View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Elsevier - Publisher Connector

CLINICAL STUDY

Early Diagnosis of Diabetic Neuropathy in Almadinah Almunawwarah

Moaz A. Mojaddidi[1] Ph.D, Moutasem Aboonq[1] Ph.D, Omar M AL Nozha[2] SSCIM Abdulkadir Allam[2] ArBIM, Mohamed Fath EL-Bab[1*] Ph.D

Departments of Physiology[1] and Medicine[2], College of Medicine
Taibah University, Almadinah Almunawwarah, Kingdom of Saudi Arabia
*Department of Physiology, College of Medicine, Suez Canal University, Ismailia, Egypt**

Abstract

Objectives

Diabetes mellitus (DM) is a major public health problem worldwide. The aim is to assess the early detection of impaired nerve function and the risk factors associated with the development of diabetic neuropathy.

Methods

It is a prospective descriptive study of age-matched 263 diabetic Saudi patients from the outpatient clinic of the Diabetic Centre in King Fahd Hospital in Almadinah Almunawwarah in Kingdom of Saudi Arabia during 2008-2009. Written informed consent was obtained from each subject after the protocol was approved by the local ethics committee. All subjects were diagnosed as diabetics using WHO criteria. We obtained detailed demographic data as age, sex, special habits, height, weight and body mass index, arterial blood pressure, type and duration of diabetes, glycosated haemoglobin (HbA_{1C}), lipid profile, management, family history of hypertension, diabetes. Assessment of neuropathy by using the Diabetic neuropathy index and diabetic neuropathy score. Asymptomatic patients who scored less than two in clinical examination were referred to be assessed by complete neurological examination, and nerve conduction studies. Data were calculated and compared by using SPSS version 13.0.

Results

The type I were 39 (14.8%) and type II were 244 (85.2%) diabetic patients and the mean duration of diabetes mellitus in all diabetic patients was 13.89 ± 8.7 years. The symptomatic diabetic neuropathy patients were 165 (62.7%) out of 263 diabetic patients and the asymptomatic were 98 (37.3%). The risk factors for neuropathy were old age, poor blood sugar control, long duration of diabetes, hyperlepidemia, Body Mass Index (BMI). There were no statistical significant differences in relation to types of diabetes mellitus. There was positive correlation which shown by the linear regression charts between the grades of nerve conduction defects in asymptomatic diabetic neuropathy patients and duration of diabetes, age, BMI and HbA_{1C}.

Conclusion

The early detection of by sub-clinical nerve conduction of diabetic patients is of a major clinical interest that could lead to more intensive supervision of diabetic patients. Further studies should be performed in order to confirm these findings.

Key words: Diabetic neuropathy, Diabetes mellitus risk factors, Nerve conduction studies.

Journal of Taibah University Medical Sciences 2011; 6(2): 121-131

Correspondence to:
Dr. Mohamed Fath EL-Bab
Department of Physiology, College of Medicine
Taibah University, ✉ 30001 Almadinah Almunawwarah
Kingdom of Saudi Arabia
☎+966 4 8460008
🖷 +966 4 8475790
mfeb70@hotmail.com

Introduction

Diabetes mellitus (DM) is a major public health problem worldwide. The World Health Organization has estimated that, the number of adults with diabetes in the world would increase alarmingly from 135million in 1995 to 300 million in 2025[1]. One study has shown that the prevalence of DM is about (23.7%) in 2004 in Kingdom of Saudi Arabia and another recent study has shown that there is a significant increase in the prevalence which became 30% in 2011 where was 34.1% in males and 27.6% in females[2-3].

Diabetic peripheral neuropathy considered as one of the commonest complications seen in up to 50% of affected patients with type 1 and type 2 DM leading to substantial morbidity, discomfort and associated with increased mortality according to its severity[4,5].

Nerve conduction studies, primarily nerve conduction velocities are considered one of the most sensitive indices of the severity of neuropathy and were used to localize lesions and to describe the type and severity of the pathophysiological process, including alterations in function that are not recognized clinically[6].

