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RESEARCH ARTICLE

Subclinical musculoskeletal, neuropathy and otorhinolaryngologic complications in children with type I DM

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Abstract

Objectives: To evaluate the subclinical MSK manifestations, subclinical sensory peripheral neuropathy and otorhinolaryngologic manifestations in type I diabetic children and correlation of these manifestations with duration and severity of DM. **Patients and Methods**: This case-control study was carried out in the period from June 2013 to April 2015. The study includes group I (64 children with type I DM) and group II (50 apparently healthy children as controls). All participants were subjected to: 1-complete history taking, 2- complete MSK examination, 3- complete neurological examination, 4- ENT examination (pure tone audiometry, speech audiometry and tympanometry and acoustic reflex), 5- laboratory investigations (RBC, HbA1C, RF, ANA, Anti-DNA, ESR, CRP), 6- MSK US of shoulder joints, 7- electrodiagnostic evaluation of sensory nerve conduction study to sensory branch of median, ulnar and nerves. **Results:** shoulder US examination revealed tendinitis, bursitis and joint effusion with significant difference between DM group and controls. Positive significant correlation between tendinitis and disease duration, RBS and HbA1C. Also significant positive correlation between bursitis, effusion and disease duration, age, HbA1C, RBS. Electrophysiological examination revealed median, ulnar and sural neuropathy with significant difference between DM group and controls. Positive correlation between RT. Median, sural neuropathy and disease duration while between RT. Ulnar neuropathy and RBS. 20% of DM group have mild SNHL, 20% of them have Eustachian dysfunction with no significant difference with controls**. Conclusion:** subclinical MSK, sensory peripheral neuropathy and otorhinolaryngologic complications are associated with children type 1 DM and correlated with disease duration and severity. MSK US and audiometry should be included in type I DM children clinical examination.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease, type 1 DM results from a complete deficiency of insulin due to the autoimmune-mediated destruction of insulin-producing β cells in the pancreas. Most diabetic patients will develop functional disabilities due to multiple factors, including musculoskeletal (MSK) manifestations [(1)].

MSK complications of DM are the most common endocrine arthro-pathies. These have been generally under-recognized and poorly treated compared with other complications, such as neuropathy, retinopathy, and nephropathy. These manifestations, which are some of the causes of chronic disability, involve not only the joints, but also the bones and the soft tissues [(2)].

Most data showed that the prevalence of MSK manifestations in the hands and shoulders in patients with type 1 is 30% that can be very incapacitating and significantly compromise their quality of life. The exact pathophysiology of most of these musculoskeletal disorders remains obscure; however, connective tissue disorders, neuropathy or vasculopathy may have a synergistic effect on the increased incidence of musculoskeletal disorders in DM [(3)].

Prolonged hyperglycemia in uncontrolled diabetic patients results in collagen glycosylation. Glyco-sylated collagen is less soluble, offers increased resistance to collagenases and accumulate in connective tissue, which not only alters the extracellular matrix structure and function but also affects cell viability[(4)].

Musculoskeletal ultrasound (US) is an imaging tool with a wide set of advantages over other imaging modalities, being safe, easily accessible, relatively cheap, not invasive and lacking of any contraindication[(5)].

Joint US is a simple and effective method for assessment of degenerative changes of the joint and joint effusion, allowing a reliable differential diagnosis for causes of soft tissue swelling. The application of Doppler US is useful in evaluation of early inflammatory changes and vascular abnormality [(6)].

Today the association between DM and hearing loss is being given a lot of attention. Complaints related to the auditory and vestibular systems and metabolic disorders affecting glycides and lipids have been pointed out as the main etiologic factors related to hearing loss, tinnitus, and dizziness [(7)]. Therefore, the diabetic population must be considered at risk for auditory conditions[(8)].

Aim of the study:

The aim of this study was to evaluate the subclinical MSK manifestations, subclinical sensory peripheral neuropathy and otorhinolaryngologic manifestations in type I diabetic children and correlation of these manifestations with duration and severity of DM.

Subjects and methods

Study design:

It is an case-control study was carried out at Rheumatology and Rehabilitation, pediatric, ENT and Radiology Departments, Zagazig University Hospitals, in the period from June 2013 to April 2015.

Informed consent was taken from the parents of the patients, after receiving adequate information about the study (the characters of the study, benefits and possible side effects).

Subjects were divided into two groups:

Group I:

It Includes 64 children wit type 1 DM (*28* males and 36 females), their ages ranged from (5.5-14.0) years with a mean of 9.5 ± 2.63 and the duration of the disease ranged from (2-8) years with a mean of 4.81 ± 2.22

Group II:

It Includes 50 apparently healthy children as a controls (23 males and 27 females), their ages ranged from (5-13) years with a mean of 9.3 ± 2.3, not suffering from any musculo-skeletal and neurological manifestation.

Exclusion criteria:

- All children complaining of any MSK and neurological symptoms.
- All children complaining of type 1 diabetes mellitus with disease duration less than 12 months.
- Any other endocrinal disorders other than JDM, fever.
- Connective tissue disease e.g. Juvenile SLE & Juvenile RA.
- Cases with history of trauma were excluded from the study.
- History of receiving drugs inducing lupus or PN.

All patients that included in the study were those attending pediatric department complaining of type 1 diabetes mellitus with high level of fasting blood sugar.

