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Study of Musculoskeletal Manifestations in Patients with Type II Diabetes Mellitus Visiting a Tertiary Care Hospital

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Abstract
The aim of this cross-sectional study was to determine the prevalence and risk factors of musculoskeletal manifestations in 441 patients with type 2 diabetes mellitus (T2DM) visiting a tertiary care hospital. Using The Nordic Musculoskeletal Questionnaire and Short Musculoskeletal Functional Assessment (SMFA), participants were recruited on the basis of detailed history, and relevant laboratory tests [(Fasting blood sugar) FBS> 126mg/dl, (Postprandial blood sugar) PPBS>200mg/dl, symptoms of diabetes and (Random blood sugar) RBS>200mg/dl]. The overall prevalence of musculoskeletal manifestations was 66.21%. Often working in slightly bent posture (55.32%), Poor ergonomics (39.00%), Pushing/Pulling loads >20kg (25.39%) were the significant work place risk factors. Older age ($\geq$ 45 years), female gender, Work Related Risk Factors, Lower socio-economic status and duration of the disease (>7) were associated with higher rates of Musculoskeletal manifestations and were statistically significant in regression model. The study is one of the first to report Work Related risk factors that are associated with the development of Musculoskeletal manifestations in the diabetic population. The study highlights the need for routine musculoskeletal screening and early intervention in diabetes care to prevent disability and improve quality of life.
Key words - The Nordic Musculoskeletal Questionnaire, Short Musculoskeletal Functional Assessment (SMFA), Diabetic neuropathy, frozen shoulder, Musculoskeletal manifestations

Introduction

Diabetes is one of the leading causes of mortality and morbidity worldwide. According to a study done by "International Diabetes Federation, Diabetes ATLAS" in 2021, 537 million adults (20-79 years) are living with diabetes. This number is predicted to rise to 643 million by 2030 and 783 million by 2045 which reports a continued global increase in diabetes prevalence [1].

In developing economies like India, diabetes is a significant burden whose prevalence is mainly fueled patient related factors like overweight/obesity and unhealthy lifestyles [2]. Type 2 Diabetes Mellitus, which accounts for majority of the cases, can lead to multiorgan complications, broadly divided into microvascular and macrovascular complications. These complications are a significant cause for increased premature morbidity and mortality among individuals with diabetes, leading to reduced life expectancy and financial and other costs of diabetes leading to profound economic burden on the Indian health care system [2].

Diabetes is associated with a range of common musculoskeletal conditions such as Diabetic Neuropathy, Diabetic Myopathy, Frozen Shoulder (Adhesive Capsulitis), Osteoporosis, Back pain, Dupuytren's contracture, Carpal Tunnel Syndrome, Lateral Epicondylitis, Rhabdomyolysis, Diabetic Cheiroarthropathy, Flexor Tenosynovitis (trigger finger), Diffuse Idiopathic Skeleton Hyperostosis (DISH), etc. [3].

Diabetes can impact the musculoskeletal system through various mechanisms, but the Pathophysiology is not fully understood [5]. Metabolic imbalances associated with diabetes, such as protein glycosylation, microvascular issues leading to damage in blood vessels and nerves, and the accumulation of collagen in skin and periarticular tissues, may lead to alterations in connective tissues [3].

As reported from previous research studies, factors that contribute to the development of musculoskeletal disorders in diabetic patients can include disturbances in the insulin metabolism, peripheral neuropathy, genetic predispositions, progressive accumulation of Advanced Glycation End products and the microvascular complications that are associated with diabetes. [4]

Musculoskeletal manifestations are often associated with pain and limitation of mobility, which reduces the ability of individuals to work and increases loss of function. Musculoskeletal manifestations in diabetic patients are not necessarily linked to higher mortality rates but can be a

major cause of pain, morbidity and disability. The Global Burden of Disease Study, which provides a comprehensive annual assessment of health loss related to specific diseases, injuries, and risk factors, consistently ranks musculoskeletal disorders among the top causes of disability [6]. Musculoskeletal conditions are also the biggest contributor to years lived with disability (YLDs) worldwide with approximately 149 million YLDs, accounting for 17% of all YLDs worldwide [7]. As the incidence of Musculoskeletal manifestations is increased in the diabetic population, there could be remarkable functional disability in such patients [8]. Despite the recent advancements in medical technology and public health that has contributed to an increase in the life expectancy of diabetic patients, it is not assured that they are living healthier. Therefore, evaluating the impact of functional disability associated with musculoskeletal manifestations in diabetics is crucial for understanding the importance of prioritizing these problems and including musculoskeletal examinations as a substantial part of regular care for diabetic patients.

