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RESEARCH ARTICLE

RHEUMATOLOGICAL MANIFESTATION IN TYPE 2 DIABETES MELLITUS

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Abstract

Rheumatological manifestations of Diabetes Mellitus may be classified in: non articular, articular and bone conditions. Among non articular conditions, diabetic cheiroarthropathy, frequent in type I diabetes, the most important disorder related to limited joint mobility, results in stiff skin and joint contractures. Adhesive capsulitis of the shoulder, flexor tenosynovitis, and Duputryen's and Peyronie's diseases are also linked to limited joint mobility. Diffuse skeletal hyperostosis, due to calcification at entheses, is frequent and early, particularly in type 2 diabetes. Neuropathies cause some non articular conditions, mainly neuropathic arthritis, a destructive bone and joint condition more common in type I diabetes. Algodistrophy, shoulder-hand and entrapment syndromes are also frequent. Mononeuropathy causes diabetic amyotrophy, characterised by painless muscle weakness. Among muscle conditions, diabetic muscle infarction is a rare, sometimes severe, condition. Among articular conditions, osteoarthritis is frequent and early in diabetes, in which also chondrocalcinosis and gout occur. Rheumatoid arthritis (RA) and diabetes I have a common genetic background and the presence of diabetes gives to RA an unfavourable prognosis. Among bone conditions, osteopenia and osteoporosis may occur early in type 1 diabetes. Contrarily, in type 2 diabetes, bone mineral density is similar or, sometimes, higher than in non diabetic subjects, probably due to hyperinsulinemia.

Introduction:-

The number of patients with type 2 Diabetes mellitus (DM), is increasing rapidly in both developed and developing countries around the world.[1] The emerging pandemic is driven by the combined effects of population ageing, rising level of obesity and inactivity, and longevity among patients with diabetes mellitus that is attributable to improved management. The vascular complications of type 2 diabetes account for the majority of the social and economic burden among patients and society more broadly. Global prevalence has rapidly increasing over the past four decade, and in 2015, diabetes was the 15th most important cause of years of life lost. Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defect in insulin secretion, insulin action, or both.[2] The chronic hyperglycemia of diabetes mellitus is associated with long- term damage, dysfunctions, and failure of various organ, especially the eye, kidneys, nerve, heart, and blood vessel.[3] DM is associated with a variety of rheumatological manifestations.[4] For most of these disorder, pathophysiologic correlations are not well established. Some of them, such as diabetic cheiroarthropathy, neuropathic arthritis, diabetic amyotrophy, diabetic

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muscle infraction, are considered intrinsic complications of diabetes mellitus. For others, like diffuse idiopathic skeletal hyperostosis or reflex sympathetic dystrophy, DM is considered a predisposing condition.[5] In most cases, these disorder cause pain and disability, affecting the quality of life of diabetic patients, but once correctly diagnosed, they often respond to the treatment.

While so much emphasis is given to micro and macro vascular complications of diabetes, other long-term complications especially musculoskeletal are often overlooked and underappreciated.[6] Nonvascular complications include gastrointestinal, genitourinary, dermatologic, infectious periodontal disease and rheumatological. There is paucity of studies on diabetes and its association with rheumatological manifestations. Therefore, the present study was conducted with the aim to determine the correlation between rheumatological manifestations and diabetes complications.

Aims and Objectives:-

1. To study the prevalence of rheumatological manifestations namely, limited joint mobility, dupuytren's contracture, carpal tunnel syndrome, trigger finger, adhesive shoulder capsulitis, diffuse idiopathic skeletal hyperostosis and tendonitis in type 2 DiabetesMellitus
2. To evaluate the correlation of these rheumatological manifestations with age, BMI, duration of diabetes and control ofdiabetes
3. To study the correlation of these rheumatological disorders with retinopathy, neuropathy and nephropathy

Background

Theburdenofdiabetesasanon-communicablediseasehassteadilyincreasedoverthepastquarter century in India and across the globe, with India contribute a major part of the global burden. Existing evidences suggests that as part of the epidemiological transition from communicable disease to non-communicable diseases, the burden of diabetes and its risk factors has been increasingacrosstheworldandAsiapacificcountriesincludingIndia.[7]Diabetesisassociatedwith a large variety of rheumatological manifestations. We review the rheumatological conditions that are associated with DM and the pathophysiologic relationships that might links these conditions. It also summarizes recent advances in the field of diabetes and rheumatic conditions, focusing on the diagnosis and management of rheumatic manifestations in patients with type 2 diabetes mellitus.

