Nephropathy Symptoms in Type-2 Diabetic Patients and Their Relationship with Daily Exerciser and Sunlight Exposure

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Abstract

Background: Type 2 Diabetes Mellitus (T2 DM) is chronic metabolic disorder withan increasing prevalence worldwide and manifolds with high morbidity and mortality in both developed and developing countries. It can cause complications if remain uncontrolled. The aim of the study was to find out the socioeconomic status, complications associated with diabetic neuropathy and correlation with life style.

Materials and methods: A cross sectional study was carried out for a period of one year (October 2020 to October 2021) among the diagnosed T2 DM patients in Southern Medical College Hospital (SMCH) Chattogram, Diabetic General Hospital (CDGH) and author's personal chamber. Total 158 patients were enrolled for this study and data were collected through a pre-structured questionnaire.Collected data were entered into the MS Excel-2010, sorted out and exported to Statistical Package for Social Sciences (SPSS) Version 20.0. Descriptive statistics were performed followed by student's t-test, Chi-square test among different groups then correlation and multiple linear regression analysis were performed.

Results: Among total enrolled patients, 72(46%) were male and 86(54%) were female where 62% patents lived in urban areas. 13.3% of the patients didn't perform any daily exercise and 27% led a sedentary life style. 61.4% had daily sunlight exposure varying from few hours to 6-8 hours where 58(80.6%) were male and 39(45.3%) were female ($p<0.00$) respectively. Chi-square test showed increase prevalence for HTN and Dyslipidaemia ($p<0.05$) regarding daily exercise. Increased prevalence of periodontitis, Feet/Leg cramps, GIT problems infemale sex were predominant as opposed to males due to less daily sunlight exposure. Multiple linear regressions confirmed that sex ($p=.000$) plays an important roleregarding diabetic neuropathy related symptoms and complications, where female had morediabetic neuropathy related symptoms and complications than males ($\beta=.341$, 95% CI=.190~.477, $p=0.000$) with less daily sunlight exposure.

Conclusion: Female has less sunlight exposure than male, so they likely have less vitamin D level than male which might triggers diabetic neuropathy symptoms. So every T2 DM patient should routinely assay vitamin D level.

Key words: Neuropathy; Sunlight; T2 DM; Vitamin D.

Introduction

Diabetes Mellitus (DM) is a chronic debilitating disease affecting the Global population for last few centuries. The rising burden of type 2 diabetes is a major concern in healthcare worldwide. In 2021, approximately 537 million individuals or 10.5% adults were affected by diabetes mellitus of which 90 million are from South-east Asia.[1] International Diabetes Federation have predicted that the expected number of adults with diabetes will reach up to 643 million by 2030 and 783 million by 2045.[2] Over 3 in 4 adults with diabetes are living in low- and middle-income countries accounting for about 79% adult diabetic cases.[3] In Bangladesh there were 8.4 million adults living with diabetes in 2019 and it is projected to increase to around 13.7 million by 2045.[2]

Type 2 diabetes (Formerly called non-insulin-dependent or adult-onset diabetes) results from the body's ineffective use of insulin.[4] Type 2 diabetes accounts for 90% of people with DM around the world.[5] Diabetes mellitus cases has been increasing as a chronic case in wider context of South East Asia due to rapid urbanization leading to increasing sedentary life style, dietary excess fat intake and stressful life. Biological factors are also associated with life style that ultimately led to 3 fold higher prevalence of Diabetes in South East Asia compared to Europe.[6,7]

Uncontrolled T2DM can be life threatening if unmanaged. T2DM can damage the eyes, heart, blood vessels, nerves, and kidneys, and increases the risk of cardiovascular disease and cerebrovascular disease over time. These damages ultimately resulting in blood flow reduction, combined with nerve damage (Neuropathy) in feet-increases the risk of foot ulcers, infection and might even lead to limb amputation.[8]