This study aims to report the prevalence of musculoskeletal manifestations in patients with Type 2 Diabetes Mellitus visiting a tertiary care hospital. The study also assesses the common locations of the musculoskeletal manifestations and Work-Related Risk Factors associated with Musculoskeletal problems in the diabetic patients. The study also determines the extent of functional disability in diabetic individuals with musculoskeletal manifestations.

Materials and Methods

Study design

This is a single-centered, Prospective Observational study (Cross-sectional study) in which the data and sample collection were done from September 2023 to February 2024, the study was conducted in the Department of General Medicine, JSS Medical College and Hospital, Mysuru.

Inclusion and Exclusion criteria/ Study population

Adult patients with (Fasting blood sugar) FBS> 126mg/dl, (Postprandial blood sugar) PPBS>200mg/dl, symptoms of diabetes and (Random blood sugar) RBS>200mg/dl, 2Hr plasma glucose >200mg/dl during oral tolerance test, patients with history of Type 2 Diabetes Mellitus for minimum of 5 years visited In-patient and out-patient department in a tertiary care hospital and

Patients who were willing to provide Informed consent form and relevant data for the study team were included in the study.

Pregnant women, Diabetic patients with history of Rheumatoid arthritis, mental disorders like depression, anxiety or psychosis or those who were physically handicapped were excluded from the study. Any patient who felt uncomfortable during or after the data collection had full access to withdraw from the study.

Study approval

The Study approval was obtained from the Institutional Ethics Committee of JSS Medical College, Mysore. (JSSMC/IEC/27102023/44 NCT/2023-24)

Study Measures

The Nordic Musculoskeletal Questionnaire [9]

This questionnaire has two sections. It has 40 items identifying body regions that have any musculoskeletal system related trouble (ache, pain, discomfort, numbness). Completion was aided by a body map illustrating the nine symptom sites, i.e. neck, shoulders (left, right, both), upper back, elbows (left, right, both), low back, wrist/hands (left, right, both), hips, knees and ankles/feet. Respondents were asked if they have had any pain/trouble at the specific sites during the past 12 months and the past seven days which has interfered with their normal activity.

Short Musculoskeletal Functional Assessment (SMFA) [10]

This questionnaire assesses the impact of a musculoskeletal condition on self-reported patient functioning and on the impact of the condition in impeding everyday life. SMFA consists of 46 items divided into two sections: 34 questions cover patient's functions (function index), while 12 questions cover how bothered patients are about their symptoms (bother index). Each question consisted of 5 options, that was scored from 0 (no disability) to 5 (severe disability).

Modified Kuppuswamy socio-economic scale [11]

The scoring is based on education, occupation, and monthly income as per the updated modified Kuppuswamy socioeconomic scale 2023.

Procedure

The research team developed a data collection form in collaboration with the senior physician. The data collection form included section like patient demographics information, socio-economic status and Work-Related Risk Factors followed by The Nordic Musculoskeletal Questionnaire (NMQ) and Short Musculoskeletal Functional Assessment (SMFA), the participants were explained about the study procedures and then the written consent was obtained. Patients were assisted while filling the data collection form and the study measures.

Statistical analysis

Statistical analysis was performed with the help of SPSS Version 16.0. Musculoskeletal manifestations were considered as the dependent variable and demographics and socioeconomic status were considered as independent variables. Comparison between the variables was done using the Odds ratio test for categoric variables and the Mann-Whitney U test for continuous variables. Impact of demographic variables on Musculoskeletal manifestations was evaluated using a bi-variate analysis followed by subsequent regression analysis by keeping Musculoskeletal manifestations as a dependent variable. Relationship between Work-Related Risk Factors as well as the duration of Diabetes and the number of locations of Musculoskeletal manifestations were analyzed using Pearson's Correlation coefficient. A 'p' value of less than 0.05 was considered as statistically significant. Parametric data were presented as Mean±95% Confidence Interval (CI).