Epidemiology Incidence and trend

Diabetes – The incidence of type 2 DM among youth is increasing in many countries, coinciding with increasing prevalence of obesity and severe obesity. As an example, in the United States, there was a sharp rise in T2DM from 9.0 cases per 100,000 in 2002-2003 to 13.8 cases per 100,000 in 2014-2015, with an adjusted annual increase of type2 DM of 4.8 percent, based on a large representative dataset from the SEARCH for Diabetes in Youth study.

Pathophysiology

General principles-The pathogenesis of type 2 diabetes is multifactorial. Patients typically present with a combination of varying degrees of insulin resistance and defective insulin secretion (beta cell dysfunction), neither of which is routinely measured in the clinical setting. Both contribute to type 2 diabetes, with heightened demands for insulin action mediated by resistance that is not matched by insulin secretions.[8]

Impaired insulin secretion and insulin resistance-

The relative importance of impaired insulin release and insulin resistance in the pathogenesis of type 2 diabetes has been evaluated in several studies as an example, in a prospective study of over 6500 British civil servants without diabetes at baseline, 505 subjects were diagnosed with diabetes during 9.7 years (median) of follow-up.[9] In those who developed diabetes compared with those who did not, there was a marked decrease in insulin sensitivity during the five years prior to diagnosis. Beta cell function (insulin secretion) increased three to four years prior to diagnosis, likely as a compensatory mechanism,andthendecreaseduntildiagnosis.Inaddition,aseven-yearprospectivestudyof714 Mexican Americans without diabetes suggested that decreased insulin secretion and insulin resistance were independent risk factors for type 2 diabetes.[10]

Pathogenesis of type 2 diabetes

Role of islet amyloid polypeptide-

Islet amyloid polypeptide (amylin) is stored in insulin secretory granules in the pancreatic beta cells. It is cosecreted with insulin, resulting in serum concentrations approximately one-tenth those of insulin, and is present in increased amounts in the pancreas of many patients with type 2 diabetes. Serum insulin and amylin concentrations are lower in patients with impaired glucose tolerance compared with patient with normal glucose tolerance, and the concentrations are very low in patients with type 2 diabetes mellitus.[11]

Rheumatological Manifestation

The wide spectrum of rheumatological manifestation related to DM can be classified according to the involved musculoskeletal structures. The rheumatologic manifestations of diabetes mellitus are the following: syndromes of limited joint mobility: diabetic hand syndrome (diabetic cheiroarthropathy), adhesive capsulitis (frozen shoulder, periarthritis), trigger finger (flexon tenosynovitis), dupuytren's contractures, osteoporosis); diffuse idiopathic skeletal hyperostosis (DISH); neuropathies: neuropathic arthritis (Charcot joints, diabetic osteoarthropathy, Carpal tunnel syndrome, diabetic amyotrophy, reflex sympathetic dystrophy, various other neuropathies; diabetic muscle infarction.[4]

Materials and Methods:-

Study setting:

Patients admitted in General medicine wards, and those attending OPD, and diabetic clinic of tertiary care center after informed written consent.

Study duration:

January 2020 to October 2021

Study design:

Hospital based cross sectional observational study with a control group

Sample Size

A minimum sample size of 100 patients per group in the two groups (casesand controls) was determined to find a statistically significant meaningful difference.

Criteria for Study enrollment Inclusion criteria for cases-Patients of either sex aged 30-70 years, History of Type 2 diabetes mellitus, Patients willing to give written informed consent.

Inclusion criteria for controls, Patients of either sex aged 30-70 years, Patients willing to give written informed consent.

Exclusion criteria for both cases and controls-Chronic liver disease, Hypothyroidism, Alcoholism, Renal osteodystrophy (diabetic end stage renaldisease), Patients with collagen vasculardisorder, Rheumatoidarthritis

Methodology:-

1. 100 consecutive patients diagnosed to have type 2 diabetes and age (+/- 5 years) matched healthy controls were enrolled after taking written informed consent satisfying the strict inclusion and exclusion criteria.
2. Detailed history about duration of diabetes, control of diabetes, any musculoskeletal complaints and details of ongoing treatment were noted.
3. Physical examination with special reference to BMI and waist-hip ratio was done. Fasting and postprandial blood sugar and HbA1c levels were estimated.

Result:-

This study titled “Rheumatological Manifestation in Type 2 Diabetes Mellitus” was conducted at General medicine wards, Outpatient department, and diabetic clinic of tertiary health care center. Consecutivepatientsofdiabetesmellitusanddiseasefreecontrolswereenrolledforthestudy.The data was available in 100 patients each over a 22-month period in this study. The detailed characteristics of patients are mentioned below.