- All patients and controls were subjected to:

1- Complete history taking, with special stress on the following:

- Duration of diabetes, management and control
- Symptoms suggestive neurological system affection.
- Cardiovascular, renal, ophthalmic evaluation & other co morbidities.
- Skin & nail problems: infections/ skin disease/blisters/Ingrown toenails.
- Present medication for Juvenile DM, (Insulin therapy, Immunosuppressive agents)
- Past Medical & Surgical history.
- History of trauma.

2- Complete musculoskeletal examination:

- Inspection: (swelling, muscle wasting, malalignment, pigmentation, scars, deformities).
- palpation: (Temperature, joint tenderness, ligament and menisci evaluation, special tests).
- Range of motion examination

3- Complete neurological examination

4-ENT examination:

- Basic audiological evaluation including : pure tone audiometry (pure audiometry or conventional audiometry) according to age of children.
- Speech audiometry according to age of child.
- Immittancemetry: tympanometry and acoustic reflex.

5- Laboratory Investigations: The following laboratory examinations were performed to the patients:

- Random blood sugar: normally less than 200mg/dl.
- Hemoglobin (HbAlc.):

Normal = 4.9-5.8%

Good control = 5

Insufficient control ≥ 8.

- Rheumatoid factor titre.
- ANA .anti DNA autoantibodies.
- Acute phase reactant (ESR & CRP)

6- Musculoskeletal ultrasound of shoulder joint:

Ultrasound examination was performed by a single radiologist. The ultrasound examiner was blinded for the clinical findings, diagnosis and patient identity. All patients were examined with commercially available equipment using a linear array transducer (5-12 MHz, Medison, R3) with fixed settings of the machine. To ensure standardization, the same ultrasound machine without software upgrading was used throughout the study.

Pathological US findings were detected for long head biceps tendon-LHB, subscapularis tendon-SSC, supraspinatus tendon-SSP, infra-spinatus tendon-ISP, subacromial/ subdeltoid bursa-SA/SD-B, gleno humeral joint effusion-JE, bone cartilage-BC, and humeral erosions-HE.

Transverse and longitudinal planes were used for all of the following investigated structures. LHB and SSC tendons were examined on the anterior aspect of the shoulder, in the seating position, with the arm held in neutral position, the elbow flexed to 90°, and the forearm in a supinated position on the thigh [(9)]. SSP and ISP tendons were examined with laterally moved transducer, with the patient's shoulder in hyperextension and internal rotation. This position allows the maximal length of tendons to be visualized [(10)]. The SA/SD-B was imaged between the deltoid muscle andthe SSP and ISP tendons. For the visualization of the joint effusion, distance between joint capsule and inferior margin of ISP tendon above 2 mm was considered as positive sign. The humeral articular cartilage was seen between the SSP and ISP tendons and the humeral head.

7- Electrodiagnostic evaluation of sensory nerve conduction study to one sensory branch of median, ulnar nerves and sural nerves by using ring recording" electrodes act as active (black) and reference (red) electrodes for sensory study of median and ulnar nerves and round plate surface electrodes as recording electrodes for sural nerves. With third surface electrode (green) used as ground electrode. The normal range of peak latencies of the nerves are as follow [(11)]:

Range of Median nerve peak latency: 3.4±0.3 ms (≤ 4.1 ms)

Range of ulnarnerve peak latency :3.4±0.3 ms (≤ 4.1 ms)

Range of sural nerve peak latency: 3.8±0.3 ms (≤ 4.5 ms)

Statistical analysis:

The collected data were organized tabulate and statistically analyzed using SPSS (Statistical Package for Social Science) software compute program version 12 (SPSS Inc, USA). The results were represented in tabular forms then interpreted. Mean, standard deviation, range, frequency and percentage were used as descriptive, chi square and Fisher exact test was used for testing significance of observed differences between studied patients. The level of significance was adopted at $p < 0.05$.

RESULTS

Table (1): Demographic data of the patients and control groups

Groups **Variables**	**Group (I)** **(no=64)**	**Group (Il) control** **(no= 50)**	**P**
Age (years) Mean ±SD **Range**	 **9.50 ± 2.63** **5.50 - 14.00**	 **9.3 ± 2.3** **5 - 13**	**0.65**
Sex **Females** **Males**	 **36 (56.2)** **28 (43.8)**	 **27 (54.0)** **23 (46.0)**	**0.96**
Duration (years) **Mean ± SD** **Range**	**4.81 ± 2.22** **2.00 - 8.00**	----	
HbAlC (% activity) **Mean ± SD** **Range**	 **9.95 ± 1.02** **8.07 - 11.50**	 **5.5 + 1.4** **4 - 6**	**0.00***
Random blood sugar (mg/dl) (RBS) **Mean ±SD** **Range**	 **374.00 ± 136.85** **105.00 - 538.00**	 **186.4 ± 20.3** **99 - 220**	**0.00***

Table (1): The demographic data of the patients revealed that their ages ranged from 5.5 to 14 years with a mean ±SD of 9.50 ± 2.36. And the disease duration ranged from 2 to 8 years with a mean 4.81±2.22 As regards the HbAlC, it ranged from 8.07-11.5 with a mean +SD of $9.95_{\pm}$ 1.02, while the random blood sugar ranged from 105 to 538 with a mean 334 ±156.85.

