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RESEARCH ARTICLE

ASSOCIATION OF PREVALENCE OF COMPLICATIONS WITH DEGREE OF HYPERGLYCEMIA IN TYPE 2 DIABETICS OF JAMMU REGION

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ABSTRACT

India is one of the epicenters of global diabetic pandemic. It is silent epidemic that disables kills and strikes people at their most productive age and reduces life expectancy of older people. Diabetes is a global issue and a threat that does not respect borders, social classes or races. It is responsible for increased morbidity and mortality and imposes a catastrophic financial burden on patients and huge burden on healthcare system. Keeping in view the prevalence of diabetic complications the present study was planned to investigate the prevalence of complications in individuals suffering from diabetes and association with degree of hyperglycemia. Out of 200 diabetic patients selected for the study, 80 (40%) patients had not developed any complication. 120 (60%) of the patients were found to have developed one or more complications of diabetes. 46 (23%) were found to have microvascular complications, 32 (16%) macrovascular and 42 (21%) have both micro as well as macrovascular complication. It was observed, as degree of hyperglycemia increased the prevalence of microvascular complications increased from 5 to 10.5% and both micro and macrovascular complications increased from 2% to 12% whereas macrovascular complications increased only from 2 to 3.5%.Thus indicating that prevalence of complications increased with increasing degree of hyperglycemia. Initial treatment of complications is prevention and that can be achieved by keeping a good glycemic control as measured by HbA1c.

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INTRODUCTION

Diabetes and its various complications are major causes of hospitalisations. Chronic complications of diabetes can be divided into vascular and nonvascular complications. Vascular complications can further be divided into microvascular and macrovascular complications. Diabetes is a chronic incurable disease which leads to significant morbidity and mortality due to various complications (Boyle PJ, Keenan 2007). Diabetes is a lifelong incurable disease which leads to significant morbidity and mortality due to macrovascular (Coronary artery disease, Peripheral arterial disease and stroke) and microvascular (diabetic nephropathy, neuropathy and retinopathy) complications (Michael J. Fowler 2008). Till now there is no treatment for diabetes but early detection and control of blood sugar may prevent or at least delay the progression of microvascular and macrovascular complications. Good glycemic control helps in preventing various diabetic complications (Vishwanathan Mohan et al 2013). It has been reported that 18% diabetics suffer from neuropathy, 50% cardiovascular diseases, 18% nephropathy, 33% retinopathy 7% foot ulcers and 10% stroke (Sherry Garg, Sophia and Ma Jamadar 2018). In another study from Goa India, prevalence of diabetic complications reported is CAD 32.3%, CVD 6.9%, PAD 11.5%, nephropathy 30.7%, neuropathy 60% and retinopathy 15.4% (Nafisa C Vaz, AM Ferreira, MS Kulkarni, Fredericks Vaz and NR Pinto 2011). The purpose of present study was to quantify various chronic complications of diabetes and their association with degree of hyperglycemia as represented by glycated hemoglobin (HbA1c).

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MATERIALS AND METHODS

This was a cross sectional study and was conducted in the department of Biochemistry in collaboration with department of Medicine, Acharya Shri Chander college Of Medical

Sciences (ASCOMS) and Hospital Sidhra, Jammu and department of biochemistry, Government Medical College Amritsar. 200 type 2 known diabetics with and without complications of diabetes, were recruited for the study. The study was approved by ethics committee of ASCOMS and hospital. Informed consent for the inclusion of the patient in study was taken and the purpose of the study was indicated clearly to the participating individuals in vernacular language. Patients suffering from other diseases like thyroid dysfunction, any type of malignancy, Alzheimer's and Asthmatics were not included. Patients on cyclosporins and steroid immunosuppressant were also excluded from study. The detailed history about duration of diabetes, hypertension, their dietary habits, life style, smoking habits and presence of any complications of diabetes were noted as per the Performa designed. Presence of complications was noted from medical records of patients.