Table 1:- Distribution of study population according to age group.

Age group (in years)	Cases	Controls
	No. of patients, Percentage (%)	No. of patients, Percentage (%)
31-40	9(9%)	12 (12%)
41-50	32(32%)	36(36%)
51-60	38(38%)	37(37%)
61-70	21(21%)	15(15%)
Total	**100**	**100**
Mean age ± SD years	**52.9 ± 8.5**	**52.2 ± 8.4**
Range	**37-69**	**37-70**

Majority of the patients were in the age group of 51-60 years with 38% patients in cases and 37% in controls group. The mean age ± SD was 52.9 ± 8.5 years and ranged from 37-69 years in cases as compared to 52.2 ± 8.4 years and ranged from 37-70 years in control group.

Table 2:- Distribution of cases according to HbA1c levels.

Control of DM HbA1C level (%)	Cases percentage (%)
Good <6.5%	1(1%)
Moderate 6.5-8%	65(65%)
Poor >8%	34(34%)

The above table showed that majority of the patients (65%) had moderate control of DM. 34(34%) patients had poor control of DM and only 1(1%) patient had good control of DM.

Table 3:- Distributions of subjects according to Rheumatological complaints.

Complaints	Cases (n=100)		Controls (n=100)		p value
	No.	%	No.	%	
Pain in joints	33	33%	9	9%	<0.001
Stiffness in muscle, joints or back	34	34%	7	7%	<0.001
Swelling of joints	10	10%	0	0%	0.001
Difficulty with stairs	2	2%	0	0%	0.155
Difficulty with washing and dressing	33	33%	9	9%	<0.001

Among cases, the most common symptom was stiffness in muscle, joints and back in 34% patients followed by pain in joints in 33% patients and difficulty with washing and dressing in 33% patients. There was a statistically significant difference between the two groups when rheumatological complaints were assessed viz. pain in joints, stiffness in muscle, joints or back, swelling of joints and difficulty with washing and dressing; p <0.001.

Table 4:- Distribution of study subjects according to rheumatological diagnosis.

Rheumatological diagnosis	Cases (n=100)	Controls (n=100)	p value		
	No.	%	No.	%	
Frozen shoulder	20	20%	7	7%	0.007
Dupuytren's contracture	7	7%	1	1%	0.030
Limited joint mobility	6	6%	1	1%	0.054
Carpal tunnel syndrome	5	5%	0	0%	0.024
DISH	2	2%	0	0%	0.155
Tendonitis	1	1%	1	1%	0.99

According the above table among cases, the most common rheumatological manifestation was frozen shoulder in 20% patients, followed by DC in 7% patients and as compared to control this was highly significant. There was a statistically significant difference seen in frozen shoulder, Dupuytren'contracture and Carpal tunnel syndrome between cases and controls.

Table 5:- Duration of diabetes and rheumatological manifestation.

Duration of diabetes (in years)	Cases with Rheumatological manifestation	
	No.	%
≤5	4	9.7%
6-10	8	19.5%
11-15	21	51.2%
>15	8	19.5%

Most of the cases (51.2%) with rheumatological manifestation had a duration of diabetes between 11 to 15 years.

Table 6:- Association between duration of diabetes with rheumatological manifestations in type 2 diabetes mellitus (n=100).

Duration	FS		LJM		DC		OTHERS	
of diabetes (in years)	P	A	P	A	P	A	P	A
≤5	1	22	1	22	0	23	4	19
6-10	2	34	3	33	1	35	8	28
11-15	10	23	2	31	6	27	21	12
>15	7	1	0	8	0	8	8	0
P <0.001	0.878		0.026		<0.001			

P present, A absent, DC Dupuytren's Contracture, FS Frozen shoulder, LJM Limited joint mobility (Others included - Carpal tunnel syndrome, DISH, tendonitis)

Positive correlation between duration of diabetes and rheumatological manifestation was observed. And this correlation was statistically significant for frozen shoulder, Dupuytren's Contracture and among others.

Table 7:- Association of rheumatological manifestations with microvascular complication of diabetes.

Complications	With Rheumatological manifestations	Without Rheumatological manifestations	P value
Nephropathy			
Yes	9	0	<0.001
No	32	59	
Neuropathy			
Yes	6	0	0.002
No	35	59	
Retinopathy			
Yes	12	0	<0.001
No	29	59	

There was a statistically significant association of diabetic complications (nephropathy, Neuropathy, Retinopathy) with the presence of rheumatological manifestations.