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Chattogram is a major and second largest densely populated city situated in the south-eastern part of Bangladesh having a population of more than 5,132,751 in 2021.[9] The city is situated on the banks of the river Karnaphully between the Bay of Bengal and Chattogram Hill Tracts. Modern Chattogram is the second most significant urban center in Bangladesh after Dhaka. A survey conducted in Chattogram Medical college Hospital in 2019 shows that women are more prone to diabetes compared to men, which is 61%. In this age distribution, it is observed from above figure 51-60 aged people are mainly suffering from diabetes mellitus. The study also shows that 32% are suffering from blood pressure, 33% from joint pain, 15% from back pain, 7% from foot pain, 10% from itching, 3% from arthritis and 9% from allergy.[10] In Bangladesh, besides the afore-mentioned studies, no detailed studies have been done regarding daily sunlight exposure and daily exercise and their association with T2 DM neuropathy symptoms and T2DM associated risk factors. Therefore, the study was conducted with the aim of finding out the prevalence of T2 DM neuropathy and T2 DM associated risk factors and correlate with lifestyle.

Materials and methods

This cross sectional study was conducted for a period of one year from October 2020 to September 2021.The target population for the study was the outdoor patients in Chattogram Diabetic General Hospital (CDGH) Author's personal Chamber and Southern Medical College Hospital (SMCH) Chattogram.Total 158 sample data has been entered for analysis. It was a cross sectional study that was conducted for the assessment of prevalence of Type 2 diabetes mellitus complications in humans in Chattogram city. Diagnosed case of T2 DM according to the International standard by American Diabetic Association (ADA) was the inclusion criteria.[4] All T2DM patients fulfilling the inclusion criteria were invited to take part in the study with their written consent.The ethical clearance was also obtained from the respective Institutional Review Boards. Detailed information regarding the study was provided to all eligible individuals. Only the subjects who agreed to participate and sign in the consent part were included in the study. Subjects were interviewed face to face using a pre-structured questionnaire by the author himself to gather the information regarding demographic details, risk factors, present diabetic problems, or complications and T2 DM associated risk factors and life style.The gathered information was entered into MS-Excel-2010, coded, decoded, sorted out and exported to Statistical Package for Social Sciences version 26. Student's t-test, Chi square test, correlation and multiple linear regression analysis were performed. The $p < 0.05$ was considered significant.

Results

The analysis of the socio-demographic status, life style behavior, general health characteristics of 158 T2DM patients are depicted in Table I which shows55.7% participants were from the author's personal chamber. 54.4% were female and 45.6% were male. Highest number (62.1%) of participants were from urban areas and lowest number (1.8%) are living in overseas. 50% participants are unemployed, 21.5% are job holders, 17.7% are businessmen, 2.8% are farmers and rest are retired. As far as the Educational status is concerned, 24.6% completed Honors and above, 8.9% were illiterate, 20.9% completed primary and the rest have completed either SSC or HSC. Almost 75% had never smoked and 20% were former and rest were current smokers. 84.7% individuals perform daily exercise starting from minimum 30 mins brisk walk per day. 61.4% have daily sunlight exposure varying in duration from few hours to 6-8 hours.In this study only 16.50% participants showed no family history of T2 DM,

Table II shows student's t-Test result of the baseline comparison between male and female regarding socio-demographic status and chronic complications of T2 DM and associated factors with related biochemical laboratory values including minimum value, maximum value and mean with standard deviation. Here duration of Hypertension ($p<.05$) and Dyslipidemia is higher in female. Percentages of diabetic neuropathy symptoms are higher in female than male.

The T2 DM associated complications and associated factors in Table III shows that among the participants having Diabetic Neuropathy related problems (36.07% have Burning sensation, 36.70% have Teeth/Gum problems, 24.05% have

GIT problems, 9.50% have Sexual function problems and rest 1.26% have Psychological problems). Analyzing the T2DM associated factors 54.43% have Hypertension and 44.90% have Dyslipidemia and 37.9% have both HTN and Dyslipidemia.