The aim of this research was to study the prevalence of asymptomatic diabetic neuropathy in Almadinah Almunawwarah in the Kingdom of Saudi Arabia as an example of the western district and find out the prevalence of the associated risk factors with symptomatic and asymptomatic diabetic neuropathy.

Material and Methods

It is a prospective descriptive study, the protocol was approved by the local ethics committee and written informed consent was obtained from each patient who attended the outpatient clinic of the Diabetic Patients Medical Centre in king Fahad hospital in Almadinah Almunawwarah in Kingdom of Saudi Arabia in the academic year of 2008/2009. All subjects diagnosed as diabetics using international standard criteria[7-10].

We obtained detailed demographic data as age, sex, special habits, height, weight and body mass index, arterial blood pressure, type and duration of diabetes, glucosated haemoglobin (HbA_{1C}), lipids profile, management, family history of hypertension, diabetes. Neuropathy was assessed by using the Michigan Neuropathy program which includes two steps; the Diabetic Neuropathy Index (DNI) and the Diabetic Neuropathy Score (DNS). Patients who scored less than 2 on routine clinical examination and were asymptomatic were referred to be assessed by complete neurological examination done by neurologist, and nerve conduction studies **(Appendices 1 and 2)**.

The electrophysiological tests were performed by the same neurophysiologist, and he was blinded to the clinical information of the subjects. The procedures were explained for the patient, and all nerve-conduction tests were performed in the same room with a comfort temperature of 22°C to 25°C using standard protocol[11].

We used The XL Calibre Ltd EMG system to perform the recording. The optimal recording amplifier frequency range of 50 Hz. to 10 KHz and a standard sensitively of 100 to 500 UV. Nerve conduction velocity was assessed in Median, ulnar, peroneal, sural nerve and posterior tibial nerves Motor nerve conduction velocity was measured on the left forearm segment of the median nerve (thenar muscle), and the left peroneal nerve (extensor digitorum brevis and tibial anterior muscle)[12-14]. Minimal F-wave latencies were acquired from the same recording and distal stimulation points, from at least eight tracings. F-wave conduction velocity was calculated as described elsewhere data were collected, calculated and statistical analyses were carried out by using Statistical Package for Social Sciences (SPSS version XIII, Inc., Chicago, Illinois). Results were considered statistically significant at *P*-value less than or equal to 0.05[18-19].

Results

The 263 diabetic Saudi patients distributed as follows: type I was 39 (14.8) and type II was 224 (85.2%) and the mean duration of diabetes mellitus was 13.89 ± 8.7 years. The distribution of the patients according to their gender and type of diabetes were 15 (51.7%) males in type I and 14 (47.3%) females, and type II they were 107 (45.7%) males and 127 (54.3%) females. The positive family history of diabetes was 66.9% and for the hypertension was 33.5%. The non-smokers representing 86.7%.

There were 122 males and 141 females' with male to female ratio of 1:1.15, aged 20-70 years (51.79 ± 10.88 years). The patients with neuropathy were 155 (58.9%) and 108 (41.1%) diabetic patients were free from signs and symptoms of neuropathy as assessed initially by the DNI. Further assessment by the DNS and the neurological examinations added 10 more patients (3.8%). So, patients became 165 (62.7%) and those clinically free 98 (37.3%). The positive DN patients diagnosed by electrophysiological studies were 43 (16.4.) The results show that positive family history of diabetes was seen in 115 patient (69.6%) and 54 (55.1%), the smokers number and percentage were 13 (0.07%) and 3 (0.03%) while type II represented as 146 (88.4%) and 78 (79.5) in the symptomatic and asymptomatic DN patients respectively. The symptomatic DN diabetic patients mean BMI was 33.42 ± 5.68 and that of asymptomatic was 33.45 ± 6.88 which makes them more susceptible to chronic disease e.g. hypertension and diabetes mellitus complications. The mean systolic blood pressure among symptomatic and the asymptomatic DN patients were (140.19 ± 18.30 and 138.77 ± 21.21mmHg) and the mean diastolic were respectively (83.30 ± 11.37 and 81.22 ± 9.47 mmHg). Hypertensive family history was 61 patients (36.9%) positive in symptomatic and 28 (28.5%) in asymptomatic patient.