Table (2): Comparison of the findings of shoulder US examination between DM group and controls

	Group I				**Group II**				**P**
	RT shoulder	**LT shoulder**	***Bilateral***	**P**	**RT shoulder**	**LT shoulder**	**Bilateral**	**P**	
Tendinitis	**44 (68.8%)**	**16 (25.0%)**	**8 (12.5%)**	**.00***	**11 (22.0)**	**4 (8.0)**	**1 (2.0)**	**0.76**	**0.00***
Bursitis	**48 (75.0%)**	**28 (43.8%)**	**20 (31.3%)**	**.00***	**6 (12.0)**	**2 (4.0)**	**1 (2.0)**	**0.34**	**0.00***
Effusion	**48 (75.0%)**	**28 (43.8%)**	**20 (31.3%)**	**.00***	**1 (2.0)**	**0 (0.0)**	**0 (0.0)**	**0.89**	**0.00***

- **Table (2):** As regard to the Musculoskeletal U/S features of the Rt. shoulder, 44 patients (68.8%) had tendinitis, while 48 patients (75%) had bursitis and effusion were evident in 48 (75%) of them, with significant difference between the 2 groups.

- As regard to the Musculoskeletal U/S features of the Lt. shoulder, tendinitis were observed in 16 patients (25%), while 28 patients (43.8%) had bursitis and effusion were observed in 28 (43.8%) of them, with significant difference between the 2 groups.

- While 8 patients (12.5%) had tendinitis, 20 patients (31.3%) and 20 patients (31.3%) of both shoulders, with significant difference between the 2 groups.

Table (3): Comparison of the findings of electrophysiological examination between DM group and controls

	Group I			Group II			P of g1/g2
	RT	LT	P	RT	LT	P	
Median nerve Mean ± SD Range	7.71 ±1.46 4.9.50-11.5	6.4 ±1.74 5.0-4.30	0.01*	3.4 ± 0.4	3.5 ± 0.3	0.11	.04*
Ulnar nerve Mean ±SD Range	6.5 ± 2.44 4.3-9.7	5.9 ± 1.70 4.8-8.7	0.00*	3.2 ± 0.3	3.4 ± 0.3	0.06	0.04*
Sural nerve Mean ± SD Rang	8.9 ±2.6 5.40-13.50	8.0 ±2.4 4.5-13.90	0.04*	3.7 ± 0.2	3.7 ± 0.34	0.98	0.00*

- Table (3) shows the comparison of the findings of electrophysiological examination of median nerve, ulnar nerve and sural nerve between DM group and controls showing significant difference between the 2 groups.

Table (4): Correlation between muscloskeletal U/S findings and disease duration, age, HB1C, RBS

	Duration	Age	**HBA1C**	**RBS**
Tendinitis	**0.41****	**0.03**	**0.26***	**0.41****
Bursitis	**0.56****	**0.37****	**0.32****	**0.43****
Effusion	**0.56****	**0.37****	**0.32****	**0.43****

- **HBAlC:** hemoglobin **A1C, RBS: Random blood sugar**
- There were highly significant positive correlations between tendinitis and duration of the disease, RBS. Also there were statistically significant positive correlations between tendinitis and HbAlC. While there were no significant correlations between tendinitis and age of the patient. There were highly significant positive correlations between bursitis, effusion and duration of the disease, age, HbAlC, RBS.

Table (5): Correlation between elrctrophysiological findings and disease duration, age, HB1C, RBS

	Duration	Age	HBA1C	RBS
Rt. Median	0.27*	0.18	0.09	0.04
Rt. Ulnar	0.11	0.20	0.18	0.26*
Rt. Sural	0.39**	0.099	0.10	0.02
Left median	0.12	0.006	0.12	0.22
Left Ulnar	0.06	0.2	0.10	0.09
Left sural	0.22	0.005	0.02	0.04

- **HBAlC:** hemoglobin **A1C, RBS: Random blood sugar**

- Table (5): In this study, there were highly significant positive correlations between neuropathy of the Rt. sural nerve and disease duration. There were statistically significant positive correlations between Rt. Median neuropathy and disease duration. Also there were statistically significant positive correlations between Rt. Ulnar neuropathy and RBS.

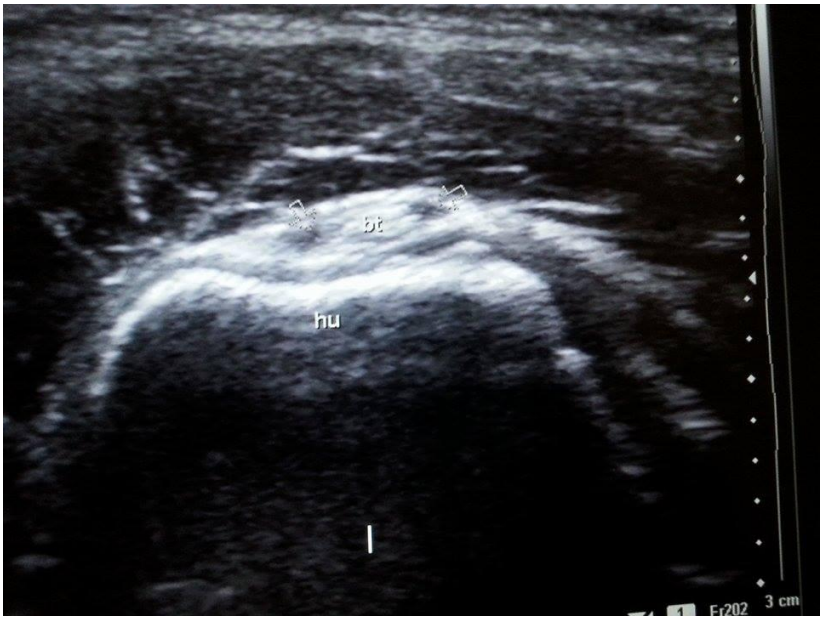
Table (6): Comparison of the findings of electrophysiological examination between DM group and controls