Results

A total of 441 patients were enrolled into this study. The mean age was found to be 62.1 years ±10.4. The patients' characteristics are shown in Table 1. The study revealed that overall prevalence of Musculoskeletal manifestations was 66.21% (n=292), the most commonly observed co-morbidities in the study participants were Hypertension, Hypothyroidism, Hyperlipidemia, and coronary artery disease. The study noted that the most frequently used medications by the participants were Tab. Glimepiride + Metformin, INJ Insulin, Tab. Telmisartan, Tab. Metformin,

Tab. Thyroxine Sodium, Tab. Glimepiride + Metformin + Pioglitazone, Tab. Cilnidipine, Tab. Amlodipine, Tab. Vildagliptin, and Tab. Voglibose + Metformin + Glimepiride.

In the study setting, the most commonly seen Work-Related Risk Factors were, Often working in slightly bent posture (55.32%), Poor ergonomics (39.00%), Often working in heavily bent posture (28.79%), and Pushing/Pulling loads >20kg (25.39%). The prevalence of various Work-Related Risk Factors observed in the study population are presented in Table 2.

The Nordic Musculoskeletal Questionnaire (NMQ) was used to assess the ache, pain, discomfort and numbness in 9 locations in the body, namely, Neck, Shoulder, Elbow, Wrists/Hand, Upper Back, Lower Back, One or both Thighs, One of both Knees, and One or both Ankles/Feet. The most commonly affected locations were observed to be, One or both Knees (46.93%), Lower Back (40.13%), One or Both Thighs (34.69%), One or Ankle/Feet (28.79%), and Both Shoulders (26.75%). (Figure 1)

Those who reported pain in one or more locations were segregated and grouped as those with Musculoskeletal manifestations (group-1), and those who did not report any musculoskeletal pain were grouped as those with no Musculoskeletal manifestations (Group-II) using the NMQ. The overall prevalence of Musculoskeletal manifestations in the present study was calculated to be 66.21%. (292/441), out of which 58.93% of males and 72.64% of females were found to have Musculoskeletal manifestations. A detailed results of the prevalence of Musculoskeletal manifestations according to the patients' characteristics are presented in Table 3.

The bivariate analysis identified female sex, age ≥45 years, low socio-economic status, Work-Related Risk Factors ≥2, and duration of disease >7 years, as statistically significant variables that predispose individuals to the development of Musculoskeletal manifestations. The detailed results of the bivariate analysis with the corresponding Odds ratio are represented in Table 3.

Five variables which were found to be significant in the odds ratio were selected for further logistic regression analysis. Finally, three variables found to be influential predictors for Musculoskeletal manifestations, namely Female sex (OR 9.297, CI 1.88 – 45.935, p value < 0.006), Age > 45 years (OR 3.120, CI 1.218 – 7.992, p value < 0.018), and presence of at least ≥2 Work-related Risk factors (OR 1.88, CI 0.02 – 0.8, p value < 0.029).

Upon performing Pearson's correlation, we observed a weak positive correlation between duration of Diabetes Mellitus and Musculoskeletal manifestations (r = 0.11, p = 0.01779) as well as the number of Work-Related Risk Factors and Musculoskeletal manifestations (r = 0.1, p = 0.045). This implies that the number of locations of Musculoskeletal manifestations increases with an increase in the number of risk factors and increase in duration of Diabetes.

