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Original Research Article

A CROSS-SECTIONAL OBSERVATIONAL DESCRIPTIVE STUDY ON GLYCAEMIC CONTROL, DURATION OF DIABETES MELLITUS, AUTONOMIC NEUROPATHY AND CUTANEOUS MANIFESTATIONS IN TYPE 2 DIABETES MELLITUS PATIENTS

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Abstract

Background: Type 2 diabetes mellitus is a global concern and public health issue in India, affecting various organs and causing skin disorders in 30% of patients with potential diabetic neuropathy and angiopathy. The present study is aimed to analyse the duration of diabetes, glycaemic control, autonomic neuropathy and dermatological manifestations in Type 2 DM. **Materials and Methods:** 100 Type 2 DM subjects in the age group between 30-70 years of both genders were randomly selected. History regarding the demographic profile, duration of Diabetes Mellitus, treatment particulars, personal and family history of DM and any other ailments were obtained. Height and weight were recorded, and body mass index was calculated for all patients. Detailed dermatological examination was done. Venous blood was collected and tested for HbA1C, fasting and postprandial blood glucose, urea, serum creatinine, and lipid profile. Patients were also tested for Sympathetic skin response (SSR). **Results:** Skin infections were the commonest cutaneous manifestations in DM, and poor glycaemic control was observed among the most of the severe infections. A positive correlation was noted between the duration of DM and the severity of skin complications. SSR was absent in most subjects with xerosis, which reflects autonomic neuropathy due to defective sympathetic nerve function. The present study showed a positive association between the duration of DM and glycaemic control with DM complications in the skin. The average age of subjects was 56 years, and females outnumbered males. **Conclusions:** The present study infers a positive association of duration of DM, glycaemic control, autonomic neuropathy with DM complications in the skin.

INTRODUCTION

Type 2 diabetes mellitus is the commonest form of diabetes worldwide. The overall prevalence of T2DM in South Asia is high and increasing. By 2030, there will be 120.9 million people with diabetes in South Asia (90–95% of these cases will be T2DM).[1] Type 2 DM has become a major public health problem in India now. It is also probable that there is also a substantial delay in the diagnosis of DM. This is partly due to provider issues and a lack of public awareness.[2] Skin is affected by both acute metabolic defects and chronic degenerative complications of diabetes. It is observed from studies that more than 33% of diabetic patients have some dermatologic manifestations on a chronic run.[3] Atherosclerosis, microangiopathy, abnormal carbohydrate metabolism, neuronal degeneration and impaired host defence mechanism all contribute to the pathogenesis of cutaneous complications.[4] Cutaneous signs and symptoms of diabetes mellitus are extremely valuable to the physician as some may reflect the status of lipid metabolism and glycaemic control.[5]

Autonomic dysfunction is a major microvascular complication of DM involving the cardiovascular, gastrointestinal, genitourinary, and sudomotor systems. Karamitsos and colleagues have reported that the progression of diabetic autonomic neuropathy is significant during the two years following its diagnosis.[6] Autonomic involvement of CVS has been studied extensively, but sudomotor function, specifically the peripheral sympathetic nerve fibers which supply the eccrine sweat glands of the skin, is an unearthed treasure. From many studies, it is evident that the duration of diabetes mellitus and

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glycaemic control are directly related to the complications of DM, and generally, glycaemic control is assessed by HbA1c.[7] Some studies have reported a continuous, but not linear, relationship between the level of glycemia and the risk of development and progression of these complications.[8]

Since the incidence and prevalence of type 2 DM is more, type 2 DM subjects were selected for this study. As Autonomic Nervous System (ANS) function tests in DM skin manifestations were not much studied, our study had been designed to analyse the duration of diabetes mellitus, glycaemic control, autonomic neuropathy and skin manifestations in type 2 DM.

MATERIALS AND METHODS

This cross-sectional descriptive observational study was conducted at Tirunelveli Medical College Hospital for six months on 100 patients. The subjects were randomly selected from the Diabetology and Dermatology outpatient departments. Informed consent was obtained from all study subjects. Institutional ethical committee clearance was obtained.