On the other hand, we found that HbA_{1C} was higher in symptomatic DN patients (10.06 ±1.91) symptomatic to (8.58 ±1.41) in a symptomatic patients indicated worst glucose control in the first group. We also revealed that there were more hyper-lepidemic symptomatic patients 47 (28.4) and has asymptomatic which were 29 (29.5), where the total cholesterol, triglycerides and the LDL were higher than the normal values in both groups **(Table 1)**.

The results show that the mean risk score for the females (2.88± 4.18) was higher than the males (1.77 ± 4.30) with no statistical differences **(Figure 1).**

The number of patients, who were clinically asymptomatic and diagnosed electro-physiologically, was as mild, moderate, and severe nerve conductions defect as shown in **(Figure 2)**.

There was a positive correlation shown by the linear regression charts between the grades of asymptomatic patients and the diabetes mellitus duration, glycosated haemoglobin, age and BMI of the nerve conduction defects among clinically free diabetic neuropathy **(Figure 3)**.

Table 1: comparison between the diabetic neuropathy patients and the asymptomatic patients according to different variables.

Features	Asymptomatic diabetic neuropathy N (%) 98	Symptomatic diabetic neuropathy N (%) 165
Age	49.84 ± 11.85	52.90 ± 10.21
Males: females ratio	1: 1.1	1:1.22
Dm duration	12.05 ± 7.43	14.32 ± 8.39
Type ii	78 (79.5)	146 (88.4)
Family history of hypertension	28 (28.5)	61 (36.9)
Family history of dm	54 (55.1)	115 (69.6)
Smokers (non-smokers)	3 (0.03)	13 (0.07)
Body mass index	33.45 ± 6.88	33.42 ± 5.68
Systolic blood pressure	138.77 ± 21.21	140.19 ± 18.30
Diastolic blood pressure	81.22 ± 9.47	83.30 ± 11.37
Glucosated haemoglobin	8.58 ± 1.41	10.06 ± 1.91
Hyperlepidemia	29 (29.5)	47 (28.4)
Total cholesterol	5.36 ± 1.04	5.68 ± 1.30
Triglyceride	2.24 ± 0.90	2.78 ± 1.17
Low density lipoprotein	3.25 ± 0.77	3.27 ± 0.67