There are a total of 2 domains assessed in the Short Musculoskeletal Functional Assessment (SMFA) Questionnaire, namely: Function Index which includes 4 categories namely Daily Activity, Emotional Status, Arm and Hand Function and Mobility; and Bother Index. Upon performing Mann Whitney U test and comparing the scores obtained from all the domains of SMFA, it was observed that the participants with Musculoskeletal manifestations (group 1) had significantly more functional disability than the patients with no Musculoskeletal manifestations (group 2). (Table 4)

Discussion

These Musculoskeletal manifestations cause pain and dysfunction in the patients thereby negatively impacting their quality of personal, social, and occupational life [12]. Despite the high prevalence of Musculoskeletal manifestations among diabetics they are often neglected [13][14]. Hence, early detection of musculoskeletal issues linked to diabetes is crucial for maintaining good quality of life and averting prolonged disability. Musculoskeletal manifestations are not specific to the diabetic however, their incidence is significantly increased in the diabetic population according to many research studies [8]. Due to the lack of a gold standard diagnostic tool to identify Musculoskeletal manifestations in Type 2 Diabetes Mellitus in the Indian population, the study team had to use Short Musculoskeletal Functional Assessment and Nordic Musculoskeletal Questionnaire.

In our study, the prevalence of Diabetic individuals with Musculoskeletal manifestations was found to be 66.21%. The global prevalence of Musculoskeletal manifestations as observed in several studies is between 16.3% - 83.5% [15-25]. The prevalence obtained from various studies conducted in India ranges from 30% – 75% [26-29]. The high prevalence of Musculoskeletal manifestations might stem from delayed detection of diabetes mellitus, lack of awareness and

screening methods, ineffective control of blood sugar levels, and/or insufficient clinical handling of musculoskeletal issues [30].

In our study, the female population was found to have a higher prevalence of Musculoskeletal manifestations which is in line with the findings in Muluneh AG et al., (2022) [25], could be attributed to oestrogen deficiency around menopause, involvement in heavy manual labour at home, poor glycaemic control and higher prevalence of vitamin D deficiency in Indian housewives due to lack of sunlight exposure [12, 25, 31, 32].

In our study setting, participants who were ≥45 years had a significantly higher prevalence of Musculoskeletal manifestations which is accordance with Dr. Manish Kumar Bansal et al., (2022) [33], which observed that with advancing age, the incidence of Musculoskeletal manifestations increases and Muluneh AG et al., (2022) [25], which observed that increasing age is a significant risk factor for the development of musculoskeletal manifestations. Possible reasons for this finding could be due to aging include bone loss, degradation of articular cartilage, degeneration, and narrowing of intervertebral discs which occurs due to substantial biomechanical changes that directly impair their function, leading to the onset of Musculoskeletal manifestations [34,35].

Individuals in the Upper lower class and Lower class were found to be susceptible to developing Musculoskeletal manifestations which is consistent with the findings in Hagen K et al., (2005) [36]. People with a lower socioeconomic status usually have less access to financial, educational, social, and health resources which results in them being in poor health with chronic health conditions and disabilities.

In the present study, it was observed that individuals with more than 7 years of Diabetes had higher prevalence of Musculoskeletal manifestations as compared to those with less than 7 years of Diabetes mellitus. The most likely explanation is that musculoskeletal changes may progress in a proportional manner as the duration of diabetes increases [25, 26, 33, 37, 38]. This finding is in line with many previous studies where people have reported Musculoskeletal manifestations with an average duration of ≥5 years after diagnosis of Type 2 Diabetes Mellitus as observed in Dr. Manish Kumar Bansal et al., (2022) [33].

From the results of the Nordic Musculoskeletal Questionnaire, it was observed that knee pain was the most prevalent (46.93%) followed by lower back pain (40.13%) and upper back pain (33.56%).

An additional objective of our study was to see if work place risk factors play a role in Musculoskeletal manifestations. It has been established that the work environment and engaging in various tasks can impact the onset and progression of musculoskeletal diseases. Exposure to these risk factors does not guarantee the disease but can increase the likelihood.

Work-Related Risk Factors were noted from the literature validated with the help of Physiotherapist and General Medicine Physician which were used to collect information from study participants. In our study the most common Work-Related Risk Factors were found to be often working in slightly bent posture (55.10%), poor ergonomics (39%), often working in heavily bent posture (28.79%), and pushing/pushing loads >20kg (25.17%). The correlation of a singular risk factor to Musculoskeletal manifestations was not established, however it was found that a combination of two or more risk factors was significantly associated with the development of Musculoskeletal manifestations which is in compliance with the existing evidence in this regard [39].