Inclusion Criteria

Patients of either sex, aged between 30 to 70 years, diagnosed with Type 2 diabetes mellitus were included.

Exclusion Criteria

Patients with Type 1 diabetes mellitus, drug-induced diabetes, gestational diabetes and comorbidities such as thyroid disorders, epilepsy, bronchial asthma, tuberculosis and on medications that can induce neuropathy, alcoholics and Hansen's disease were excluded.

Methodology:

The demographic details of the subjects, namely age, sex, education, occupation, address and history related to personal habits like smoking, alcoholism, and family history regarding DM in parents and siblings, were obtained by a pretested questionnaire. History associated with the duration of DM, and medications for DM, whether on oral hypoglycemic agents, insulin, or any alternative medicine, were enquired. Pre and present histories of skin diseases were elicited, and a history of thyroid disorder, bronchial asthma, tuberculosis and epilepsy were enquired. History of other drug intake and neuropathy due to other diseases were enquired. Height and weight were measured, BMI was calculated, and pulse rate and blood pressure were recorded for all the patients.

Patients were subjected to a detailed dermatological examination by a dermatologist. Under strict aseptic precautions, venous blood samples were collected in appropriate containers in fasting and postprandial states. The blood samples were analysed in Central Laboratory Tirunelveli Medical College Hospital, Tirunelveli, for HbA1c, sugar, urea, creatinine and lipid profile.

SSR test was done in the Department of Neurology using the Medicaid EMG-200 Digital polygraph 4-channel Neurostim machine. We followed the standard method described by Kucera et al. in their study.[9] Single electrical stimulus was given for 0.1msec duration with 10mA intensity to the contralateral median nerve, contralateral posterior tibial nerve, ipsilateral median nerve and ipsilateral posterior tibial nerve. Recording from all four extremities was done, and the absence of SSR from at least two extremities after electrical stimulation followed by deep inspiration was considered abnormal. One stimulus per minute was given to avoid habituation, and after 2 minutes, the next stimulus was given. Likewise, five stimuli were given, and the presence or absence of a response was observed and recorded.

Statistical Analysis

All the results were analysed by using IBM SPSS statistical software version 16. The demographic profile was analysed. Skin manifestations were cross-tabulated with a duration of DM and analysed. Glycaemic control was studied with skin manifestations. SSR test was cross-tabulated and analysed with skin manifestations.

RESULTS

The study population showed female predominance accounting for 64% and a mean age of 56. Most patients had done schooling (64%), and predominantly (40%) the cases were housewives. 58% of the patients were from urban residency. A total of 44% of the patients reported positive family history of DM and 25% were smokers, and 54% were overweight and obese [Table 1].

79% were reported with DM duration of <10 years. Of all patients, 28% showed good, 22% fair, and 50% poor glycaemic control. Fasting blood sugar was normal in 20% and high in 80%. Postprandial blood sugar values were high in 89% of patients. Observed urea values showed 93% having normal results and 7% having high values. It was observed that 92% of subjects had Creatinine values within the normal range, and 8% of subjects had high creatinine values. SSR was present in 72% and absent in 28% [Table 2].

Among the reported cases, the most common skin manifestations were fungal infections and xerosis, each accounting for 27% and 26% of the cases, respectively. Bacterial infections were also relatively common, occurring in 13% of the cases. Viral and parasitic infections, psoriasis vulgaris, pityriasis rosea, lichen planus, diabetic dermopathy, diabetic bullae, diabetic ulcer, and vitiligo were less frequent, ranging from 4% to 1% of the cases [Table 3].

Diabetic dermopathy, diabetic bullae, and diabetic foot ulcers were observed in subjects with > 10 years of DM [Table 4]. The observation was that a major

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percentage of skin infections, diabetic bulla, diabetic ulcer foot, and diabetic dermopathy occurred with poor glycaemic control. Of 45 subjects with infection, 31 had poor glycaemic control. Sympathetic skin response was tested and observed, whether recordable or not recordable. We observed that in 72% it was recordable, and in 28%, SSR was not. In diabetic bullae, diabetic dermopathy, and diabetic ulcer foot SSR was not recordable [Tables 5,6].

