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GENDER WISE ASSESSMENT OF CLINICAL RISK FACTORS AND COMPLICATIONS AMONG DIABETIC PATIENTS: A RETROSPECTIVE STUDY FROM LAHORE, PAKISTAN

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ABSTRACT

Objective: Diabetes-associated complications can be ruled out and prevented through control of diabetes in relation to risk factors of complications. The aim of the study was to find the gender wise correlation of risk factors and complication of Diabetes in the local population.

Design: A retrospective study was carried on the diabetic patient in 3 major hospitals of Lahore.

Method: The medical record was assessed of enrolled patients underwent treatment with insulin, oral anti-diabetic or both. The descriptive statistics/ inferential statistics were applied to find the correlation between the demographics, risk factors and complications related to the disease using SPSS 20.0.

Results: Mostly female (73%) of diabetes was at risk of infections. Blood pressure was majorly associated with the diabetic patient, a major risk factor for diabetes. Obesity was also a risk factor for not only diabetes but abnormal lab values and hypertension as well. Cholesterol, HbA1c, Hb, uric acid etc. were prominently abnormal due to metabolic disorder, which is resourceful element indicating diabetes. High salt intake also disturbs salt metabolism in patients which could lead towards high blood pressure and related infections.

Conclusion: Diabetes is related to many of the risk factors which have been rapidly advancing in underdeveloped countries like Pakistan. These risk factors are finally then associated with complications in patients of which major risk factors were physical inactivity and obesity leading to micro and macrovascular complications.

Abbreviations:

DM (Diabetes Mellitus), MODY (maturity onset diabetes of young), UTIs (urinary tract infections), HBAIc (Glycated hemoglobin level), Hemoglobin (Hb)

Keywords: Diabetes Mellitus, Insulin, Infection, Risk factor, Complication

INTRODUCTION

Diabetes Mellitus is the abnormal in blood glucose level due to the inability of beta cells to secrete insulin/lack in insulin action or both factors, causing metabolic disturbances in proteins, fats, and carbohydrate [1]. It is of four types. Type I, Type II, Type III and Type IV. Type I is described as absolute insulin deficiency and usually occurs in childhood and adolescence. Type II is characterized by increased insulin resistance or relative insulin deficiency and beta-cell dysfunction and has adult onset and usually occurs in old age. Type III is also called maturity-onset diabetes of young (MODY). It is inherited as an autosomal dominant disease by the mutation in glucose kinase gene (glucose kinase is a "glucose sensor" in pancreatic insulin secretion). And type IV is known as gestational diabetes mellitus which usually occur during pregnancy and returns to normal postpartum. Complications of diabetes are characterized by retinopathy (blindness), nephropathy leading to renal failure, foot infections and ulcers, blurring of vision, weight loss, polyuria, ketoacidosis, stupor, and coma leading to death in severe cases so require serious medical examination [1]. The ratio of people having diabetes is increasing dramatically particularly in the United States and other Western countries. The most particular reason for this sudden expansion is obesity and population aging.

The burden of disease can be lowered by proper diet control and exercise along with proper treatment of hypertension, hyperglycemia, and dyslipidemia [2]. Diabetic patients have often altered immune system due to the abnormality in glycemic control so there is increased the risk of infection in them. The prevalence of some ailments is more in diabetic patients and some are more complicated in them. T-cell function, leukocyte adherence, antioxidant system, chemotaxis, phagocytosis may also be depressed. Polymorph nuclear leukocyte (PNL) function is depressed particularly if acidosis is present due to metabolic disturbance. Improving glycemic control will improve the immune system. Infections commonly occurring in diabetic patients with increased incidence are respiratory tract infection, skin and soft tissue infection, foot infections, urinary tract infections (UTIs), and retinopathy [3]. According to one of the studies, 132 out of 515 patients admitted to hospital due to acute infection had diabetes mellitus. Among diabetic patients 3% were suffering from osteomyelitis, 1% with infection in extremities, 24% with urinary tract infection, and 10% with *Staphylococcus aureus* infection; whereas the ratio of these infections was far less in nondiabetic patients than in the diabetic patients. The gross mortality rate in the diabetic patient was 10% as compared to non-diabetics 12% [4]. In Pakistan, the overall risk of diabetes mellitus in urban areas was 22.04% and rural areas were 17.15%. The major risk factors associated were age, family history and obesity [5]. Proper management of diet and lifestyle modifications are easier than treating by medications. Diabetes is continuously increasing in Pakistan every year and this study aimed to find the causes and risk factors of this increase in the incidence of diabetes and related complications either by obesity or family background in diabetic patients.