	Group I (n= 10)	Group II (n=10)	P
Mild SNHL (high frequency)	2(20%)	0(0%)	0.47
Eustachian tube	2(20%)	3(30%)	1.00

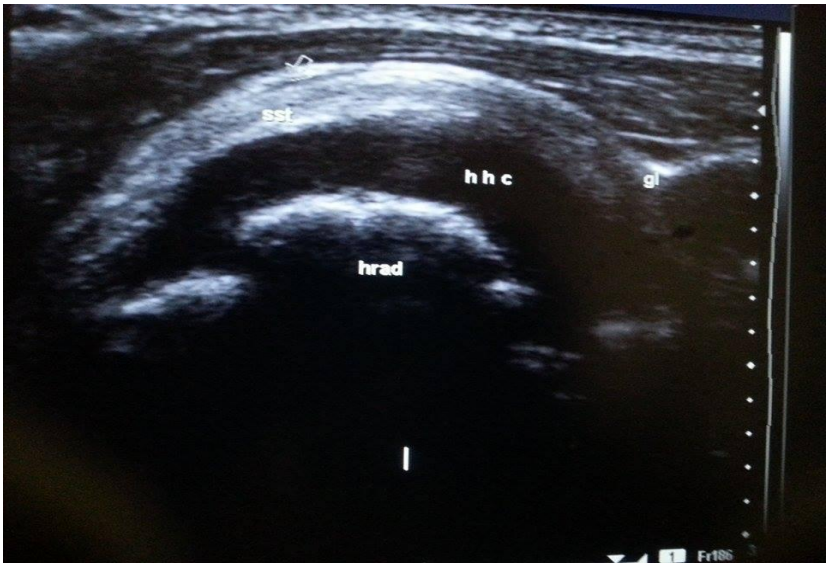
dysfunction			

SNHL: Sensorineural hearing loss.

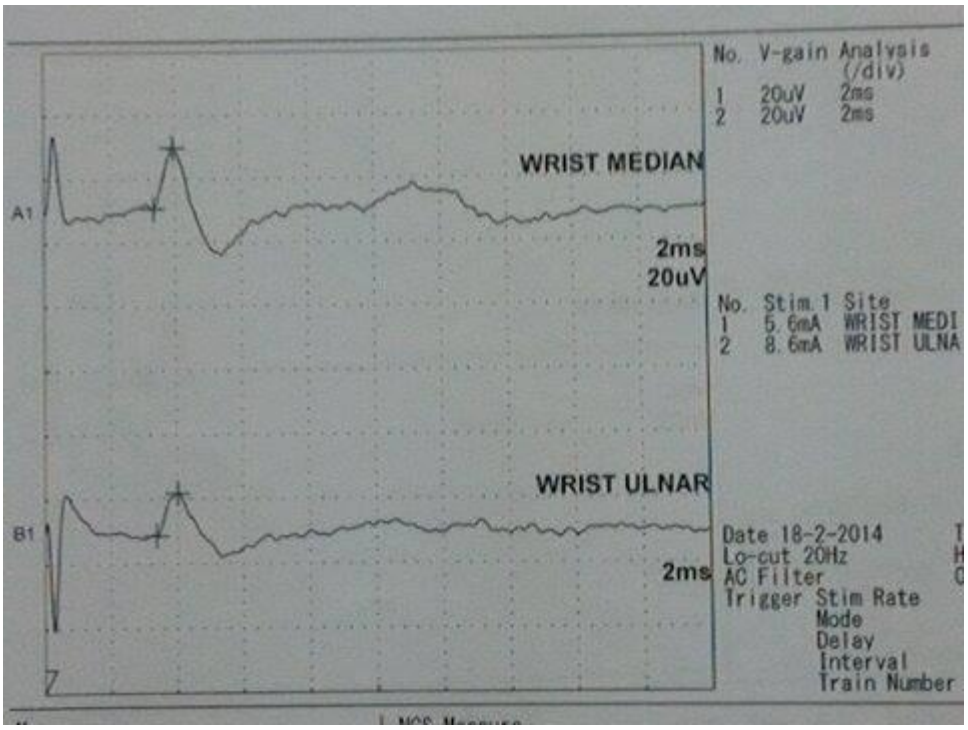
- Table (6) shows comparison between the 2 study groups regarding audiological examination findings revealing (20%) of DM group have mild SNHL and 20% of them have Eustachian tube dysfunction with no statistical difference with controls.



