

## Frequency of Limited Joint Mobility and its Association with Some Chronic Diabetic Complications among Type 1 Diabetic Patients

Zahra Razavi<sup>1\*</sup>, Fariba Mohammadi<sup>2</sup>

1-Associated Professor, Pediatric Endocrinologist, Department of Pediatrics, Hamedan University of Medical Sciences.

2-Medical student, Faculty of Medicine, Hamedan University of Medical Sciences.

### \*Correspondence:

Zahra Razavi, Department of Pediatrics, Besat Hospital, Motahari Boulevard, Resalat Square, Hamedan, Iran

Fax: +811-2640064

Tel: +98-918-3122066

Email: razavizahra@yahoo.com.au

Received: 5 May 2012

Accepted: 10 June 2012

### Abstract

**Objective:** Limited joint mobility (LJM) has been described as the earliest clinical complication of diabetes mellitus.

This study was performed to determine the frequency of limited joint mobility and to evaluate the association between LJM and some chronic diabetic complications.

**Materials and Methods:** A total of 125 patients with type 1 diabetes mellitus aged  $11.89 \pm 3.75$  years, with  $4.2 \pm 2$  years mean duration of disease were studied. Diabetic patients were compared with 125 healthy young controls that were group-matched for age and sex. Variables such as age, sex, duration of disease and mean HbA1c level were obtained from the patients' medical records. LJM was assessed by observing the small joints of the hands in the prayer position. Student t-test and chi-square ( $X^2$ ) were used for comparisons between groups.

**Results:** The frequency of LJM was significantly higher in diabetic patients compared to healthy controls (19.2% vs. 4%,  $p=0.001$ ). Diabetic patients with LJM had not longer duration of diabetes than those without LJM (4.33 years compared to 4.08 years,  $p=0.55$ ). Its presence was significantly related to microalbuminuria ( $p=0.017$ ) and higher systolic blood pressure ( $p=0.001$ ).

**Conclusion:** Diabetic patients showed a significantly higher frequency of LJM than non-diabetic patients. LJM in the hands of patients with type 1 DM was associated with microalbuminuria but it was not related to retinopathy.

**Key Words:** limited joint mobility, type 1 diabetes mellitus, prayer maneuver

## Introduction

Limited joint mobility (stiff hand syndrome) is characterized by limitation of joint movement in people with both type 1 and type 2 diabetes. It occurs as a painless, asymptomatic and non-disabling thickening of skin, tendons, ligaments and joint capsules primarily affecting the small

joints of the hand and feet. Large joints may be involved as well. Of major importance is documented evidence on the relationship between limited joint mobility (LJM) and subsequent microvascular complications (1-3). Evidence for this is however still conflicting. Previous data showed that LJM may be a

possible factor in causing high plantar pressures and may also contribute to the formation of diabetic foot ulcers in the susceptible patients (4, 5). The pathogenesis of LJM is probably the enzymatic and non-enzymatic glycosylation of collagen and increased collagen hydration. Microangiopathy, neuropathy and vasculopathy may also contribute to the contractures (6-8).

Limited joint mobility can be found in 8 to 58% of patients with type 1 diabetes compare to 1% in non-diabetic control subjects (9-12). According to published studies, the prevalence of limited joint mobility increases with poor glycaemic control, duration of diabetes and age (1,11-13), but it was also reported in patients with recent onset diabetes (14).

To our knowledge, frequency of LJM and its association with other microvascular diseases in type 1 diabetic patients have not been assessed in our region. We aimed to determine the frequency of LJM and its association with the clinical characteristics in children with type 1 diabetes. We also assessed the association between LJM and retinopathy, microalbuminuria and hypertension.

### Materials and Methods

One hundred and twenty five patients with type 1 DM (62 females and 63 males) who met inclusion criteria were recruited from the Pediatric Endocrine Clinics of Besat hospital, Hamadan, Iran. The control group consisted of 125 non-diabetic subjects well matched for gender, age, socioeconomic background, ethnic group, and geographic location who were randomly recruited from the school population.