MATERIALS AND METHODS

Study design and center

A cross-sectional study of four months duration was designed to assess the prevalent risks and complications in diabetic patients presenting in three major hospitals of Lahore, Sir Ganga Ram, Sheikh Zaid and Jinnah hospital.

Inclusion Criteria: All diabetic patients irrespective of their age, gender, concomitant disease, education and ethnic background undergoing treatment were enrolled for the study. An informed consent was obtained from the patients.

Exclusion Criteria: Diabetic or Non-diabetic patients not taking oral anti-diabetic agents or insulin were excluded from the study.

Ethical Approval:

Ethical approval for the study was obtained from the ethical committee of the University College of Pharmacy, University of the Punjab, reference number **(EC/UCP/092/2015)** and hospital committee of ethics on human research.

Study Population:

A total of **250** patients were enrolled form all the three hospitals. As per the hospital wise patient distribution; **70** of them were enrolled from Sir Ganga Ram, **150** from Sheikh Zaid hospital and **30** from Jinnah hospital.

An instrument of measure and Data collection:

A comprehensive questionnaire based on basic demographics, clinical characteristics, non-pharmacological and pharmacological interventions, risks and complications was designed for data collection. Notable parameters include lab values. Informed consent was obtained from all the enrollees.

Data analysis:

Data were analyzed by applying independent T-test using SPSS (statistical process for social sciences) version 21. An α **0.05** or less is considered statistically significant (p<0.05).

RESULTS:

Patient Basic Demographic Data:

Patient basic demographic characteristics, confirmed by patient medical history and as per clinician's judgment, are summarized in **Table 1.** The study population was divided into two arms, male (n=66) and female (*n*=183), mostly males (33.3%) and females (90.1%) were unemployed. According to age (96.9%) of males and (55.4%) of females are in the range of (<45 yrs), while (37.8%) of males and (43.9%) of females are in the range of (>45 yrs) with an average age of 54.78787879 and 49.78142077 in males and females respectively as in **Figure 1.** The BMI shows that 41% of males and 33% of females have BMI <30 as in **Figure 2**. Clinical presentation represents that 41% of males and 56% of females are hypertensive. Medication history shows that were undergoing therapy by Insulin (46.97% in males and 35.51% in females), oral anti-diabetics (53.03% in males and 64.5% in females) and both insulin and oral anti-diabetics (19.69% in males and 12.08% in females).

Risks and Complications:

Social lifestyle and dietary habits of both the male and female are summarized in **Table 2.** It has been seen that 64% of males and 57.1% of females have physical activity less

than 30 minutes. As far obesity is concerned 86.3% of males were obese and none of the females are obese. The salt, sweet and oil intake is almost normal in both male and female.

Complications associated with Diabetes Mellitus are classified as macrovascular and microvascular complications. Macrovascular complications such as 29% of male and 66.4% of females had cognitive impairment and similarly, females have a higher rate of cerebrovascular diseases 34% while males only 1.5%. The incidence of retinopathy was higher in males (21%) than in females (6.59%) while 0.06% of males and 48.3% of females face visual disturbances. Ulceration was also more in females (43%) than in males (28%).

Amongst the microvascular complications, Neuropathy was more prevalent in females as 32% of males and 46% of females have numbness and cramps issues. Other micro-vascular complication such as kidney disease (males: 12.12% & females: 15.93%), frequent diarrhea (males: 34.8% & females: 38.4%), and Nausea & vomiting (males: 45.45% & females: 29.67%). Complications related to lower appendages includes foot numbness (males: 66.66% & females: 53.29%), tingling in foot (males: 68.18% & females: 54.39%) and foot pain (males:

54.54% & females: 53.84%) was more prevalent in males than females. Unusual sweating was also more in males than in females.