Table 1: Observation of demographic and other evaluation variable of patients

Parameters		**Frequency (%)**
Gender	Male	36 (36%)
	Female	64 (64%)
Age group	30 - 40	7 (7%)
	40 - 50	26 (26%)
	50 - 60	31 (31%)
	60 - 70	36 (36%)
Mean Age (Years) (Mean± SD)		56.02± 3.5
Educational status	Illiterate	3 (3%)
	Schooling	64 (64%)
	Diploma/ITI	8 (8%)
	Undergraduate	18 (18%)
	Postgraduate	3 (3%)
	Professional	4 (4%)
Occupation	Cooley	19 (19%)
	Housewife	40 (40%)
	Business	8 (8%)
	Private	16 (16%)
	Government	17 (17%)
Place	Rural	42 (42%)
	Urban	58 (58%)
Smoking	Non-smoker	75 (75%)
	Smoker	25 (25%)
Family history of DM	Mother and father	12 (12%)
	Mother alone	20 (20%)
	Father alone	12 (12%)
	Neither parent	56 (56%)
Weight	Under Weight	1 (1%)
	Normal weight	45 (45%)
	Over Weight	37 (37%)
	Obesity 1	16 (16%)
	Obesity 2	1 (1%)

Table 2: Duration of DM and other biochemical parameters

Parameters		**Frequency (%)**
Duration of DM (years)	<1	13 (13%)
	1 - 5	38 (38%)
	5 - 10	28 (28%)
	10 - 20	19 (19%)
	>20	2 (2%)
HbA1c%	< 7	28 (28%)
	7 - 8	22 (22%)
	> 8	50 (50%)
Blood sugar fasting (mg/dL)	Normal (70 -110)	20 (20%)
	Abnormal (>110)	80 (80%)
Blood sugar postprandial (mg/dL)	Normal (110-140)	11 (11%)
	High (>140)	89 (89%)
Blood Urea (mg%)	Normal (15 - 40)	93 (93%)
	Abnormal (>40)	7 (7%)
Serum creatinine (mg%)	Normal (0.2 - 1.2)	92 (92%)
	Abnormal (>1.2)	8 (8%)
Sympathetic skin response (SSR)	Absent	28 (28%)
	Present	72 (72%)

Table 3: Distribution of skin manifestations

Skin Manifestations	**Frequency (%)**
Bacterial Infection	13 (13%)
Fungal Infection	27 (27%)
Viral Infection	4 (4%)
Parasitic Infection	1 (1%)
Psoriasis Vulgaris	4 (4%)
Pityriasis Rosea	1 (1%)
Lichen Planus	1 (1%)
Xerosis	26 (26%)

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Diabetic Dermopathy	2 (2%)
Diabetic Bullae	1 (1%)
Diabetic Ulcer	1 (1%)
Vitiligo	4 (4%)
Others	15 (15%)

Table 4: Observation of Skin manifestations with Duration DM

Skin Manifestations	Duration of DM in years					Total
	<1	1-5	5-10	10-20	>20	
Bacterial Infection	0	5	4	4	0	13
Fungal Infection	7	11	7	2	0	27
Viral Infection	0	3	1	0	0	4
Parasitic Infection	0	1	0	0	0	1
Psoriasis Vulgaris	0	3	0	1	0	4
Pityriasis Rosea	0	1	0	0	0	1
Lichen Planus	0	0	0	1	0	1
Xerosis	1	4	12	7	2	26
Diabetic Dermopathy	0	0	0	2	0	2
Diabetic Bullae	0	0	0	1	0	1
Diabetic Ulcer	0	0	0	1	0	1
Vitiligo	0	1	3	0	0	4
Others	5	9	1	0	0	15