χ^2-test result on the basis of comparison among complications and associated factors where independent variable is daily exercise is shown in Table IV. It shows the diagnosed case of HTN and Dyslipidemia now doing daily exercises are 95.4 % and 95.7% respectively. But neuropathy symptoms are more in the subjects who don't do daily exercises. The males conducted daily exercise more than females respectively.

Table V shows the male-female comparison on the basis of correlation between Diabetic neuropathy symptoms and T2 DM associated factors. This table shows highly significant difference between male and female where neuropathy symptoms (Burning sensation, teeth gum problem, GIT problem, Bone-Joints pain) HTN and Dyslipidaemia are more in female in correlation. In correlation to daily sunlight exercise, this is negatively correlated in female than male which indicates female has less sunlight exposure.

In Table VI, the results of χ^2-test are shown on the basis of comparison among complications and associated factors where the independent variable is daily sunlight exposure. Here sex ($p<.000$), teeth/gum problem ($p<.017$), Feet/Leg cramp ($p<.008$), GIT problem ($p<.045$) shows significant differences between factors.

On the basis of comparison among complications and associated factors where dependent variable was daily sunlight exposure and the independent factor was sex, the multiple linear regressions were done through different models adjusted for different chronic complications and risk factors associated with T2 DM. On the basis of p value of independent factor male sex, the comparison between male and female was done by the using following calculation (Here predictor value of male is, e=1) and Female predictor value = e^x (χ= value of β coefficient) were shown in Table VII.

Table I Socio-Demographic information of T2 DM patients (n-158)

Variable	Category	n	%
Patient's source	CDGH	22	14
	Author's personal chamber	88	56
	SMCH	48	30
Sex	Male	72	46
	Female	86	54
Residence Type	Urban	98	62
	Slum	16	10
	Rural	41	26
	Overseas	3	2
Educational Status	Illiterate	14	9
	Primary	33	21
	SSC	32	20
	HSC	40	25
	Honors and above	39	25
Religion	Muslim	149	94
	Hindu	7	4
	Christian	1	1
	Buddhists	1	1
Smoking status	Never	119	75.3
	Former	32	20.3
	Current	7	4.4
Performing physical exercise everyday:	No	21	13.3
	Heavy (Brisk walk>90mins)	7	3.7
	Moderate (Brisk walk60-90mins)	31	20
	Mild (brisk walk 30-59mins)	56	36
	Sedentary (Brisk walk<30mins)	43	27
Daily Sunlight exposure	No	61	38.6
	Yes	97	61.4
Family history of T2DM	Father	25	15.8
	Mother	38	24.1
	Father & Mother	22	13.9
	Brother, sister & other 1st degree family member	47	29.7
	No family history	26	16.5

Table II Baseline characteristics between male and female T2 DM individual (n=158): t-test

	Variable				Male			Female	
	n	Min	Max	Mean ± SD	n	Min	Max	Mean ± SD	p
Diabetic duration (Years)	72	0.5	30	7.34±7.28	86	0.5	32	6.73±6.60	.581
Hypertension (Years)	38	1	10	3.9474±2.59	48	1	40	6.13±5.98	.026
Dyslipidemia (Years)	30	0.5	10	3.27±2.72	40	0.5	10	3.35±2.41	.887
BS (Years)	24	0.5	8	3.08±2.42	33	0.5	6	2.96±2.33	.859
TGP (Years)	24	2	30	7.92±7.26	33	0.5	50	7.02±9.57	.627
FLP (Years)	20	1	5	2.31±1.37	28	0.5	10	2.82±2.06	.348
GIT problems (Years)	13	1	6	3.15±1.67	25	0.5	6	2.63±1.55	.344
SP (Years)	9	0.5	5	1.83±1.63	6	0.5	3	1.50±1.18	.676
BJP (Years)	11	0.5	7	2.67±1.86	23	0.5	7	2.99±1.97	.691

(Min=Minimum, Max=Maximum, BS= Burning sensation, TGP= Teeth/Gum problem, FLP= Foot/Leg Problem, GIT= Gastrointestinal Tract, SP= Sexual Problem, BJP= Bones and Joints Problem.)