Chronic pain and loss of function are the primary means by which Musculoskeletal manifestations lead to functional disability. As the incidence of Musculoskeletal manifestations is increased in the diabetic population, there could be remarkable functional disability in such patients which can compromise daily activities and can also cause hindrance in recreational activities, social connections, and family relations.

The Short Musculoskeletal Functional Assessment (SMFA) score was used to assess functional disability among diabetic individuals with Musculoskeletal manifestations. Individuals with Musculoskeletal manifestations had significantly more Functional disability and were more bothered by their disability than those without Musculoskeletal manifestations.

Developing markers and identifying early symptoms of Musculoskeletal manifestations in diabetic patients can lead to development of effective screening tools for diagnosis. Incorporating routine musculoskeletal examinations in regular health screening and follow up of diabetic patients allow early detection of these disorders which can help provide prompt and effective therapy thereby improving patient outcomes. The results from the study imply that there is a significant association between Type 2 Diabetes Mellitus and Musculoskeletal manifestations and since the pathophysiological mechanisms behind this is still unclear, further research in this area can help

elucidate the same. This can in turn help in developing novel therapies for the prevention and treatment of Musculoskeletal manifestations in diabetic patients.

This study is one of the first of its kind from this region and is one of the first to report Work-Related Risk Factors associated with the development of Musculoskeletal manifestations in diabetics. It also assesses the degree of functional disability experienced by the participants.

Although our study is the first of its kind from this region, it is not devoid of limitations. Present work may have possible limitations such as the patients were not subjected to radio diagnostic procedures and were handled by senior endocrinologist but not further evaluated by orthopedist/rheumatologist. It is important for the rheumatologist/orthopedist to diagnose and understand this association.

Conclusion

In the present study, the prevalence of Musculoskeletal manifestations associated with Type 2 Diabetes Mellitus was relatively high as compared to the results observed in studies from various other locations in India. Most patients received appropriate drug treatment in accordance with latest treatment guidelines. This study is one of the first to report the association of Work-Related Risk Factors in the development of Musculoskeletal manifestations in diabetic individuals. Several other factors reported by previous research studies are similar to our study findings namely Female gender, Low socio-economic status, longer duration of diabetes, more than 2 Work-Related Risk Factors and increasing age. Early identification, evaluation and management of diabetes and its complications can reduce the duration of pain and illness in vulnerable individuals.

TABLE 1: Patient Characteristics

CHARACTERISTICS		N= 441
GENDER	Male	207 [46.9%]
	Female	234 [53%]
AGE	25-55	130 [29.47%]
	56-85	310 [70.29%]
	>85	1 [0.22%]
LIVING CONDITION	Own home	441 [100%]
MARRIAGE STATUS	Married	397 [90%]
	Unmarried	6 [1.36%]
	Widow/Divorced	38 [8.61%]
ALCOHOLIC STATUS (self-reported)	Yes	33 [7.48%]
PHYSICAL ACTIVITY (self-reported)	Yes	378 [85.71%]
SMOKING (Self -reported)	Yes	22 [4.98%]
SES CLASS	Upper class	7 [1.58%]
	Upper middle class	59 [13.37%]
	Lower middle	86 [19.50]
	Upper lower	239 [54.19%]
	Lower	50 [11.33%]

BMI	≤18.5 (Underweight)	3 [0.68%]
	18.5 - 24.9 (Healthy)	206 [46.71%]
	25-29.9 (Overweight)	198 [44.89%]
	≥30 (Obese)	34 [7.66%]
DRUGS	0	3 [0.68%]
	1	96 [21.76%]
	2	191 [43.31%]
	3	93 [21.08%]
	≥4	58 [13.15%]
DISEASE	1	153 [34.69%]
	2	230 [52.15%]
	3	43 [9.75%]
	≥4	15 [3.40%]