Table 5: Observation of Skin manifestations with HbA1C

Skin Manifestations	HbA1c%			Total
	<7%	7-8%	>8%	
Bacterial Infection	0	1	12	13
Fungal Infection	3	7	17	27
Viral Infection	1	1	2	4
Parasitic Infection	1	0	0	1
Psoriasis Vulgaris	3	1	0	4
Pityriasis Rosea	1	0	0	1
Lichen Planus	1	0	0	1
Xerosis	5	8	13	26
Diabetic Dermopathy	0	0	2	2
Diabetic Bullae	0	0	1	1
Diabetic Ulcer	0	0	1	1
Vitiligo	3	0	1	4
Others	10	4	1	15

Table 6: Observation of Skin manifestations with SSR

Skin Manifestations	SSR		Total
	Not recordable	Recordable	
Bacterial Infection	4	9	13
Fungal Infection	1	26	27
Viral Infection	1	3	4
Parasitic Infection	0	1	1
Psoriasis Vulgaris	0	4	4
Pityriasis Rosea	0	1	1
Lichen Planus	0	1	1
Xerosis	15	11	26
Diabetic Dermopathy	2	0	2
Diabetic Bullae	1	0	1
Diabetic Ulcer	1	0	1
Vitiligo	1	3	4
Others	2	13	15

DISCUSSION

Analysis of demographic profiles showed that the mean age in this study was 56 years, and the maximum number of patients (36%) were 60 to 70 years old. Our study population, and age group distribution, were consistent with Goyal et al. study, in which the mean age was 57.44 years.[10] The male: female ratio of 1:1.77 was reported in our study. In their studies, the female predominance seen in our study was also reported by Mahajan et al. and Romano et al.[11,12] Residential status showed an urban: rural ratio of 1.08:1. International Diabetes Federation (IDF) statistics showed more incidence and prevalence of DM in the urban population when compared to the rural population.[13] But nowadays incidence and prevalence of DM among the rural population is increasing. Educational status observed in this study was illiterate 3% (criteria based on census India), and 97% literates and housewives were more in this study.

A family history of DM revealed that 44% of subjects had a positive family history, and 56% had a negative one. Our study observation showed significant

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positive family history, as reported in the literature. If both parents had DM, an individual's chance of getting DM increased by 70%.[14] Alcoholics were excluded from the study because alcohol-induced neuropathy can induce abnormalities in SSR. Of all subjects, smokers were 25%, and smoking, hyperglycaemia, and disordered lipid metabolism make the individual more prone to both microvascular and macrovascular complications of DM.

In our study, skin infections were the predominant skin manifestations seen in 45% of the population. Among infections, fungal etiology was predominant, and the next was bacterial. It was similar to the study done by Mahajan et al.[11] In our study, the observed skin manifestations of infective origin included 27% of fungal, 13% of bacterial, 4% of viral and 1% of parasitic. Among fungal infections, candidal infection (13%) was predominant, followed by dermatophyte infection (12%). According to Duff M et al., candidal vulvovaginitis is the most common form of candidal infection in type 2 diabetics.[15]

In their study, Al-Mutairi outlined bacterial infection as more common than dermatophyte, candida and viral infections.[16] In our study, bacterial infections ranked second in overall skin infections, wherein among 13% of bacterial infections, furunculosis was the most observed one (9%), followed by cellulitis (4%). The relatively high observation of skin infections can be explained as uncontrolled diabetes mellitus, which increases the risk of developing microangiopathy and related sequelae. Xerosis was observed in 26% of the total study population, which was the second commonest observation in our study. The clinical observations are supported by objective findings of a reduced hydration state of the stratum corneum and decreased sebaceous gland activity in patients with diabetes mellitus.[17] Fluctuations in glucose levels seem to be the reason for dry skin in diabetes. However, autonomic neuropathy may also play a significant role in skin dehydration in diabetic patients and, thereby, Xerosis.[18]