Table 3 shows the laboratory values of the patients such as B.P, blood glucose, HBAIc lipid profile (HDL, LDL), uric acid and hemoglobin level in Diabetic patients. Systolic B.P was within normal in most of the patients in both genders while it was more in males (27%) than in females (17.5%) within 141-190mmHg which is a Hypertensive range. Diastolic B.P was also higher in males 45.45% and 37.9% in females within 81-110mmHg range. Average Fast blood glucose was 173mg/dL with range of (60-600) in males and 158mg/dL in females (60-370) with p-value 0.016466091 higher than that of normal value which is 100 -150mg/dL. Random blood glucose level was 227mg/dL (40-500) and 200mg/dL (30-500) with p-value 0.008255012 in males and females respectively. Glycated hemoglobin level (HbAIc) was normal (9mg/dL) in both study arms. Lipid profile of the patients shows that HDL and LDL level was within normal range in both arms with p-value 0.155449 and 0.567357804 respectively. Hemoglobin and the uric acid level were also normal in the patients.

Table 1: Basic demographics and history of the patients enrolled for study

PARAMETER	MALE (n=66)	FEMALE (n=183)
Marital status		
Married	**63 (95.45%)**	**173 (94.54%)**
Single	**3 (4.55%)**	**10 (5.46%)**
Literate	**18 (27.21%)**	**65 (35.71%)**
Illiterate	**40 (60.5%)**	**77 (42.56%)**
Occupation		
Employed	**31 (46.9%)**	**15 (8.24%)**
Unemployed	**22 (33.3%)**	**164 (90.1%)**
Concomitant disease		
Hypertension	**27 (40.9%)**	**102 (56.04%)**
Treatment		
Insulin	**31 (46.97%)**	**65 (35.51%)**
Oral anti-diabetic agents	**35 (53.03%)**	**118 (64.5%)**
Both	**13 (19.69%)**	**29 (12.08%)**

Table 2: Risk factors and complications of Diabetes Mellitus in enrolled patients

PARAMETERS	MALE (n=66)	FEMALE (n=183)
Salt intake		
Low <1500mg	**40 (60.6%)**	**132 (72.5%)**
Moderate 1500-2300mg	**17 (25.7%)**	**37 (20.3%)**
High >2300mg	**5 (7.57%)**	**11 (6.04%)**
Oil intake		
Low <10g	**46 (69.69%)**	**140 (76.9%)**
Moderate 10-15g	**4 (6.06%)**	**30 (16.4%)**
High >15g	**6 (9.09%)**	**9 (4.94%)**
Sweet intake		
Low <15g	**39 (59.09%)**	**137 (75.27%)**
Moderate 15-25g	**20 (30.30%)**	**30 (16.48%)**
High >25g	**4 (6.06%)**	**13 (7.14%)**
Stress	**15 (22.7%)**	**64 (35.1%)**
Physical activity		
<30 minute walk	**42 (63.6%)**	**104 (57.1%)**
>30 minute walk	**20 (30.3%)**	**74 (40.6%)**
Obesity (BMI)		
30-40	**7 (10.6%)**	**Nill**
>40	**57 (86.3%)**	
Macro-vascular complications		
Cognitive impairment	**19 (28.7%)**	**121 (66.4%)**
Cerebrovascular disease	**1 (1.5%)**	**62 (34.06%)**
Retinopathy	**14 (21.21%)**	**12 (6.59%)**
Blindness	**0**	**3 (1.64%)**
Cataract	**3 (4.54%)**	**5 (2.74%)**
Glaucoma	**4 (6.06%)**	**3 (1.64%)**
Visual disturbance	**4 (6.06%)**	**88 (48.3%)**
Ulceration	**19 (28.7%)**	**79 (43.4%)**
Micro-vascular complications		
Neuropathy		
Muscle cramp	**8 (12.12%)**	**22 (12.08%)**
Numbness	**6 (9.09%)**	**30 (1.64%)**
Muscle cramp + numbness	**21 (31.8%)**	**81 (44.5%)**
Bloating	**3 (4.54%)**	**2 (1.09%)**
ECG		
Abnormal	**2 (3.03%)**	**10 (5.49%)**
Kidney disease	**8 (12.12%)**	**29 (15.93%)**