**Inclusion criteria:** All Type 1 DM patients with diabetes duration of more than 2 years who received at least two daily insulin injections.

**Exclusion criteria:** Type 1 diabetic patients and controls with the following hand pathologies were excluded from the study:

- Previous history of trauma, infection, or deformity of the hands, or any joint disease
- Family history of limited joint mobility
- Diabetes duration of <2 years.

- Patients with established diabetic nephropathy (proteinuria or increased creatinine)

The protocol was performed according to the principles of the declaration of Helsinki and was approved by the local ethics committee and research of Hamadan University of medical sciences in 2008. Written informed consent was obtained from all subjects or their parents. The diabetic patients were investigated in terms of the following characteristics: Sex, age, diabetes duration, the number of blood glucose tests/day, HbA<sub>1c</sub> hypertension, background and proliferative retinopathy, albuminuria or overt proteinuria.

Appropriate physical examination was performed by the same observer who was blinded to the study. Glycohemoglobin (HbA<sub>1c</sub>) level which reflects diabetes control was measured every 3 months by high performance liquid chromatography (HPLC) assay (Bayer DCA 2000+ analyzer). The mean HbA<sub>1c</sub> value for each patient was derived from all measurements recorded over the 1 year of enrollment. Blood pressure was measured by an aneroid sphyngomanometer (Reichter Co) in the supine position with a cuff of appropriate size twice at 10 minutes interval in three separate visits. The mean of three readings was calculated and reported as the mean blood pressure. Hypertension was defined as over 95 percentile of blood pressure according to standardized table of age, gender and height. Diabetic retinopathy was assessed by a consultant ophthalmologist using standardized examination of the fundus through dilated pupils. Urinary albumin excretion (UAE) and protein excretion rate was determined in at least two 24- hour urine samples. Microalbuminuria was evaluated by measuring the urinary albumin-to-creatinine ratio (ACR) by an immunoturbidometric assay (Hitachi 902 auto analyser; Roche Diagnostics.).

LJM of the hand was assessed qualitatively by visual clinical examination using prayer maneuver: Subjects were asked to approximate the palmar surfaces of both hands in a praying position with fingers fanned and wrists maximally extended. The number of missing joint contacts between the fingers was counted and correlated to LJM.

Joint limitation was assessed by the method and classification used by earlier investigators (10,15):

-stage 0: no joint limitation

-Stage I: limitation of one or two proximal inter-phalangeal or metacarpo-phalangeal joints, usually fifth proximal inter-phalangeal joints in one or both hands.

-Stage II: limitation of two or more proximal inter-phalangeal joints.

-Stage III: limitation of all fingers of each hand plus limitation of one large joint bilaterally (obvious hand deformity).

**Statistical analysis:** The data were analyzed using SPSS software version 11. Means and standard deviations were computed for continuous variables. Chi-squared test ( $\chi^2$ ) was used to test associations between categorical data in patients with and without LJM. The intergroup comparisons were made using student's t-test.  $P < 0.05$  was considered statistically significant.

## Results

A total of 250 subjects were included in the study. 125 had DM1 (DM1 group) and 125 were healthy (control group). In both groups 63 subjects (50.4%) were males. The mean age of the patients was  $11.89 \pm 3.75$  years; the mean diabetes duration was  $4.2 \pm 2.1$  years. The mean age of controls was  $12.26 \pm 2.67$  years. The DM1 patients and controls did not differ regarding age ( $p = 0.36$ ). The characteristics of diabetic patients with and without LJM are shown in table 1.

Overall, twenty four (19.2 per cent) out of 125 diabetic patients had limited joint mobility, whereas LJM was present in only five (4%) of the 125 controls. 14.4% had stage 1 and 4.8% stage 2 changes. Diabetic patients with and without LJM did not differ regarding age. Frequency of LJM was the same in both sexes ( $p = 0.08$ ). LJM was not associated with duration of the disease ( $p = 0.55$ ). We found an association between LJM and frequency of self monitoring of blood glucose (SMBG) ( $p = 0.05$ ) and between LJM and microalbuminuria ( $p = 0.017$ ). Mean systolic blood pressure was significantly higher in patients with LJM than those without LJM ( $p = 0.001$ ). There was not a significant correlation between LJM and presence of retinopathy. Mean HbA<sub>1c</sub> levels were higher in those with LJM than those without LJM but the difference was not statistically significant ( $p = 0.71$ ).