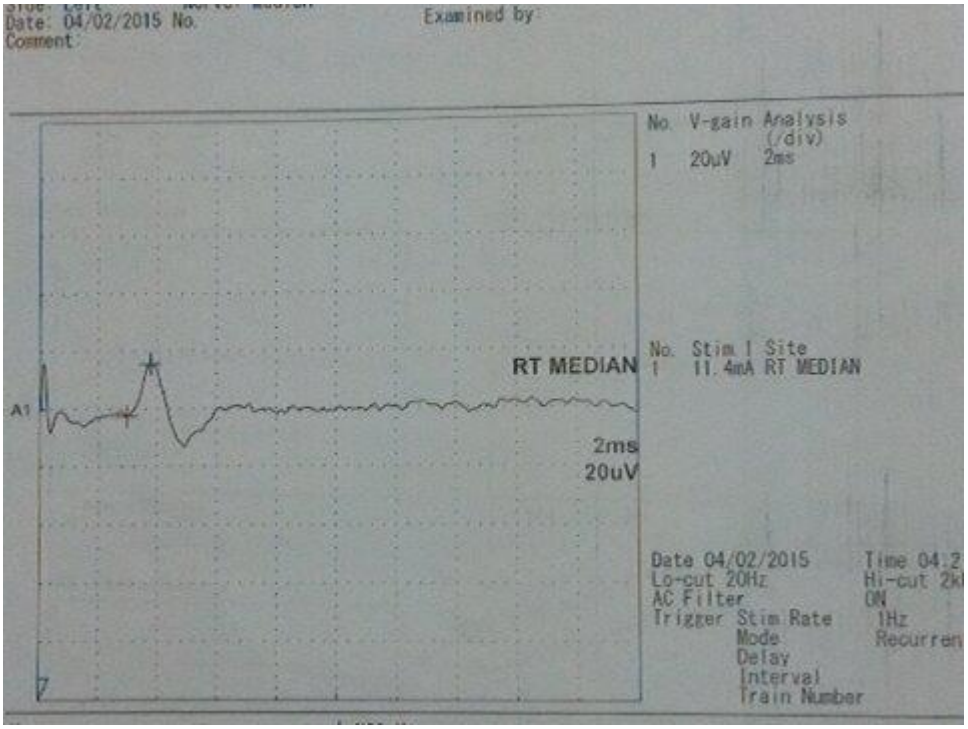
- Fig. (1): High resolustion ultrasonography image of Bicipital groove and long head of the biceps brachii tendon in short axis view . There is two buckets of fluid collections wthin the tendon sheath that not normally present .normally there is hypoechoic halo of thin fluid rim around the oval shaped hyperechoic tendon



- Fig. (2): High resolution ultrasonography of the supraspinatus tendon in short axis view that show a mid degrees of subdeltoid bursal effusion [arrow].Note the signs of immature skeleton in the form of increase in cartilage thickness of humeral head[hhc] and non closure of the proximal humeral epiphysis .



- Fig. (3): sensory nerve conduction study of both median and ulnar nerves at right side showed peak latency 3.9 ms median and 4.02 ms ulnar