Table III Diabetic neuropathy symptoms and associated factors of T2DM (n=158)

Variable	Category Symptoms/Problems	n	%
Diabetic Neuropathy symptoms	Paraesthesia/Burning	57	36.07
	Periodontitis/Teeth and Gum problems	58	36.70
	GIT problems (IBS, Constipation)	38	24.05
	Sexual function problems (Erectile dysfunction, Loss of libido, Frigidity)	15	9.50
	Psychological problems (Anxiety, Depression)	02	1.26
	Hypertension	86	54.40
Associated risk factor	Dyslipidemia	70	44.30
	No HTN or Dyslipidemia	02	1.3
	Both HTN & Dyslipidemia	60	37.97

(GIT= Gastrointestinal Tract).

Table IV Prevalence of complications between daily exercise and without daily exercise in T2 DM patients (n=158): χ^2-test

Variable	Category	Total(n)	With DE (%)	Without DE (%)	p
Hypertension	Yes	86	95.4	4.6	.000
	No	72	77.8	22.2	
Dyslipidemia	Yes	70	95.7	4.3	.003
	No	88	79.5	20.5	
Burning problem	Yes	57	84.2	15.8	.487
	No	101	88.1	11.9	
Teeth/Gum problem	Yes	57	87.7	12.3	.779
	No	101	86.1	13.9	
Feet/Leg cramp problem	Yes	48	87.5	12.5	.768
	No	110	86.4	13.6	
GIT problem	Yes	38	89.5	10.5	.553
	No	120	85.0	15.0	
Sexual Function problem	Yes	15	93.3	6.7	.427
	No	143	86.0	14.0	
Sex	Male	72	90.3	9.7	.249
	Female	86	83.7	16.3	

(DE= Daily Exercise, GIT= Gastrointestinal Tract).

Table V Male-female comparison in correlation between Diabetic neuropathy symptoms and T2 DM associated factors (n=158)

VAR	DE		HTN		DLP		BUP		TGP		GITP		BJP		SLE	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
DE			.218	.364**	.153	.342**										
HTN	.218	.364**			.517**	.586**			.281*	.299**			.050	.215*		
DLP	.153	.342**	.517**	.586**	-	-	.120	.247*	.212	.296**	.189	.325**				
BUP			.197	.199	.120	.247*							.316**	.330**		
TGP			.281*	.299**	.212	.296**					.492**	.499**			-.010	-.348**
GITP					.189	.325**			.492**	.499**						
BJP			.050	.215*			.316**	.330**			.371**	.342**				
SLE									-.010	-.348**	-.134	-.151				

(VAR= Variable, DE=Daily Exercise, HTN= Hypertension, DLP=Dyslipidemia, BUP=Burning Problems, TGP=Teeth/GumProblems, GITP= Gastrointestinal Tract problems, SP= Sexual Problems, BJP= Bones & Joints Problems, SE= Sunlight Exposure).

* Significant correlation.

** Strongly correlated.

Table VI Prevalence of complications between daily sunlight exposure or not in T2 DM patients: χ^2-test

Variable	Category	Total (n)	DSLE, Yes (%)	DSLE, No (%)	p
Sex	Male	72	80.6	19.4	.000
	Female	86	45.3	54.7	
Hypertension	Yes	86	54.6	45.4	.057
	No	72	69.4	30.6	
Teeth/Gum problem	Yes	57	49.1	50.9	.017
	No	101	68.3	31.7	
Feet/Leg cramp	Yes	48	45.8	50.9	.008
	No	110	68.2	31.8	
GIT problem	Yes	38	47.4	52.6	.045
	No	120	65.8	34.2	
Bones & Joints problem	Yes	34	47.0	53.0	.053
	No	124	65.3	34.7	

(DSLE=Daily Sunlight Exposure, GIT= Gastrointestinal Tract)

- Selection criteria: $p < 0.06$.