Frequent diarrhea	**23 (34.8%)**	**70 (38.4%)**
Nausea & vomiting	**30 (45.45%)**	**54 (29.67%)**
Foot numbness	**44 (66.66%)**	**97 (53.29%)**
Tingling in feet	**45 (68.18%)**	**99 (54.39%)**
Foot pain	**36 (54.54%)**	**98 (53.84%)**
Unusual sweating	**41 (62.12%)**	**71 (39.01%)**

Table 3: Laboratory parameters among the enrolled patients related to the risk factors and complications of the disease

PARAMETER	MALE (n=66)	FEMALE (n=183)	P-value
Systolic B.P **100-140mmHg** **141-190mmHg**	**43 (62.1%)** **18 (27.27%)**	**144 (79.1%)** **32 (17.5%)**	**-** **-**
Diastolic B.P **60-80mmHg** **81-110mmHg**	**25 (37.8%)** **30 (45.45%)**	**99 (54.39%)** **69 (37.90%)**	**--**
Fasting glucose (mg/dL)	**173 (60-600)**	**158 (60-370)**	**0.01****
Random glucose (mg/dL)	**227 (40-500)**	**200 (30-500)**	**0.01****
HBA1c	**9 (5-13)**	**9 (3.5-13)**	**0.91**
HDL (mg/dL)	**48(20-250)**	**50 (15-315)**	**0.16**
LDL (mg/dL)	**138 (40-210)**	**124 (40-320)**	**0.56**
Uric Acid (mg/dL)	**4.8 (2.5-8)**	**4.75 (2-9)**	**0.91**
Hemoglobin (mg/dL)	**11.6 (5-15)**	**10.7 (4.5-16)**	**0.62**