Discussion:-

Diabetes mellitus (DM) is a chronic systemic disease with a wide range of complications, including those in the musculoskeletal system. DM is a common disease in nearly all countries and continues to increase in numbers and significance. Though a lot of research work has been done in microvascular and macrovascular complications of T2DM but rheumatological manifestations in T2DM have been less studied subject. The present study was conducted with the aim to analyze the commonly encountered rheumatological manifestations amongst patients with type 2 diabetes. Consecutive patients of diabetes mellitus and disease free controls were enrolled for the study. The data was available in 100 patients each over a 22-month period in this study.

Age group comparison-
Majority of the patients were in the age group of 51-60 years. The mean age ± SD was 52.9 ± 8.5 years and ranged from 37-69 years in cases as compared to 52.2 ± 8.4 years and ranged from 37- 70 years in control group (Table 1). The difference in the mean age at presentation for treatment was not statistically significant; p=0.504. The mean values of age of patients with T2DM in the various studies conducted by[12,13] were 61±10, 57.72±10, 57.59±10.44 years respectively. In a study by patients had a median age of 54 years.[14] The average age of patients was 53 years old ranging from (31-63).[15] The mean age of patients in our study among cases was 52.9 ± 8.5 years.

Duration of Diabetes-
Majority of the patients (36%) had duration of diabetes between 6-10 years, followed by 33% patients who had duration of diabetes between 11-15 years and 23% patients had duration of diabetes between 1-5 years. The mean duration of diabetes was 9.4 ± 4.17 years. We also observed a positive correlation between rheumatological complications and disease duration. It was observed that with increase in duration of diabetes, the occurrence of rheumatological complications increases. The mean duration of diabetes was 7.8± 4.6 years in a study by but no association was found.[16]showed that duration of diabetes was significantly associated with hand disorders in T2DM.[17] found a positive correlation between duration of diabetes and the presence of musculoskeletal manifestations; however it was not statistically significant.

Diabetes control and HbA1C-
Majority of the patients (65%) had moderate control of DM. 34(34%) patients had poor control of DM and only 1(1%) patient had good control of DM. Majority of the Cases (63.4%) with rheumatological manifestation had an HbA1C level >8% indicating poor control of diabetes. 14 (34.1%) patients had HbA1C level 6.5-8%. One patient had good control of diabetes with HbA1C level <6.5%. The mean reading of HbA1C was 8% in a study from Saudi Arabia.[15] When HbA1C level was studied for the relation to rheumatological manifestation, there was a statistically significant difference seen in patients with frozen shoulder and among others.

Rheumatological diagnosis-
In the present study, the most common symptom was stiffness in muscle, joints or back in 34% patients followed by pain in joints in 33% patients and difficulty with washing and dressing in 33% patients.[18]found shoulder pain to be present in 25.7% of diabetic patients compared with 5% of general medical patients.

Diabetes and microvascular complications-
Majority of the patients had frozen shoulder, and limited joint mobility among diabetic complications (Neuropathy, Nephropathy, Retinopathy) and carpal tunnel, dupuytren's contracture were noted in patients with diabetic neuropathy. When patients with diabetic neuropathy were studied for rheumatological manifestation these patients commonly had frozen shoulder, carpal tunnel, dupuytren's contracture and limited joint mobility.

Conclusion:-
Considering the high prevalence of diabetes mellitus in India and its associations with musculoskeletal abnormalities worldwide, it is the need of hour to study musculoskeletal manifestations and its association with different factors.

In the present study.
1. The prevalence of rheumatological manifestation in the studied subjects was41%.
2. The most common symptom was stiffness in muscle, joints and back and the commonest rheumatological manifestation was frozen shoulder followed byDC.
3. Thecommonestrheumatologicalmanifestationwasfrozenshoulderin20%patients,followed by DC in 7%patients.
4. The rheumatic manifestations were closely related to age, prolonged disease duration, control of diabetes and microvascularcomplications.
5. There was a statistically significant association of diabetic microvascular complications with the presence of rheumatologicalmanifestations.
6. Exercise is a vital part in the management of DM and related complications. Therefore, it is important to achieve and maintain optimal glycemic control and provide a sensible physiotherapy program to all patients with DM. Identification and treatment of these complications in the form of pharmacotherapy, diet and physiotherapy are important in order to improve the quality of life of diabetic patients and thereby reducing

the frequency and severity ofcomplications.

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