Table VII Risk of complications among T2 DM patients by category of daily sunlight exposure among total participants

Model no.	β (95% CI)	Male	Female	p
Model 1	.341 (.190~.477)	1	1.40	.000
Model 2	.345 (.194~.480)	1	1.41	.000
Model 3	.345 (.194~.480)	1	1.41	.000

(HTN= Hypertension, GIT= Gastrointestinal Tract).

Model 1: Predictor value for Female 1.40 means, 1.40-1= 0.40 or 40% more problems in Female than Male, adjusted for Sex, HTN, Teeth/gum problem, Feet/leg problem, GIT problem, Bones & Joints problem.

Model 2: Predictor value for Female 1.41 means, 1.41-1= 0.41 or 41% more problems in Female than Male, adjusted for Sex, HTN, Teeth/gum problem, Feet/leg problem, GIT problem

Model 3: Predictor value for Female 1.41 means, 1.41-1= 0.41 or 41% more problems in Female than Male, adjusted for Sex, Teeth/gum problem, Feet/leg problem, GIT problem.

Discussion

In this present study, 54.4% participants were female and 45.6% were male. 86.7% participants perform daily exercise where 80.6% male and 45.3% female have daily sunlight exposure varying from few hours to 6-8 hours. Majority of participants have family history of T2DM either Father or Mother, or both or siblings and other 1s^t degree family members which prove a strong association of running T2 DM in family.

Analyzing the diabetic self-care behavior, 86.7% participants perform daily exercise which varies from minimum 30 minutes brisk walking up to 90 minutes brisk walking and 13.3% don't. Of these 158 individuals, 38.6% don't go for daily sunlight exposure and 61.4% have daily sunlight exposure which varies from few hours to 6-8 hours. The Chi-square test shows sex ($p<.000$), teeth/gum problem ($p<.017$), Feet/Leg cramp ($p<.008$), GIT problem ($p<.045$) shows significant differences between sunlight exposure and not (Table V). Linear regression analysis of the correlations regarding sunlight exposure adjusted for multiple chronic complications and associated factor of T2 DM also shows sex is the most important factor in Model 1, Model 2, Model 3 and Model 4. In this study 81% male have daily sunlight exposure where only 45.3% female have. Other studies suggest that daily sunlight exposure of less than 5 hours is needed to avoid sunlight associated complications and important for Vitamin D deficiency associated Diabetic peripheral neuropathy and Diabetic nephropathy.[11-13] Diabetic neuropathy symptoms such as teeth/gum problem (Periodontitis) occurs due T2DM (Caused by insulin resistance) also an early sign of fasting Glucose impairment.[14]

Student's t-Test shows the result of baseline comparison between male and female regarding neuropathy symptoms of T2 DM and associated factors where, percentages of diabetic neuropathy symptoms are higher in female than male.

Previous studies conducted in different countries all over the world including Bangladesh demonstrate similarities with current study regardingT2 DM associated complications and associated factors. A previous study in Bangladesh showed IHD in 30.5% individual, CVD in 10.1% case andone or more of the complications were more in females than males.[15]

The T2 DM associated complications and associated factors in Table III shows that among the participants having diabetic neuropathy related problems (36.07% have burning sensation, 36.70% have Teeth/Gum problems, 24.05% have GIT problems, 9.50% have sexual function problem and rest 1.26% have psychological problems). Analyzing the T2 DM associated factors here shows 54.43% have hypertension and 44.90% have dyslipidemia and 37.9% have both HTN and dyslipidemia.

A study in Ethiopia showed the percentage of complications related to T2 DM was HTN and renal disease 35.4% and impotency 23.4%.[16] Another study in Northern Africa (Tunisia, Egypt and Sudan) from January 1990 to July 2012 showed that, the prevalence of complications are higher in urban area than rural area where the T2 DM patients suffered from diabetic neuropathy ranges from 21.9% to 60%.[17] In Ghana, a study reflects 76.8% of the diabetic patients had complication where the prevalence were more in females (42.7%) than males (34.1%).[18] A community-based study was carried out in a rural setting in Goa, India in 2011which also showed a high prevalence of Diabetic neuropathy (60%).[18]This study result shows some similarities with above study results.