- Fig. (4): Rt median peak latency 3.7 ms

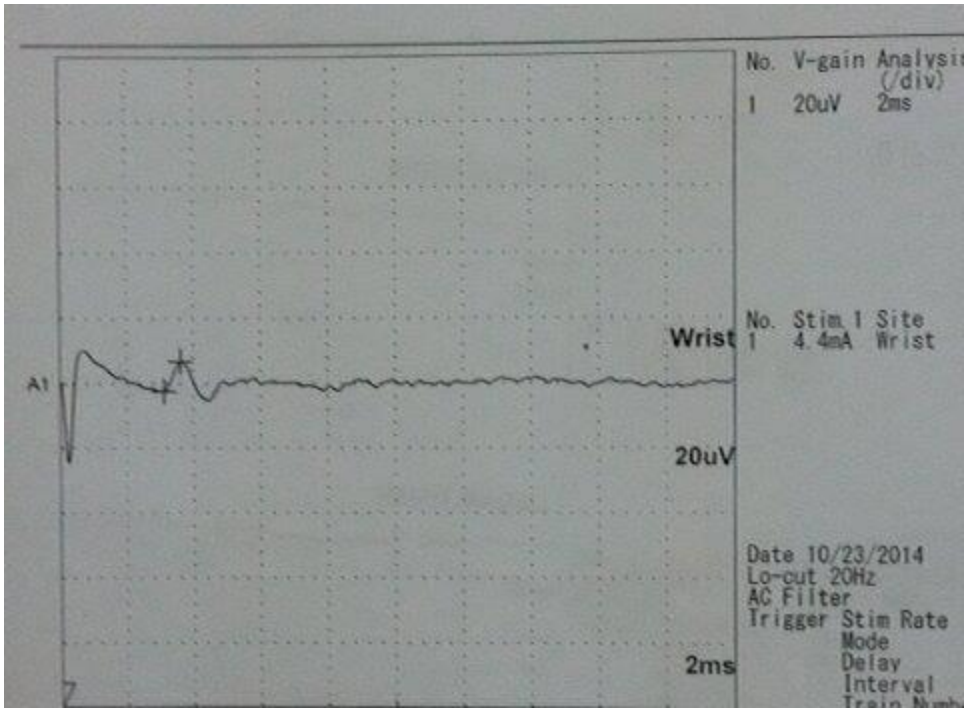


Fig. (5): .left median peak latency 3.7 ms

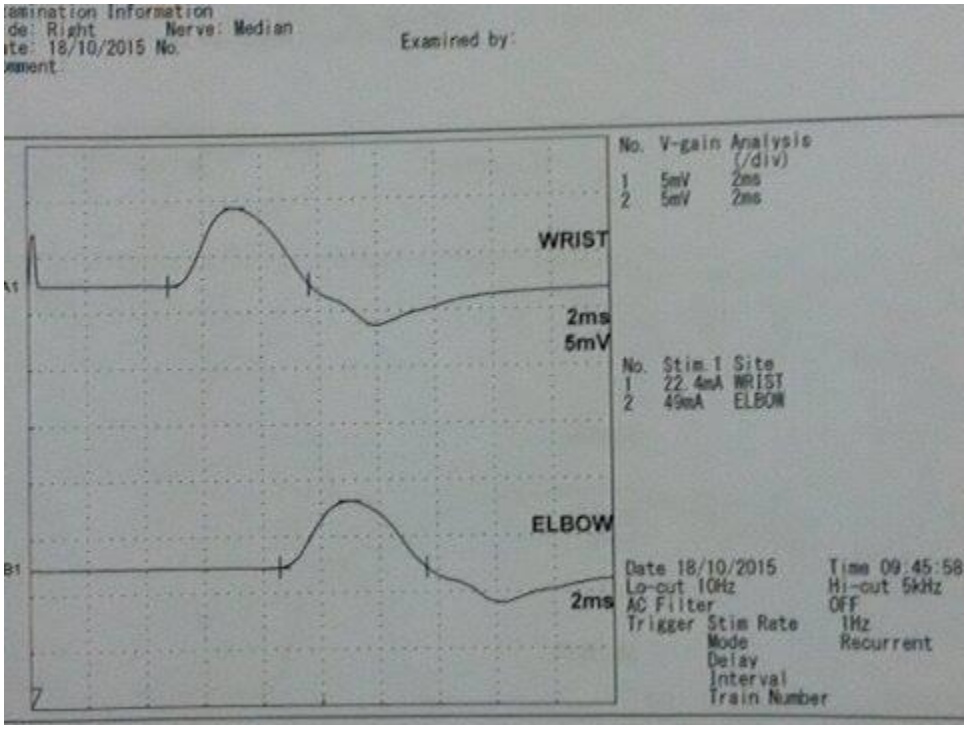


Fig. (6): motor study of right median with terminal latency 4.8 ms and amplitude 6.9 mv Velocity 58.5 m/s

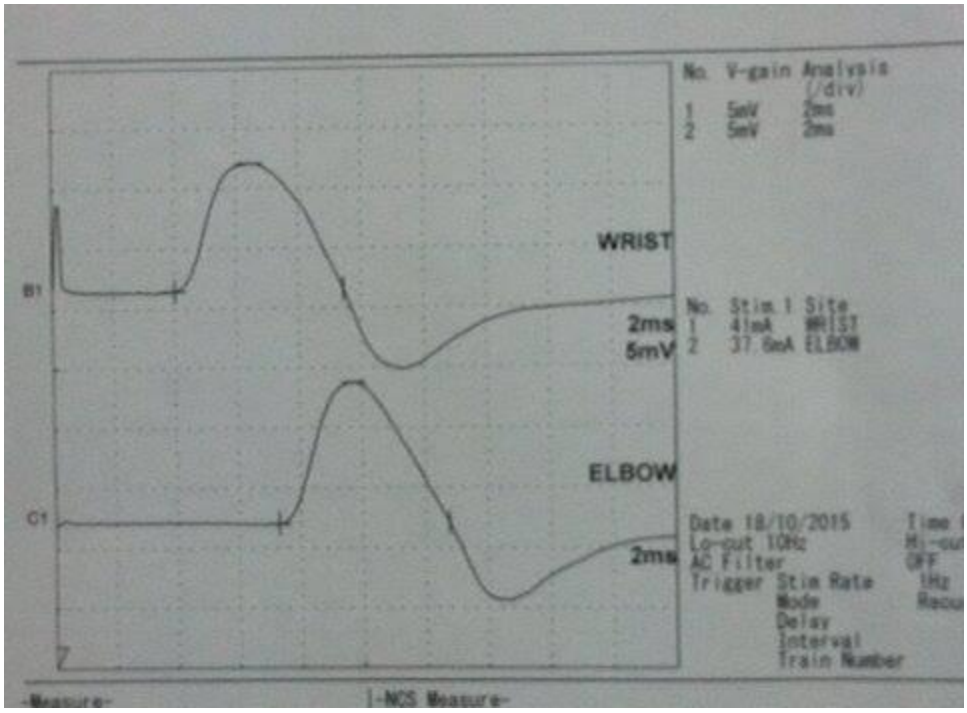


Fig. (7): terminal latency 4.02 ms Amplitude 10.6 mv Velocity 61.3m/s

DISCUSSION

This study was designed to evaluate the subclinical MSK manifestations, subclinical sensory peripheral neuropathy and otorhino-laryngologic manifestations in type I diabetic children and correlation of these manifestations with duration and severity of DM.

Musculoskeletal disorders were more common in patients with type 1 diabetes than in those with type 2 diabetes[(12)], diabetic peripheral neuropathy commonly develops insidiously in type 1 diabetes , with various clinical manifestations. In the early stages, diagnosis is difficult as there are no symptoms. Fortunately, increasing use of electrophysiological techniques that allow the identification of sub-clinical pathological changes has made early diagnosis of diabetic peripheral neuropathy possible[(13)].

Neuropathy is a common and serious complication of diabetes, which leads to increased morbidity and mortality. In children, its prevalence is difficult to determine and is estimated at 9% to 72%, depending on the diagnostic methods and diagnostic criteria [(14)], diabetic neuropathy includes clinical and subclinical abnormalities of the somatic or autonomic part of the peripheral nervous system in patients with diabetes that are diagnosed after exclusion of other possible causes of peripheral neuropathy [(15)].

Jin and park (2015) [(16)] concluded that the role of early NCS and good metabolic control during the early years of type 1 diabetes was important to detect and predict PN development, although not commonly recognized as complications of diabetes.