TABLE 2: Work-Related Risk Factors

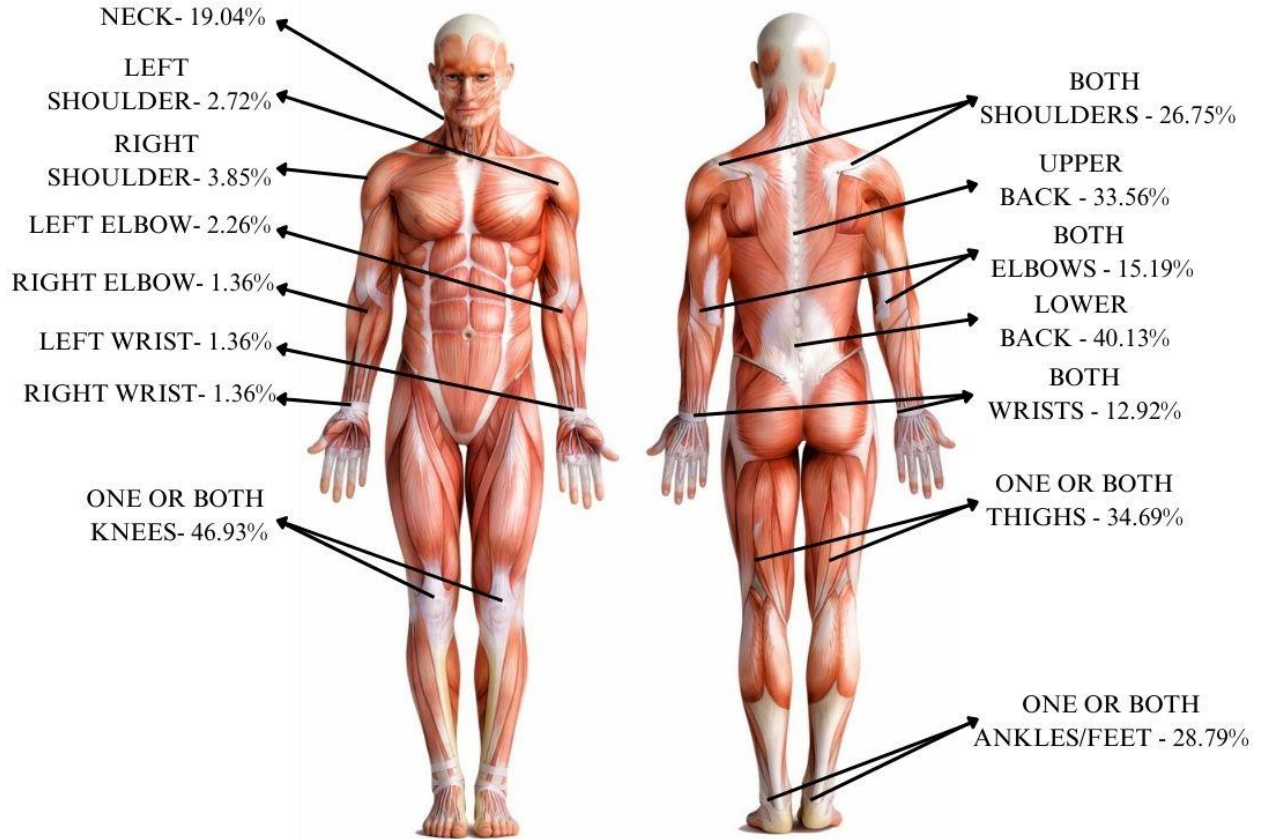| Risk Factors	Prevalence
Pushing/Pulling loads >20kg	112 [25.39%]
Often work in slightly bent posture	244 [55.32%]
Often work in heavily bent posture	127 [28.79%]
Slightly twisted posture for long	36 [8.1%]
Repetitive Motion	85 [19.27%]
Vibration	36 [8.1%]
Lack of Physical activity	63 [14.28%]
Poor ergonomics	172 [39.00%]
Mental Exhaustion	23 [5.21%]

FIGURE 1: The Musculoskeletal pain manifestation's location distribution.