## Discussion

**Table 1- Characteristics of type I diabetic patients with and without limited joint mobility**

		With LJM	Without LJM	p value
Sample size		24	101	
Sex (M:F)		11:13	52:49	0.62*
Age	mean ( $\pm$ SD) yr	12.90 $\pm$ 2.84	11.65 $\pm$ 3.91	0.08***
Duration of diabetes	mean ( $\pm$ SD) yr	4.33 $\pm$ 2.57	4.08 $\pm$ 1.62	0.55***
Mean HbA <sub>1c</sub>	mean ( $\pm$ SD) %	10.07 $\pm$ 2.25	9.86 $\pm$ 2.50	0.71***
Number of blood glucose tests/day	mean ( $\pm$ SD)	1.4 $\pm$ 0.5	1.74 $\pm$ 0.7	0.05***
retinopathy	(number)	2	5	0.62**
microalbuminuria	(number)	10	19	0.017*
systolic blood pressure	(Mean $\pm$ SD)MM/Hg	117.5 $\pm$ 11.03	108.5 $\pm$ 10.9	0.001***
Diastolic blood pressure	(Mean $\pm$ SD)MM/Hg	72.5 $\pm$ 10.32	68.6 $\pm$ 7.7	0.09***

\*Chi-square test

\*\*Fisher exact test

\*\*\*independent two samples test

This is the first study to estimate the frequency of LJM and its association with the clinical characteristics among type 1 diabetic patients in our region. Overall frequency of LJM was 19% which is significantly higher than control group. Since the first description presented by Rosenbloom in 1974, many studies have reported variable frequencies (8 - 58 %) for LJM in diabetic children (11-12, 15-17). The frequency of 19% in our study is therefore similar to other reports.

In this study, the frequency of LJM was similar in both sexes. Our findings are consistent with other previous studies by Kennedy et al. and Amin et al. (18,19) who demonstrated LJM was equally prevalent in diabetics males and females. While Frost et al. and Montana et al. found a male predominance among their type 1 diabetic patients (8,20).

The mean absolute HbA<sub>1c</sub> value of our patients with and without LJM was 10.07±2.25 and 9.86±2.50 respectively, which is higher than the normal value and it can be considered a poor glycaemic control state within 1 year of enrollment; however, consistent with previous studies (21,22), we failed to demonstrate a close correlation between glycaemic control and presence of LJM. In contrast, in the study of Rosenbloom et al. (23) the risk of LJM was related to poor glycaemic control. Silverstein et al. (1) also found that for every 1% increase in HbA<sub>1c</sub> level, there was a 2.5-fold increase in the occurrence of LJM. Previous investigators have shown marked changes in prevalence of LJM during two decades due to improved standards of glycaemic control and diabetes care of patients (23, 24). The lack of close correlation between glycaemic control and presence of LJM in the current study may reflect that the host factors could modulate metabolic influence. In addition, we could detect no correlation between LJM and duration of diabetes. This differs from the studies conducted by Strakman et al. (11) and Lindsay et al. (24) who confirmed the association between LJM and duration of diabetes. Clarke et al. (14) showed a trend towards an

increasing prevalence and progression of LJM and other complications with increasing age and duration of diabetes, but it was also found in patients with recent onset diabetes. Our interesting findings may be partly due to selecting a younger patient population with a short duration of diabetes. Similarly, Rosenbloom et al. (12) demonstrated that age regardless of duration of diabetes may be important for occurrence of LJM. Overall, these conflicting findings reinforce three previous studies that demonstrated different host factors and genetic predisposition regardless of diabetes duration, age and glycaemic control may be important for development of LJM recently highlighted in the journal (8,21,25-27).