(*P <0.05, **P≤ 0.01, ***P = 0.000)
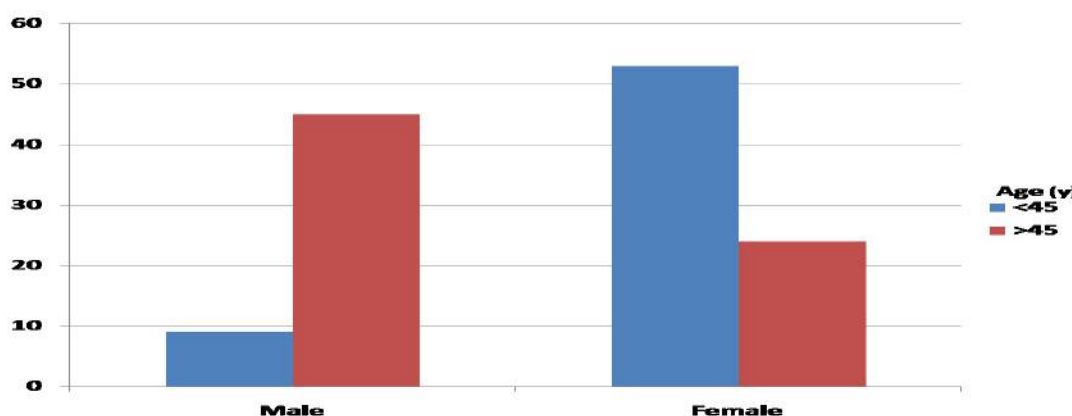

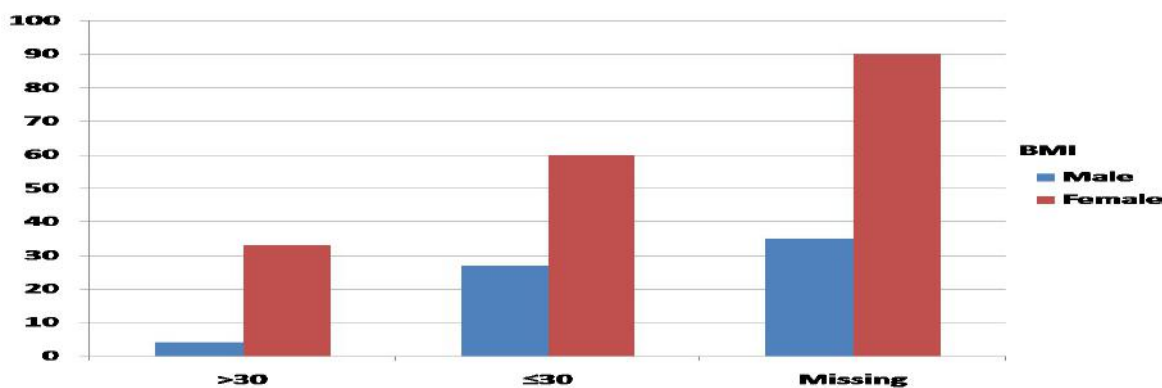**Figure 1: Number of the patients enrolled in the study of two age groups (<45 & >45yrs).**

Figure 2: Number of the patients enrolled in the study of two BMI groups (>30 & <30).

DISCUSSION

This study was conducted to find the find the gender wise correlation of risk factors and complications of diabetes in local population of Lahore. Findings of this study suggest that females are more prone to diabetes as compared to males. Whereas, most of the males having diabetes were obese because abdominal fats cause a body to become less sensitive towards insulin due to the release of pro-inflammatory chemicals, interfering the functions and release of insulin-responsive cells. According to one research, it has been seen that obese patients express 2.5 fold more TNF-alpha mRNA in fat cell which leads to insulin resistance. While gradual weight reduction decreases the expression of TNF- alpha mRNA and as a result patient shifted towards normal health [6]. Our study showed that women are more likely to eat oily products as compared to males however research indicate that saturated (solid at room temperature) and monounsaturated fatty acids do not increase the risk of Type II diabetes in women whereas polyunsaturated fatty acids (simply fat molecules having more than one unsaturated carbon bond in the molecule e.g. soybean oil and corn oil etc) reduces the risk while trans fats (liquid oils, converted to solid fats by the process called hydrogenation) increases risks [7]. Females

are more affected by cognitive impairment as compared to male patients a macrovascular complication of diabetes. The relation between cognitive dysfunction and diabetes is rather unclear but it has been viewed that cognitive dysfunction occurs in both hypoglycemia and hyperglycemia [8]. As far as cerebrovascular diseases concerned, 34% of females are affected by these diseases as compared to males which are only 1.5%. The epidemiological studies and autopsy findings indicate that diabetic patients are more susceptible to atherosclerotic occlusive disease and ischemic stroke. Pathology of stroke related to diabetes is associated with insulin resistance, platelet aggregation, impaired fibrinolysis, endothelial dysfunction, glycation and oxidation [9]. Visual disturbances in Retinopathy are more commonly to be found in women (48%) as compared to male (6%) [8]. The ratio of ulcers in females and males is 43% and 29% respectively. Acute and chronic hyperglycemia leads to GIT complications which seem to be related with dysfunction of neurons supplying the enteric nervous system which may lead to abnormalities in intestinal motility, secretion, sensation, and absorption [10].

Microvascular complications associated with DM including leg cramps and pain occurs

frequently in diabetic patients, due to the nerve damage called diabetic neuropathy. Damage of nerves of arms and legs due to diabetes is called diabetic peripheral neuropathy with 44% in females and 32% in males. The causes of muscle cramps and numbness are sustained elevated blood glucose level which results in deprivation of nutrition and inappropriate supply of oxygen to the nerves. It should be monitored and immediately treated otherwise it may cause limb amputation [11]. According to the research done by Colleen M. Story and reviewed by George T. Krucik, MD, MBA (2014) the diabetic neuropathic association stated that neuropathy in diabetics is "skyrocketing". The potential causes of nerve damage according to research include High blood sugar level, Duration of disease, Low level of insulin, Inflammation in nerves, Lifestyle factors e.g. smoking and alcohol [12]. Foot numbness is more in diabetic male patients (67%) as compared to females (53%). Similarly, nausea and vomiting occur more frequently in males. The ratio of male and female are 46% and 29% respectively. Prolonged diabetes results in an increase in excitatory innervations due to the decrease in Cajal volume of interstitial cells and inhibitory innervations. These changes associated with enteric nerves and Cajal

volume is the causes of gastrointestinal complications [13]. During hyper and hypoglycemia body's metabolism gets interrupted and confused which leads to the mixed feeling of nausea [14].