All the patients were advised to observe an overnight fast and to comply with the instructions. Blood and urine samples were collected early in the morning. About six ml of blood was collected by venepuncture of the ante-cubital vein. The blood sample was divided into three vials, one containing anticoagulant (sodium fluoride and potassium oxalate) for plasma separation for estimation of blood glucose, in plain vials for serum separation and a vial containing EDTA for Glycated haemoglobin (HbA1c). Fasting blood glucose was estimated by enzymatic GOD/POD Method (Trinder, 1969), Blood Urea was estimated by GLDH-Urease method (Tiffany *et al,* 1972), Serum creatinine was estimated Jaffes Alkaline Picrate Method (Bowers, 1980), Glycated hemoglobin was estimated by ion exchange chromatography (Nathan *et al,* 1984) Microalbumin in urine was estimated by Pyrogallol Red method (Phllpou *et al,* 1989), Serum Cystatin-C was estimated by automated immunoassay (Newman *et al*, 1995). Serum total cholesterol was estimated by enzymatic (CHOD-PAP method of Allain CC 1974). Serum HDL was estimated by the autozyme precipitation reagent method in conjunction with autozyme cholesterol reagent–for enzymatic determination of HDL cholesterol in the supernatant (Burstein *et al,* 1970). Serum LDL-C was calculated (by Friedwald's formula 1972). Serum triglyceride was estimated by enzymatic method (Trinder, 1968). Serum electrolytes sodium and potassium were analyzed with ion selective electrodes (Levy, 1981). Serum calcium was estimated by Orthocresolphthalein method (Harold *et al,* 1966). Comparison of means of various biochemical parameters was done using student t test. Analysis of variance (ANOVA) was applied for comparison between groups.

RESULTS

All the individuals were divided into 3 groups depending on values the values of glycated hemoglobin i. e ≤7%, 7-9% and >9%. Out of 200 patients 46 (23%) had HbA1c ≤7%, 90 individuals were in the range of >7-9% HbA1c and 64 (32%) were having HbA1c >9%. When degree of hyperglycemia was as low as ≤7%, 46 (23%) individuals suffered hypergycemia, out of which 27 (13.5%) had no complications whereas 19 (9.5%) had begin with diabetic complications. Out of 19, 5 (2.5%) suffered both macrovascular and microvascular complications, 4 (2%) macrovascular complications and 10 (5%) suffered microvascular complications. It was observed that 90 (45%) diabetic individuals were having HbA1c >7-9%.

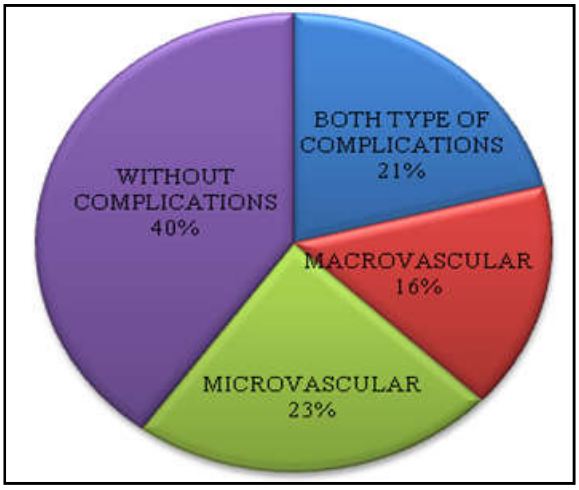

Fig. 1. Prevalence of different complications in Type 2 diabetics of Jammu Region