TABLE 3: Demographic characteristics of patients with and without MSDs

SUBJECT CHARACTERISTICS		GROUP 1 (MSDS)	GROUP 2 (NO MSDS)	OR	95% CI	P VALUE
Sex	**Females**	170 (72.64%)	64 (27.35%)	1.85	(1.2416 to 2.7585)	**0.002**
	Males	122 (58.93%)	85 (41.06%)	1	(Reference)	
Age	**≥45 years**	284 (67.78%)	135 (32.21%)	3.68	(1.5080 to 8.9875)	**0.004**
	<45 years	8 (36.36%)	14 (63.63%)	1	(Reference)	
BMI*	**25-29.9**	136 (68.68%)	62 (31.31%)	1.33	(0.8843 to 2.0093)	0.169
	≥ 30	26 (76.47%)	8 (23.52%)	1.9750	(0.8524 to 4.5763)	0.1124
	≤24.9	130 (62.20%)	79 (37.79%)	1	(Reference)	
No. Of Disease	**≥ 3**	39 (67.24%)	19 (32.75%)	1.054	(0.5860 to 1.8984)	0.859
	≤ 2	253 (66.05%)	130 (33.94%)	1	(Reference)	
No. Of Drugs	**2**	130 (68.06%)	61 (31.93%)	1.444	(0.8731 to 2.3909)	0.152
	≥ 3	103 (68.21%)	48 (31.78%)	1.454	(0.8583 to 2.4660)	0.163
	≤ 1	59 (59.59%)	40 (20.20%)	1	(Reference)	
Marital Status	**Married**	266 (67.00%)	131 (32.99%)	1.465	(0.7440 to 2.6563)	0.294
	Unmarried/Divorced /Widowed	26 (59.09%)	18 (40.90%)	1	(Reference)	
Physical Activity	**In-active**	41 (65.07%)	22 (34.92%)	0.943	(0.5385 to 1.6512)	0.837
	Active	251 (66.40%)	127 (33.59%)	1	(Reference)	
Alcohol Intake	**Alcoholic**	25 (75.75%)	8 (24.24%)	1.650	(0.7255 to 3.7540)	0.232
	Non - Alcoholic	267 (65.44%)	141 (34.55%)	1	(Reference)	
Smoking Habit	**Smoker**	15 (68.18%)	7 (31.81%)	1.098	(0.4379 to 2.7556)	0.841
	Non - Smoker	277 (66.10%)	142 (33.89%)	1	(Reference)	
SES*	**Upper lower/Lower class**	202 (69.89%)	87 (30.10%)	1.599	(1.0619 to 2.409)	**0.024**
	Upper/Upper middle/lower middle class	90 (59.21%)	62 (40.78%)	1	(Reference)	
WRRF*	**≥ 2**	172 (70.78%)	71 (29.21%)	1.574	(1.0586 to 2.3423)	**0.025**
	0-1	120 (60.60%)	78 (39.39%)	1	(Reference)	
Duration Of Disease	**> 7 years**	202 (69.41%)	89 (30.58%)	1.513	(1.0032 to 2.2822)	**0.04**
	≤ 7 years	90 (60.0%)	60 (40.0%)	1	(Reference)	

BMI*: Body Mass Index; SES*: Socio-Economic Status; WRRF*: Work-Related Risk Factors

TABLE 4: Comparison of Function Index and Bother Index of SMFA in study participants with MSDs vs participants with no MSDs

DOMAINS	GROUPS	MEAN ± STANDARD DEVIATIONS	P Value	Z Value
Daily Activities	GROUP 1	17.56 ± 6.99	**<0.05**	**13.50**
	GROUP 2	10.37 ± 1.21		
Emotional status	GROUP 1	14.31 ± 4.74	**<0.05**	**15.48**
	GROUP 2	7.38 ± 1.26		
Arm and Hand function	GROUP 1	9.60 ± 3.17	**<0.05**	**6.61**
	GROUP 2	8.04 ± 0.22		
Mobility	GROUP 1	17.36 ± 5.97	**<0.05**	**15.32**
	GROUP 2	9.44 ± 1.33		
Overall Function Index	GROUP 1	58.8 ± 17.8	**<0.05**	**16.00**
	GROUP 2	35.24 ± 3.63		
Bother Index	GROUP 1	21.50 ± 7.06	**<0.05**	**15.11**
	GROUP 2	12.30 ± 1.01		

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