creatinine, same level of urinary albumin was found in 44.9% of individuals with RBS of 301-400mg/dl percentage of individuals with similar albumin level increases up to 65.9% when RBS level reaches 400 or above, which shows that as the level of RBS increases the chances for increase of urinary albumin increases which shows that nephropathy ensues and chances for chronic kidney disease increases, as the level of RBS increases.**(TABLE III).**

### **DISCUSSION:**

As diabetes is one of the most prevailing diseases in humans and renal problems being major complication of diabetes, lots of efforts have been made in evaluating and solving problems related to this disease. Quite a lot of studies have been done in this field. One of these studies were performed by M.-A. Gall and his fellows regarding the prevalence of micro and macro albuminuria in 557 diabetic patients in which 27.5% patients were found to have micro-albuminuria and 13.66% patients had macro albuminuria [52]. When we compare these results to our study, 139(46.33%) patients had micro albuminuria and 119(39.66%) patients had macro albuminuria which is comparatively high compared to M.-A. Gall's study. The probable reasons may be poor glycemic control in this area and lack of proper education and awareness regarding diabetes and its complications.

Hertzal C. and his team had conducted a study regarding effects of diabetes on cardiovascular disease. During this study they observed that 32.6% of diabetic patients had micro albuminuria[53] whereas in our study it was present in 46.33% of diabetic patients. The difference may be due to huge difference in sample size and difference in inclusion and exclusion criteria as they only selected patients who had previous cardiovascular history.

In a survey conducted by Hans-Henrik Parving and fellows, they selected 957 diabetic patient to assess their renal function and concluded that 22.4% patients had micro albuminuria and 18.8% patients had macro albuminuria[54]. These numbers are again low compared to our study. The reason being that our study included all patients below 70 years of age and this study only included patients below 41 years of and as age is an important prognostic factor in renal problems accounting for higher percentages in our study.

Hans-Henrik Parving conducted another study regarding prevalence and causes of type 2 diabetes in which 363 patients completed the requirements and he concluded that 13.8% of these patients had persistent

albuminuria[55] compared to 39.66% in our study highlighting the importance and need of proper education, better glycemic control through proper medications and patient compliance and screening in this part of world and efforts required so that these patients with sub-clinical albuminuria can be prevented from advancing to clinical proteinuria and nephropathy.

### **CONCLUSION:-**

This study shows that as the duration of diabetes and level of RBS increases the chances for nephropathy increases exponentially so in order to reduce the risk of Diabetic Nephropathy (which is very much common in our society) doctors has to counsel their patients about the diabetes, its risk ,and most importantly its complications as by doing this we can control the complications of diabetes like nephropathy , ultimately reducing the ratio of mortalities and morbidities caused by the silent killer of the society, **‘THE DIABETES’**

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**TABLE -1:-**

RANDOM BLOOD SUGAR LEVEL (mg/dl)	DURATION OF DIABETES (numbers in table shows number of individuals)					P-VALUE
	<5 years	5-10 years	10-15 years	15-20 years	>20 years	
<140	18(20.9%)	8(10.6%)	1(3.5%)	0(0%)	0(0%)	0.000
140-200	14(16.3%)	5(6.6%)	5(17.9%)	10(13.3%)	1(2.9%)	
201-300	24(27.9%)	25(33.3%)	9(32.1%)	9(12%)	0(0%)	
<b>301-400</b>	<b>19(22.1%)</b>	<b>22(29.3%)</b>	<b>9(32.1%)</b>	<b>16(21.3%)</b>	<b>22(62.8%)</b>	
>400	11(12.8%)	15(20%)	4(14.3%)	40(53.3%)	12(34.3%)	

\*Highlighted part is explained in results heading

**TABLE II:-**

URINE ALBUMIN LEVEL(mcg/mg of creatinine)	DURATION OF DIABETES (NUMBERS IN TABLE SHOWS NUMBER OF INDIVIDUALS)					P-VALUE
	<5 YEARS	5-10 YEARS	10-15 YEARS	15-20 YEARS	>20 YEARS	
<30	18(23.7%)	14(21.8%)	5(10.8%)	6(7.3%)	0(0.0%)	0.000
30-300	55(72.2%)	47(73.4%)	15(32.6%)	16(19.4%)	6(18%)	
<b>&gt;300</b>	<b>3(3.9%)</b>	<b>3(4.7%)</b>	<b>26(56.44%)</b>	<b>60(73.2%)</b>	<b>27(82%)</b>	

\*Highlighted part is explained in results heading

**TABLE III:-**

URINE ALBUMIN LEVEL (IN mcg/mg of Creatinine)	RANDOM BLOOD SUGAR LEVEL (in mg/dl)					P-VALUE
	>140	140-200	201-300	301-400	>400	
<30	6(26.1%)	10(25.6%)	14(20.9%)	6(6.7%)	6(7.3%)	0.000
30-300	15(65.2%)	19(48.7%)	40(59.7%)	43(48.3%)	22(26.9%)	
<b>&gt;300</b>	<b>2(8.7%)</b>	<b>10(25.65%)</b>	<b>13(19.4%)</b>	<b>40(44.9%)</b>	<b>54(65.9%)</b>	

\*Highlighted part is explained in results heading