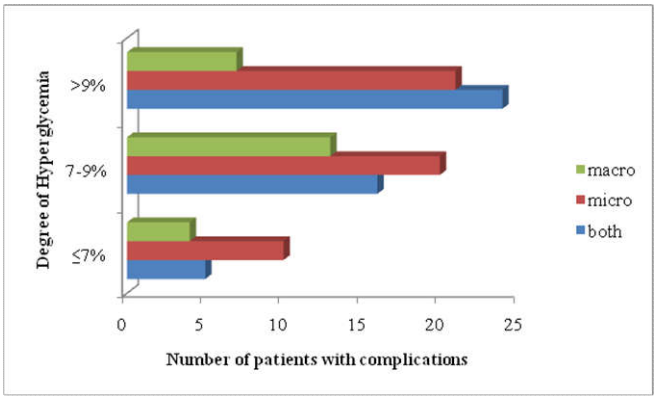

Fig. 2. Prevalence of complications in relation to Degree of hyperglycemia

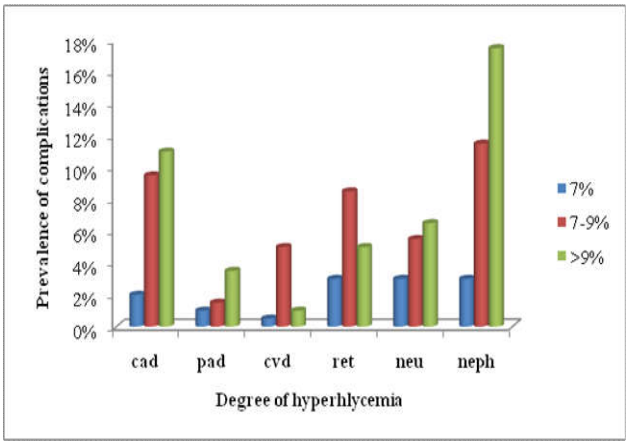

Fig. 3. Prevalence of macrovascular and microvascular complications

Out of 90, 41 (20.5%) individuals had not developed any complication and 49 (24.5%) individuals suffered complications. Out of 49, 16 (8%) individuals suffered both macrovascular and microvascular complications, 20 ((10%) suffered microvascular complications 13 (6.5%) and macrovascular complications. When degree of hyperglycemia was >9%, out of 64 (32%) individuals, 12 (6%) individuals had not suffered any complications and 52 (26%) had developed complications. Out of 52, 24 (12%) individuals suffered macrovascular and microvascular complications, 21

((10.5%) suffered microvascular complications and 7 (3.5%) macrovascular complications (Table 1 and Figure 2).

Table 1. Diabetic patients with and without complications

Degree of hyperglycemia	Total no of Patients	Diabetics without complications	Diabetics with complications
≤7%	46(23%)	27(13.5%)	19(9.5%)
7-9%	90(45%)	41(20.5%)	49(24.5%)
>9%	64(32%)	12(6%)	52(26%)

Table 2. Baseline metabolic parameters of patients and degree of hyperglycemia

Parameters	Degree of Hyperglycemia			
HbA1c	**≤7%**	**>7-9%**	**>9%**	**p value**
Blood Glucose	141±65	164±79	221±27	0.001
Urea	40±20	51±43	66±40	0.001
Creatinine	1.35±0.9	1.59±1.4	2.19±1.6	0.004
Cystatin-C	1.52±0.7	1.68±0.9	2.22±1.2	0.001
Microprotein	143±44	305±218	380±158	0.001
Cholesterol	183±40	195±42	181±42	0.09
Triglyceride	162±43	185±82	178±55	0.11
HDL-C	42±6	44±12	38±8	0.17
LDL-C	106±41	120±44	137±18	0.04
VLDL-C	32±18	41±14	37±18	0.05
HsCRP	2.2±1.6	3.1±2.2	5.4±2.3	0.05
Plasma Proteins	7.1±0.7	6.2±1.0	5.9±1.2	0.5
Albumin	4.1±1.3	3.9±0.9	3.6±1.1	0.2
Sodium	136±3.5	134±3.2	130±3.8	0.4
Potassium	4.0±0.5	4.1±0.5	4.2±0.7	0.8
Calcium	9.4±1.1	9.0±1.3	8.3±1.1	0.001

Further the type of micro and macrovascular complication was studied in the individuals and it was observed that when degree of hyperglycemia was ≤7%, among microvascular complications 6 (3%) individuals suffered retinopathy, 6 (3%) neuropathy and 6 (3%) individuals suffered nephropathy. Among macrovascular complications 4 (2%) individuals suffered CAD, 2 (1%) individuals suffered PAD and 1 (0.5%) individuals suffered CVD. When degree of hyperglycemia was >7-9%, number of individuals suffering from microvascular complications increased to 17 (8.5%) retinopathy, 11 (5.5%) neuropathy and 23 (12.5%) nephropathy. Number of individuals suffering from macrovascular complications also increased to CAD 19 (9.5%), PAD 3 (1.5%) and CVD 10 (5%).