Ultrasound is a useful tool for discovering in pre-symptomatic stages the subjects that may undergo shoulder symptomatic pathologies[(17)]. Examination of the hands and shoulders should be included in the evaluation of patients with diabetes. Individuals with type 1 diabetes mellitus have a greater propensity of developing adhesive capsulitis [(18)].

In this study, the demographic data of the patients revealed that their ages ranged from 5.5 to 14 years with a mean ±SD of 9.50 ± 2.36. And the disease duration ranged from 2 to 8 years with a mean 4.81±2.22 As regards the HbAlC, it ranged from 8.07-11.5 with a mean +SD of $9.95_{\pm}$ 1.02, while the random blood sugar ranged from 105 to 538 with a mean 334 ±156.85.

As regard to the Musculoskeletal U/S features of the Rt. shoulder, 44 patients (68.8%) had tendinitis, while 48 patients (75%) had bursitis and effusion were evident in 48 (75%) of them, with significant difference between the 2 groups. As regard to the Musculoskeletal U/S features of the Lt. shoulder, tendinitis were observed in 16 patients

(25%), while 28 patients (43.8%) had bursitis and effusion were observed in 28 (43.8%) of them, with significant difference between the 2 groups. While 8 patients (12.5%) had tendinitis, 20 patients (31.3%) and 20 patients (3 L3%) of both shoulders, with significant difference between the 2 groups.

There were highly significant positive correlations between tendinitis and duration of the disease, RBS. Also there were statistically significant positive correlations between tendinitis and HbAlC. While there were no significant correlations between tendinitis and age of the patient. There were highly significant positive correlations between bursitis, effusion and duration of the disease, age, HbAlC, RBS.

This was in accordance to **Ramchurn,** [19] that reported (75%) of diabetic patients had MSK complications, However **Kidwai et al.,** [20], reported that (32.9%) of the diabetic patients had MSK manifestations, which can be explained by the duration of DM, which was less than ten years in most of their patients.

Cagliero, et al., [21] showed that diabetic patients who had upper limb musculoskeletal manifestations had significantly longer DM duration than those without. Also the study of **Arkkila et al.**[22] included the correlation of different MSK manifestations in the upper limb of our diabetic patients with the mean of the most recent HBA1c.

In this study, regarding the comparison of the findings of electrophysiological examination of median nerve, ulnar nerve and sural nerve between DM group and controls showing significant difference between the 2 groups.

Our study reveals highly significant positive correlations between neuropathy of the Rt. sural nerve and disease duration. There were statistically significant positive correlations between Rt. Median neuropathy and disease duration. Also there were statistically significant positive correlations between Rt. Ulnar neuropathy and RBS.

Lee et al., 2010 [23] investigated a total of 37 patients (14 males and 23 'females) aged 3-19 yr (mean 12.0 ± 3.7) with newly diagnosed IDDM underwent bilateral nerve conduction studies (NCS) of median, ulnar, posterior tibial, peroneal, and sural nerves annually for 5 yr. Children with type 1 frequently have nerve conduction abnormalities without clinical neuropathy at initial diagnosis. The frequency of abnormalities of any attribute of nerve conduction increased over the 5 yr follow-up. The duration of diabetes and poor glycemic control proved to be more important' risk factors over 5 yr as related to the development of subclinical neuropathy.

Another study by **Cenesiz et al, (2003)** [24] noted that all nerve conduction values of children with type 1 were found to be significantly lower ($P < 0.0001$) as compared to the control group. 60% of diabetic children were found to suffer peripheral neuropathy. The peripheral neuropathy is rather a frequently observed complication in diabetic children. The duration of disease and impaired glycemic control play an important role in the development of neuropathy. The introduction of new methods designed to ensure better glycemic control will reduce the incidence of the complication.

Regarding the comparison between the 2 study groups regarding audiological examination findings revealing (20%) of DM group have mild SNHL and 20% of them have Eustachian tube dysfunction with no statistical difference with controls.

Patients had sensorineural hearing loss, predominantly at higher frequencies. Thirty-three (37.5%) of the tested 88 ears had hearing loss; 24 (72.7%) ears had mild hearing loss and nine (27.3%) had moderate hearing loss. Twelve (27.3%) subjects had bilateral hearing loss (7).

Mitochondrial deafness is a bilateral symmetrical sensorineural type of hearing loss. The degree of impairment and age of onset vary, and it may or not be associated with syndromic conditions as DM [25]. This study showed higher probabilities of hearing loss in the case group (23 patients with hypacusis) when compared to the control group (12 patients).

Conclusion :

We observed a significant association between subclinical shoulder MSK abnormalities and peripheral neuropathy with type 1 DM.

We found a strong relationship between duration and degree of hyperglycemia of DM and MSK and neuropathy complications.

Ultrasound was a satisfactory method for diagnosis of shoulder articular and periarticular disorders. In addition to nerve conduction study to diagnose diabetic neuropathy.

Recommendations:

It is recommended that type I DM patients should be screened for presence of rheumatic complications and peripheral neuropathy since early recognition lessens chance of irreverisble damage.

Also high frequency audiometry should be included in the patients' clinical examination protocol.

REFERENCES

1- Marilia Barreto Gameiro Silva; Thelma Larocca Skare (2012): Musculoskeletal disorders in diabetes mellitus; Rev. Bras. Reumatol. vol.52 no.4. http://dx.doi.org/10.1590/S0482-50042012000400010.

2- Suzan M. Attar: Musculoskeletal manifestations in diabetic patients at a tertiary center; Libyan J Med. 2012; 7: 10.3402/ljm.v7i0.19162. Published online Oct 29, 2012. doi: 10.3402/lim.v7i0.19162 PMCID: PMC3484174.