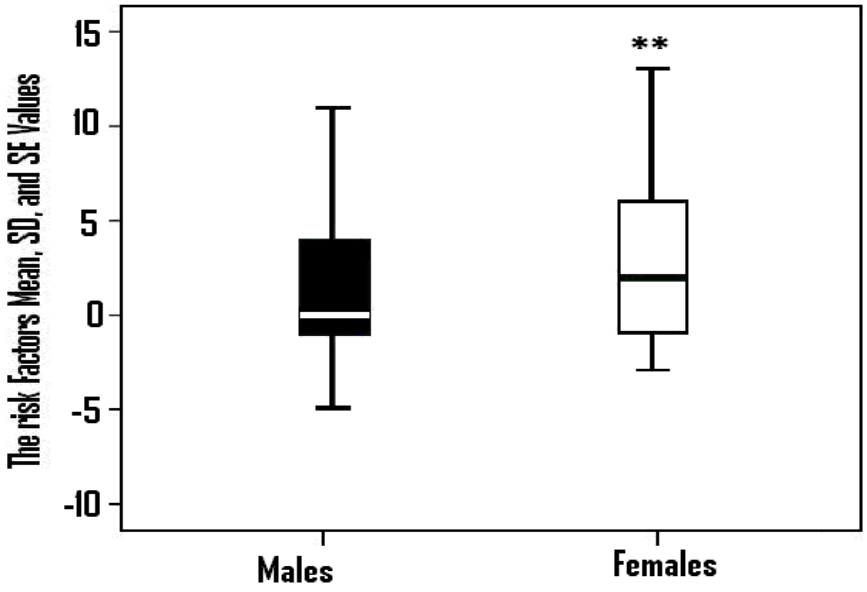

Figure 1: *The box plot chart shows the female and the male diabetic patients mean values risk factors score.*

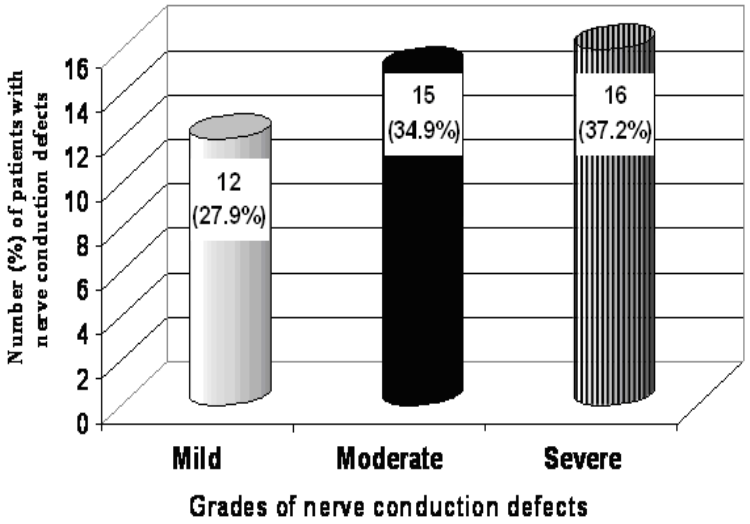

Figure 2: *The column with a cylindrical shape charts shows the grades of nerve conduction defects in clinically free diabetic neuropathy (asymptomatic) patients.*