We found significant association between LJM and microalbuminuria consistent with other clinical studies (8,20,28, 29). Furthermore, LJM was associated with high systolic blood pressure. This is in agreement with the findings of Garg et al. (29) who demonstrated that the presence of contractures was significantly related high blood pressure. In contrast, Montana et al. (20) did not find any association between LJM and blood pressure.

There was not however a strong relationship between LJM and development of retinopathy in this study. This finding is difficult to interpret and we could not explain it. This is in contrast to the results of some other studies (8, 16, 29).

It is notable that according to our results, quality of glycaemic control was generally poor in both groups of diabetic patients. This is important and should be considered a priority; therefore, improved metabolic control should be a strategy in our diabetes patients by effective intervention and additional education.

### Limitations

Given the fact that our work was a cross-sectional study, we could only draw conclusions for the association between LJM and other complications, not for a possible risk marker of LJM.

Longitudinal studies are needed in order to ascertain whether the presence of LJM in insulin-dependent patients is a risk factor for subsequent diabetic microvascular complications. We also had small number of type 1 diabetic patients, so we do not know whether the results would be sufficiently powered to be extrapolated to the large study population. These findings have yet to be confirmed in larger, population based, longitudinal studies.

## Conclusion

There were no significant differences between diabetic patients with and without joint limitation regarding age, sex, duration of diabetes and glycemic control. It was only significantly associated with the frequency of SMBG, microalbuminuria and higher systolic blood pressure. LJM was not a risk factor for retinopathy. This study extends our observations on the relationship between LJM and retinopathy.

## References

1. Silverstein JH, Gordon G, Pollock BH, Rosenbloom AL. Long-term glycemic control influences the onset of limited joint mobility in type 1 diabetes. *The Journal of pediatrics* 1998;132(6):944-7.
2. Brik R, Berant M, Vardi P. The scleroderma-like syndrome of insulin-dependent diabetes mellitus. *Diabetes/metabolism reviews* 1991;7(2):121-8.
3. Yosipovitch G, Hodak E, Vardi P, Shraga I, Karp M, Sprecher E, et al. The prevalence of cutaneous manifestations in IDDM patients and their association with diabetes risk factors and microvascular complications. *Diabetes Care*. 1998;21(4):506-9.
4. Zimny S, Schatz H, Pfohl M. The role of limited joint mobility in diabetic patients with an at-risk foot. *Diabetes Care*. 2004 ;27(4):942-6.
5. Dinh TL, Veves A. A review of the mechanisms implicated in the pathogenesis of the diabetic foot. *The international journal of lower extremity wounds*. 2005;4(3):154-9.
6. Vlassara H, Brownlee M, Cerami A. Nonenzymatic glycosylation: role in the pathogenesis of diabetic complications. *Clinical chemistry* 1986;32(10 Suppl):B37- B41.
7. Rosenbloom AL. Limitation of finger joint mobility in diabetes mellitus. *Journal of Diabetic Complications* 1989;3(2):77-87.
8. Frost D, Beischer W. Limited joint mobility in type 1 diabetic patients: associations with microangiopathy and subclinical macroangiopathy are different in men and women. *Diabetes Care*. 2001;24(1):95-9.
9. Ramchurn N, Mashamba C, Leitch E, Arutchelvam V, Narayanan K, Weaver J, et al. Upper limb musculoskeletal abnormalities and poor metabolic control in diabetes. *European Journal of Internal Medicine* 2009;20(7):718-21.
10. Grgic A, Rosenbloom AL, Weber FT, Giordano B, Malone JJ, Shuster JJ. Joint contracture. Common manifestation of childhood diabetes mellitus. *Journal of Pediatrics*. 1976; 88(4) :584-8.
11. Starkman HS, Gleason RE, Rand LI, Miller DE, Soeldner JS. Limited joint mobility (LJM) of the hand in patients with diabetes mellitus: relation to chronic complications. *Ann Rheum Dis*. 1986;45(2):130-5.
12. Rosenbloom AL. Limited joint mobility in insulin dependent childhood diabetes. *Eur J Pediatr*. 1990;149(6):380-8
13. Vukovic J, Dumic M, Radica A, Filipovic-Grcic B, Jovanovic V: Risk factors for expression and progression of limited joint mobility in insulin-dependent childhood diabetes. *Acta Diabetol*33;15-18,1996
14. Clarke CF, Piesowicz AT, Spathis GS. Limited joint mobility in children and adolescents with insulin dependent diabetes mellitus. *Ann Rheum Dis*. 1990;49(4):236.
15. Beacom R, Gillespie EL, Middleton D, Sawhney B, Kennedy L: Limited joint mobility in insulin-dependent diabetes: relationship to retinopathy, peripheral nerve function and HLA status. *Q J Med* 56:337-344, 1985
16. Arkkila PE, Kantola IM, Viikari JS, Rönnemaa T, Vähätalo MA. Limited joint mobility is associated with the presence but does not predict the development of microvascular complications in type 1 diabetes. *Diabet Med*. 1996;13(9):828-33.
17. Sauseng S, Kästenbauer T, Irsigler K. Limited joint mobility in selected hand and foot joints in patients with type 1 diabetes mellitus: a methodology comparison. *Diabetes Nutr Metab*. 2002;15(1):1-6
18. Kennedy L, Beacom R, Archer DB, Carson DJ, Campbell SL, Johnston PB, Maguire CJ. Limited joint mobility in Type I diabetes mellitus. *Postgrad Med J*. 1982;58(682):481-4.