The overall prevalence of complications among female subjects was significantly higher than in male subjects ($\chi^2 = 9.75$, $p = 0.002$), mainly in neuropathy ($p < 0.001$) and also in Ghana.[20] Then the comparison between male and female was done, which also shows the prevalence is greater in female than male. On the basis of male -female comparison Chi-square test was done for several dependent variables withdaily exercise and daily sunlight exposure respectively. On the basis of p value ($p<0.05$)in separate χ^2 test, multiple linear regressions were done. Multiple linear regressions for daily sunlight exposure on the basis of sex shows females have more diabetic neuropathy related complications or symptoms than males ($p<0.000$) (Model 1 shows 40%, Model 2 shows 41% and Model 3 shows 41% respectively). Study shows diabetic persons having less sunlight exposure suffer from more Diabetic neuropathy symptoms than those T2 DM patients who are having more sunlight exposure.

Vitamin D is a neurotropic hormone which has a neuroprotective effect through down regulation of L-type calcium channel expression and upregulation of Vitamin D Receptor (VDR) expression. In vivo studies show vitamin D improves axonogenesis and sensory neural response in peripheral nerves and electrophysiological recovery improvement. Study also found lower serum vitamin D in patients with DN than those without DN. Vitamin D increases Nerve Growth Factor (NGF) synthesis in human

cells and DN is associated with decreased NGF expression in human nerve cells.Triggering hyperglycemia and inflammation, Vitamin D deficiency promotes DN development. Vitamin D deficiency may increase pain sensitization and beneficial effects by vitamin D supplementation on neuropathic pain are reported. Patients with DN have more balance disturbance and study also shows relationship between vitamin D and balance. Vitamin D replacement therapy for lack of vitamin D in patients may improve balance. The study found significant effect of vitamin D replacement therapy on neuropathic pain and recommended vitamin D levels measurement and vitamin D replacement therapy.[21]

During sunlight exposure Ultra Violet B radiation is absorbed by 7-dehydrocholesterol in the skin and converted to pre-vitamin D3 which isomerizes into vitamin D3 (Also called Vitamin D). Vitamin D is metabolized in the liver and kidneys respectively into 25-hydroxyvitamin D (A major circulating form) and 1,25-dihydroxy vitamin D (Biologically active form) respectively. Maintenance of metabolic functions and skeletal health, 1,25-dihydroxy vitamin D has an important role in regulating calcium and phosphate metabolism.[22]

Limitation

The limitation of this study are the inability to perform routine neuropathy screening tests due to resource limitations andthe inability to assess all the necessary biochemical laboratory values associated with Type 2 DM complications and associated factors which could have been more helpful.

The study was based on a cross sectional study with a small sample size which cannot demonstrate properly the cause- effect relationship.

Conclusion

T2 DM chronic complications are a global economic and social burden. Maximum number of T2 DM patients mostly suffering from microvascular complaints specifically of diabetic neuropathy symptoms.This study shows female has more diabetic neuropathy symptoms than male. As vitamin D has a relationship with diabetic neuropathy symptoms, which indicates daily sunlight exposure (Less than 6 hours) playsan important role to reduce the diabetic neuropathy related complications or symptoms. So every diabetic person should assess vitamin D level routinely and go for daily exercise under sunlight to reduce diabetic neuropathy symptoms. Poor glycemic control and sedentary life style are the provoking factors. Diabetic education shouldbe given to every T2DM patient.

Recommendation

A comprehensive and multi approach study is necessary regarding large sample size, different study locations covering nationwide where all categories of citizens should be included. The essential laboratory biochemical value related to daily sunlight exposure specifically Vitamin D level in blood should be assessed for every T2 DM patient to assess the T2 DM diabetic complications.

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Contribution of authors

MMA-Conception, acquisition of data, data analysis manuscript writing & final approval.

SRC-Design, acquisition of data, interpretation of data, critical revision & final approval.

SKMAI-Data analysis, critical revision & final approval.

Disclosure

All the authors declared no conflict of interest.

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