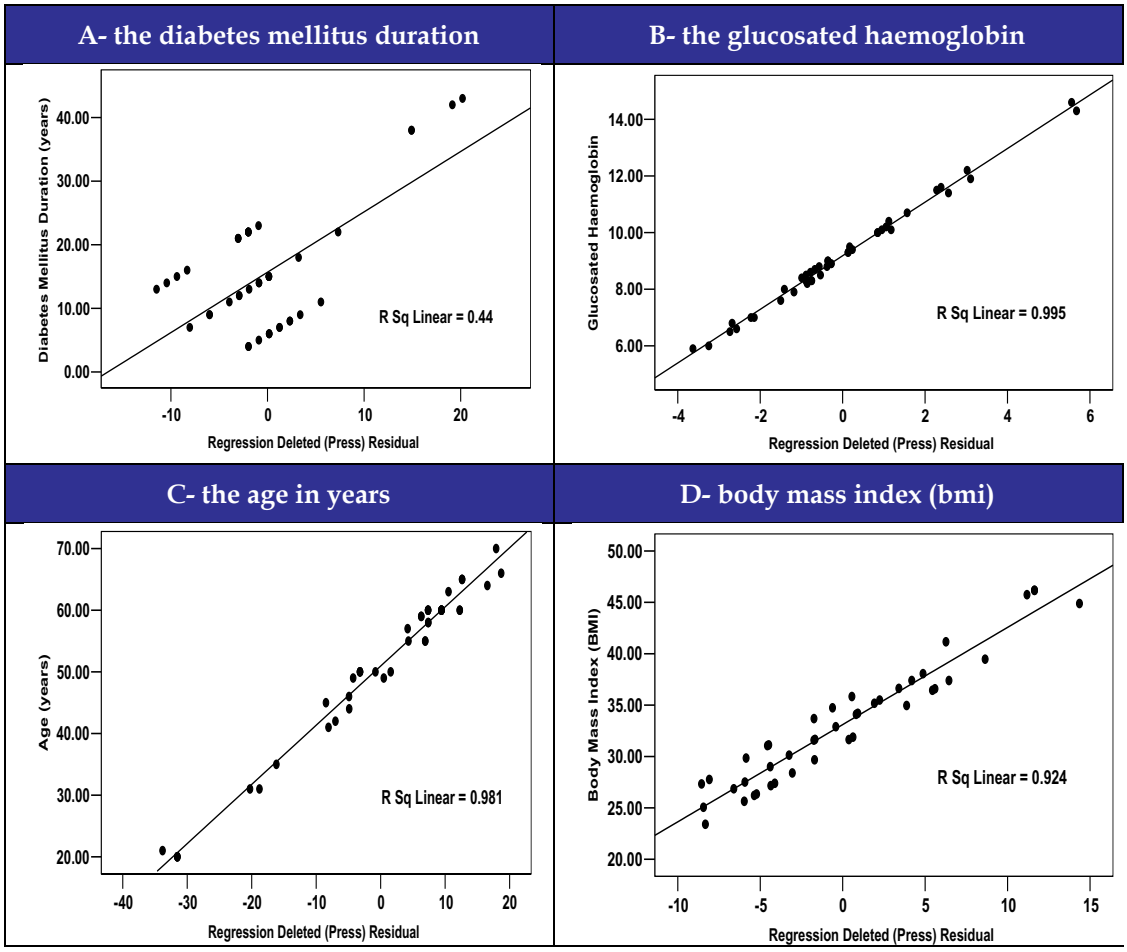

Figure 3: *The linear regression charts showing correlation between different risk factors (A- the diabetes mellitus duration, B- the glucosated haemoglobin, C- the age, D- the BMI) and the grades of the nerve conduction defects among clinically free diabetic neuropathy (asymptomatic) patients.*

Discussion

Our study has endeavoured to provide a part of the picture of the sub clinical pattern of diabetic neuropathy in DM from Kingdom of Saudi Arabia as a developing area in the Middle East. Polyneuropathy prevalence varies greatly depending on the clinical and the electrophysiological diagnostic criteria of ADA[9-10]. The electrophysiological measu-res include the studies of sensory and motor nerve conduction, F-wave recordings, and surface electrodes electromyography. In Kingdom of Saudi Arabia, the prevalence of diabetic neuropathy was observed to be 35.9% after screening 1000 diabetics[17].

From our results we found that the diabetic neuropathy is mainly in sensory nerves more than motor nerves particularly in the lower limbs, which affect the small caliber nerves as sural nerve, and the abnormalities were in the nerve conduction velocity, latencies, and F-wave studies results, rather than in the amplitudes, as well it was more in type II diabetes mellitus Patients

The early diagnosis of diabetic poly neuro-pathy (DPN) is important in that it allows for immediate interventions, which decrease both mortality and morbidity a rise in the prevalence of the commonly associated complications, namely the various forms of diabetic neuropathy, is therefore anticipated[18-22]. The present study focused on a group of type II and type I diabetic patients who were free from neurologically symptoms. Diagnosis of DPN on clinical ground alone is not accurate and there is difficulty in detecting a small alteration of neuropathy[23-24].

Therefore, as a surrogate measure, nerve conduction study (NCS) is widely used as an evaluation of DPN. In general, it has been accepted that the ideal diagnosis of DPN is made by both the compatible clinical findings and the related electrophysiological changes[25].

Diabetes is the leading cause of neuropathy in the Western world, and neuropathy is the most common complication and greatest source of morbidity and mortality in diabetes patients[26]. It is estimated from a comprehensive collection of epidemiologic studies that the prevalence of neuropathy in diabetes patients is approximately 30% in hospital patients and 20% in community patients[22]. The overall annual incidence of neuropathy was < 2%[27].