When degree of hyperglycemia was >9%, number of individuals suffering from microvascular complications increased to 10 (5%) retinopathy, 13 (6.5%) neuropathy, 35 (17.5%) nephropathy. Number of individuals suffering from CAD and PAD increased to 22 (11%) and 7 (3.5%) respectively whereas number of patients suffering from CVD decreased to 2 (1%) perhaps those with cerebrovascular disease may not have survived due to cerebrovascular accidents like stroke. Prevalence of both type of complications increased with increasing degree of hyperglycemia (Figure 3). Blood levels of various biochemical parameters like glucose, urea, creatinine, Cystatin-C LDL Cholesterol, HsCRP increased significantly and those of calcium decreased with increasing degree of hyperglycemia (P< 0.05) (Table 2).

DISCUSSION

As prevalence of diabetic complications is increasing with degree of hyperglycemia there is an urgent need to slow down epidemic of diabetes to reduce the burden of various associated complications. Premature mortality occurs in patients with diabetes under the age of 60 because of various complications like CAD, stroke and ESRD. In our study two third patients were suffering from at least one complication. Among microvascular complications prevalence of retinopathy was 16.5%, same figures were reported from South India (Vishwanathan Mohan *et al,* 2013). This prevalence is lower than another study where it was reported to be 33% from Goa (Nafisa C Vaz *et al,* 2011). Our study shows that 32% patients were suffering from nephropathy the finding is consistent with study at Chennai (CUPS no 5), higher than reported from China 29.3% (Jia et al., 2009) little higher than a study from Tamil Nadu 30.7% (Karthikeyan Manirasu, Logaraj Muthunarayanan 2017) and much higher than a study from Solapur (Sherry Garg et al., 2018). Prevalence of end stage renal diseases is up to 10 times higher in people with diabetes. Prevalence of neuropathy was 15%, consistent with a study from Goa (Vaz *et al*, 2011). Prevalence of CAD is 22.5% almost consistent to a study done in Chennai which revealed a prevalence of 21.4% (Mohan *et al,* 2001) and higher than which reported a prevalence of 16.2% (Krishan, 2012).

Diabetes is characterised by hyperglycemia, dislipidemia and insulin resistance. Prevalence of PAD in our study is 6% which is lower than reported in a study from Goa 11% (Nafisa C Vaz *et al.,* 2011) and another study reported a prevalence of 14.3% (Aggarwal *et al.,* 2012). Prevalence of cerebrovascular diseases in our study is 6.5%, consistent with a study from Saudi Arabia (Alaboud *et al,* 2016) and higher than another study which reported a prevalence of 10% from Goa (Sherry Garg et al., 2018). Chronic hyperglycemia is responsible for various acute and chronic complications of diabetes. Several mechanisms responsible for various vascular complications are activation of polyol pathway, hexosaminase pathway, activation of Protein Kinase C, increased oxidative stress, and increased production of advanced glycation end products (AGE), increased production of growth factors, cytokines and angiotensin 11. These factors are responsible for inducing endothelial damage, development and progression of various microvascular and macrovascular complications. There are lot many studies showing that an early intensive control of hyperglycemia can prevent intensive control of hyperglycemia can prevent the development of various micro and macrovascular complications. The development of diabetic

complications is due to oxidative stress, epigenetic changes, chronic inflammation, formation of advanced glycation end products and form basis for metabolic memory or legacy effect. Hyperglycemia causes production of superoxide anions in mitochondria of endothelial cells responsible for various diabetic complications. All these mechanisms may persist when hyperglycemia is achieved after treatment. Development and progression of diabetic complications can be prevented by preventing the damage caused by hyperglycemia induced stress if treatment started early. Reversal of complications becomes impossible if persistent hyperglycemia occurs for prolonged time and then normoglycemia is achieved. (Roberto et al., 2017). Prevalence of all complications is increasing with degree of hyperglycemia.

Conclusion

Economic burden of diabetes is due to complications responsible for hospitalizations, leading to morbidity disability and mortality. Prevalence of complications increased with increasing degree of hyperglycemia and hyperglycemia which is a modifiable factor in pathogenesis of diabetic complications. Initial treatment of complications is prevention and that can be achieved by keeping a good glycemic control as measured by HbA1c. Patient self management, education regarding diabetes and its various devastating complications, adherence to proper treatment regime, good exercise, healthy life style and good dietary habits can prevent, delay the development of complications and halt the progression of complications.

Conflict of Interest: There is no conflict of interest.

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