19. Amin R, Bahu TK, Widmer B, Dalton RN, Dunger DB. Longitudinal relation between limited joint mobility, height, insulin-like growth factor I levels, and risk of developing microalbuminuria: the Oxford Regional Prospective Study. *Arch Dis Child.* 2005;90(10):1039-44.
20. Montana E, Rozadilla A, Nolla JM, Gomez N, Escofet DR, Soler J: Microalbuminuria is associated with limited joint mobility in type 1 diabetes mellitus. *Ann Rheum Dis* 54:582 -586, 1995
21. Komatsu WR, Gabbay MA, Dib SA. Early subclinical limited axial and large joint flexibility in type 1 diabetes mellitus adolescents. *J Diabetes Complications.* 2004;18(6):352-5
22. Starkman H., Brink S. Limited joint mobility of the hand in type 1 diabetes mellitus *Diabetes Care,* 5 (1982), pp. 534–536
23. Rosenbloom AL, Silverstein JH, Lezotte DC, et al. Limited joint mobility in childhood diabetes mellitus indicates increased risk for microvascular disease. *N Engl J Med* 1981;305:191–4.
24. Lindsay JR, Kennedy L, Atkinson AB, Bell PM, Carson DJ, McCance DR, et al. Reduced prevalence of limited joint mobility in type 1 diabetes in a U.K. clinic population over a 20-year period. *Diabetes Care.* 2005 Mar;28(3):658-61
25. Brik R, Berant M., Vardit P, The scleroderma-like syndrome of insulin-dependent diabetes mellitus *Diabetes Metabolism Review,* 7 (1991), pp. 121–128
26. Brownlee M. Glycation products and the pathogenesis of diabetic complications *Diabetes Care,* 15 (1992), pp. 1835–1843
27. Friedman E.A Advanced glycosylated end products and hyperglycemia in the pathogenesis of diabetic complications *Diabetes Care,* 22 (Suppl. 2) (1999), pp. B65–B71
28. Yosipovitch G 2, Mukamel M, Karp MDiabetic hand syndrome in juvenile diabetics]. *Harefuah.* 1990 ;119(3-4):63-6.
29. Garg SK, Chase HP, Marshall G, Jackson WE, Holmes D, Hoops S, . Limited joint mobility in subjects with insulin dependent diabetes mellitus: relationship with eye and kidney complications *Arch Dis Child.* 1992 ;67(1):96-9.