Excessive sweating is an unusual phenomenon in diabetes mellitus which is a prominent feature of autonomic neuropathy. It may be further complicated by retinopathy, nephropathy, and neuropathy [15]. Our research shows that males are more affected by unusual sweating as related to females 62% and 39% respectively. It is majorly caused by dysfunctioning of the autonomic nervous system. It has been seen that increased salt intake results in rising blood pressure in the patient with diabetes. A diabetic patient should reduce a salt intake of 5-6g/day according to recommendations [16]. According to one survey, it has been observed that patients with diabetes have some abnormality in salt regulating mechanisms and have been observed with some of the observations like delay in excretion of salts and inability of the kidney to concentrate salts etc [17]. The diabetic patient is also seen correlated with higher or abnormal lab values particularly the cholesterol. During diabetes, good cholesterol level (HDL) gets lower in the body while bad cholesterol (LDL) is raised.

Due to this diabetes, the patient is also at a risk of developing heart diseases and strokes. And commonly this condition is referred to as diabetic dyslipidemia. And this condition is representing an abnormal lipid profile. It has been further seen that an observable increase in lipid and cholesterol synthesis results in the risk of atherosclerosis in patients with diabetes mellitus, especially if they are hyperglycemic [18]. Moreover, it has also been seen that diabetic female patient experiences more adverse effects due to triglycerides, lipoprotein and cholesterol concentrations than in men. This reveals that sex difference is also a major concern in abnormal cholesterol and triglyceride levels in patients with diabetes. Our retrospective study of diabetes in Pakistan also show us that females are with more risks and possibilities of diabetes than in men [19]. Furthermore, a high uric acid level in patient leads towards a chance of having diabetes majorly type 2 as it leads to hyperuricemia and other metabolic syndromes. Mostly adults with high uric acid level are at risk of having type 2 diabetes [20]. Although an exact mechanism of high uric acid association with diabetes is still unknown but can be independently determined by the components of metabolic syndrome like body mass index(BMI), oral glucose tolerance test

(OGTT), triglycerides etc [21]. Glycated hemoglobin (HbA1c) is also a factor that indicates a risk of having diabetes. A survey suggests that a person with normal HbA1c does not require rescreening before 3 years, but if he is having an elevated HbA1c level then he may need screening sooner than 3 years. As the high level of HbA1c indicating a chance of having diabetes so people that are diabetic will also have raised the HbA1c level. And this condition is mostly associated with obese and overweight patients. So this HbA1c level indication is quite helpful in diabetic screening [22]. An HbA1c of 6.5% is recommended as the cut point for diagnosing diabetes. A value less than 6.5% does not exclude diabetes diagnosed using glucose tests. The expert group concluded that there is currently insufficient evidence to make any formal recommendation on the interpretation of HbA1c levels Below 6.5 % [23]. Moreover, it has been seen in another survey that in the hyperglycemic patients, the red cell viscosity is observable which also leads towards abnormalities in polymorph nuclear leukocytes, which causes chemotaxis, phagocytosis killing adherence etc. Furthermore, in vitro abnormalities of platelets has also been seen [24]. Lastly, it can be summarized that diabetes is related to many of the risk factors which has been

rapidly advancing in underdeveloped countries like Pakistan. And these risk factors are finally then associated with complications in these patients.

CONCLUSION

It is concluded that diabetes is related to many of the risk factors which has been rapidly advancing in underdeveloped countries like Pakistan. These risk factors are associated with complications in these patients of which major risk factors for developing diabetes mellitus was the physical inactivity and obesity leading to micro-vascular as well as macro-vascular complications of diabetes if it is not properly controlled.

CONFLICT OF INTEREST

There is no conflict of interest between the authors. "NONE TO DECLARE"

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