In our study, psoriasis vulgaris was observed in 4%, and Sezai Sasmaz et al. noted that 11.2% had psoriasis with type 2 DM. There have been reports of a significant association between DM and psoriasis in many studies.[19] Vitiligo was observed in 4% of cases in this study. It was known that type 1 DM is associated with autoimmune skin conditions, and type 2 DM is commonly associated with skin infections. But in a study conducted by Raveendra et al., they reported that Vitiligo can occur in type 2 DM.[20] We also observed Vitiligo in type 2 DM in our study. Acanthosis Nigricans was observed in 3% of patients in this study, whereas Mashkoor Ahmed Wani reported 11.64% in their study, which is almost three times more than our study.[21] Acanthosis nigricans is considered a cutaneous marker for insulin resistance, and insulin resistance can be associated with the development of type 2 DM.[22]

Duration of DM and glycaemic control are crucial factors in microvascular and macrovascular complications. Regarding DM duration, out of 100 subjects, 79 subjects had DM for < 10 years, and 21 subjects had DM for > 10 years. Our study observation of a greater number of subjects in < 10-year duration and a smaller number of subjects in > 10-year duration was consistent with Chatterjee et al. study.[23] Long-term effects of DM on the microcirculation and dermal collagen eventually result in skin disorders in almost all diabetics.[10] On considering duration and skin manifestations, in our study, diabetic dermopathy, diabetic bullae, and diabetic foot ulcer were observed in subjects with > 10-year duration of DM. Diabetic dermopathy was observed in 2% of study subjects, and it may serve as a clinical sign of an increased likelihood of vascular complications in diabetic patients. Shahzad et al. noticed a positive correlation of skin lesions with disease duration.[24] In our study, out of 45% of subjects with skin infections, 31% had poor glycaemic control, 9% had fair control, and 5% had good control. Severe form of skin infections was noted in patients with poor glycaemic control. Chatterjee et al. reported that the mean HbA1c level was higher in patients with infective lesions.[23] Possibility of cutaneous infection is explained as increased blood glucose level leading to white blood cell dysfunction, which allows microbes to proliferate.[25]

In our study, SSR was recordable in 72% of study subjects and not recordable in 28% of study subjects. SSR was not recordable in 57.69% of the xerosis subjects of our study. Al-Moallem et al. showed a significant association of autonomic neuropathy with SSR.[26] Jha and Nag found SSR was not recordable in 42% of asymptomatic diabetics, but in DM subjects with autonomic dysfunction, SSR was not recordable in 66%.[27] As the disease progresses from asymptomatic to symptomatic polyneuropathy and symptomatic autonomic neuropathy, the frequency of abnormalities increases in SSR. Xerosis with absent SSR subjects must be evaluated for other ANS dysfunction, mainly cardiovascular ANS dysfunction. Of 100 study subjects, 8% had nephropathy with serum creatinine > 1.2 mg %, and all 8 had poor glycaemic control. Out of 8 subjects with increased serum creatinine, 4 had a severe bacterial infection, 2 had diabetic dermopathy, 1 had diabetic bullae, and 1 had a fungal infection.

CONCLUSIONS

As the duration of diabetes gets longer, the complications become severe. It is imperative to diagnose diabetes mellitus early to prevent the morbidity and mortality associated with microvascular complications. DM is in increasing trend among the rural population. Proper awareness programmes can reduce the percentage of undiagnosed diabetics by bringing the individuals voluntarily to the healthcare providers. Commonest observed skin manifestations in our DM study

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subjects were skin infections. The factor responsible for this was considered to be poor glycaemic control. Xerosis observed in most subjects in our study could be considered as the earliest indicator of DM cutaneous autonomic neuropathy. SSR was not recordable in a reasonable number of diabetic subjects. Absent SSR signifies that the subjects have autonomic neuropathy related to sudomotor function. So, skin examination and SSR tests can be included in the routine examination of diabetic individuals because these are relatively simple, less time-consuming, non-invasive methods yet with enormous positive outcomes for human wellbeing.

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