3-Tasoglu O, Dogan-Aslan M, Yenigun D, et al.: challenging case of diffuse diabetic musculoskeletal system involvement: diagnostic confusion with rheumatoid Arthritis. Reumatol Port., 2014.

4- Saad M. Alzokm, Abdullah Hussein and Sherief M. Al Shazely : Assessment of Upper limb musculoskeletal comp-lications of diabetes mellitus by ultrasonography and nerve conduction study: Correlation with duration and severity of diabetes mellitus. J Am Sci 2015;11(165-175).

5- Filippucci E, Lagnocco A, Meenagh G et al: Ultrasound imaging for the rheumatologist VII. Ultrasound imaging in rheumatoid arthritis. Clin Exp Rheumatol; 25:5-10, 2007.

6- Moller B, Banel H. And Rotzetter M: Measuring Joint Cartilage by ultrasound as Promising alternative to conventional radiograph imaging. Arthritis Rheum. 61:435-41, 2009.

7- Ferreira Jr. CA, Guimarães RES, Becker HMG, Silva CDL, Gonçalves TML, Crosara PFTB, et al. Avaliação metabólica do paciente com labirintopatia. Arq Otorrinolaringol. 2000; 4 (l):28-32.

8- Marchiori LMM, Gibrin PCD. Diabetes mellitus: prevalência de alterações auditivas. Arq Bras Endocrinol Metab. 2003; 47(l):82-6.

9- VanHolsbeeck M, Introcaso JH. Sonography of theshoulder. In: Van Holsbeeck M, and Introcaso JH, eds. Musculoskeletal ultrasound. Chicago: Mosby Year Book, 1991:265-284.

10- Crass JR, Craig EV, Feinberg SB. The hyperextendedinternal rotation view in rotator cuff ultrasono-graphy.JClin Ultrasound 1987; 15: 416-420.

11- Henry L.Lew and Su -Ju Tsai 2007: pictoral guide to nerve conduction techniques. Practical electromyography. Chapter (9) 213-255.

12- Enrico Cagliero, William Apruzzese, Gary S. Perlmutter, David M. Nathan. Musculoskeletal Disorders of the Hand and Shoulder in Patients with Diabetes Mellitus 2002, The American Journal of Medicine. Volume 112.487-490.

13- Smith A, Lessard M, Reyna S, Doudova M, Robinson Singleton J.: The diagnostic utility of Sudoscan for distal symmetric peripheral neuropathy. J Diabetes Complications. 2014;28:511-516.

14- Dos Santos L, Bruck I, Antoniuk A et al. Evaluation of sensorimotor polyneuropathy in children and adolescents with type I diabetes: associations with microalbumin-uria and retinopathy. Pediatric Diabetes 2002; 3: 101.108.

15- Wysocka-Mincewicz M, Trippenbach-Dulska H, Emeryk-Szajewska B, Zakrzewska-Pniewska B, Kochanek K, Pankowska A: Co-existence of abnormalities in the peripheral nervous system and in the auditory and visual evoked potentials in children with type 1 diabetes. Diabetologia, 7 (1): 44,49.

16- Jin H and Park T:Can nerve conduction studies detect earlier and predict clinical diabetic neuropathy? J Diabetes Invest Vol. 6 No. 1 January 2015.

17- Papatheodorou A, Ellinas P, Takis F, Tsanis A, Maris I, Batakis N: US of the shoulder: rotator cuff and non-rotator cuff disorders. Radiographics 2006, 26 (l):e23.

18- Martin J. Kelley, Michael A. Shaffer, John E. Kuhn, Lori A. Michener, Amee L. Seitz, Timothy L. Uhl, Joseph J. Godges, Philip W. Mcclure : Shoulder Pain and Mobility Deficits: Adhesive Capsulitis. J Orthop Sports Phys Ther 2013; 43 (5) : A1-A3.1.

19- Ramchurn, Chiedza Mashamba, Elizabeth Leitch, et al: Upper limb musculoskeletal abnormalities and poor metabolic control in diabetes. European Journal of Internal Medicine 20: 718-721, 2009.

20- Kidwai, Lubna Wahid, Shaista A Siddiqi, et al: Upper limb musculoskeletal abnormalities in type 2 diabetic patients in low socioeconomic strata in Pakistan. BMC Research Notes, 6:16, 2013.

21- Cagliero E: Rheumatic mani-festations of diabetes mellitus. Curr Rheumatol Rep.; 5: 189-94, 2003.

22- Arkkila, Ilkka M Kantola, Jorma S A Viikari, et al: Shoulder capsulitis in type I and II diabetic: association with diabetic complic-ations and related diseases; Ann Rheum Dis 55:907-914. 1996.

23- Lee S, Han H_5 Kim H.: A 5-yr follow-up nerve conduction study for the detection of subclinical diabetic neuropathy in children with newly diagnosed insulin-dependent diabetes mellitus. Pediatr Diabetes. 2010; 11 (8): 521-8.

24- Cenesiz F, Tur B, Tezic T, Gurer Y: Nerve conduction in children suffering insulin dependent diabetes mellitus.Indian J Pediatr. 2003 Dec; 70 (12) : 945-51.

25- Carvalho MFP, Ribeiro FAQ. As deficiencias auditivas relacionadas às alterações do DNA mitocondrial. Rev Bras Otorrino-laringol. 2002; 68 (2) : 268-75.