The following factors increase the susceptibility to nerve damage: Poor blood sugar control, Length of time the patient has diabetes, Age, Sex, High cholesterol, Smoking[28].

The American Diabetes Association recommends that glycosylated haemoglobin (HbA_{1c}) should be less than 7%[9-10]. Most previous studies, which reported HbA_{1c} correlation with polyneuropathy, used higher HbA_{1c} cut points and focused on neurologically symptomatic patients.

We showed in our results that diabetic patients had poor glucose control as indicated by high Haemoglobin A_{1c} as it was 10.06 ± 1.91 in symptomatic DN patients and 8.58 ± 1.41 in asymptomatic. Hyperinsuline-mia and hyperglycaemia might affect through their co-morbidities as hyper-tension, dyslipidemia, and central body fat distribution[29-30].

Hypertension was found in 57.8% of our diabetic patients with no statistically significant difference between males and females. The mean age of diabetic patients was significantly higher in hypertensive than non-hypertensive. There were only 14.2% of hypertensive diabetic patients in whom blood pressure was controlled. Poor control was significantly associated with obesity, and a higher rate of complications, so our results are in agreement with what was reported that the blood pressure control correlated positively and significantly with the age of patients, and negatively with duration of diabetes and hypertension as observed regarding the anthropometrical variables, the BMI values obtained about the excessive weight in all groups' patients are similar to those found in a multi-centric study carried out with more than 2,500 type II DM patients in 12 cities of different Brazilian regions[31-32]. The high prevalence of overweight diabetic patients has been appointed by epidemiological research in the South and Southeast of Kingdom of

Saudi Arabia, estimating that between 80 and 90% of individuals with type II DM are obese or overweight[33].

However, despite awareness about the importance of excessive body weight for morbidity and mortality of patients with type II DM, the control of this variable in diabetic populations has rarely been emphasized in most studies. In addition, the approach to this problem in basic health care has been neglected, since recommendations on the control of these variables exist in most services, but are not accompanied by resources that can adequately support individuals in an effective change that results in weight loss[34].

Laboratory data indicate high prevalence of dyslipidemia in our patients, similar to that found in a survey with type II DM patients, performed in Rio Grande do Sul 67% presented total cholesterol over 200mg/dL; 65% triglycerides > 150 mg/dL and 47% low HDL cholesterol >50 mg/dL[34]. Peripheral neuropathy is a common clinical problem confronting the practicing neurologist. Several groups have demonstrated a 30% to 45% prevalence of impaired glucose tolerance (IGT) in patients with otherwise idiopathic neuropathy[35]. In concordance with the results of the DCCT, UKPDS and Booya et al, our study shows the same risk factors published in different reports such as poor blood sugar control, the duration of having diabetes, the age, the high level of low-density lipoprotein (LDL) cholesterol which damaged the small blood vessels that nourish the nerves, and smoking where they enhance the atherosclerotic effect and reduce the blood flow to the legs and feet ending in damage of the peripheral nerves[36-38]. Other researchers reported that the diabetic neuropathy was significantly associated with age, duration of disease, negative association with arterial blood pressure, smoking status, low HDL cholesterol level, high triglyceride level, BMI and HbA_{1c} [38-42].

The diabetic individuals were, on average, more obese than the control group, with higher values for body mass index (BMI), Waist Hip Ratio and percentage body fat. The mean systolic and diastolic blood pressures were higher in the diabetic group than in the control group, as was the serum triglyceride[43].

Our results showed no statistical significant differences and there was no correlation between the diabetes mellitus type I and type II and the risk factors score which indicates that the risk factor effects were equal in both types of diabetes mellitus.

Our study is in agreement with Tesfaye et al, and DCCT findings, that the mean glycosylated haemoglobin had a strong correlation with neuropathy[35,44].

Clinical spectrum of diabetic neuropathy is variable; it may be asymptomatic, but once established as neuropathy, it is irreversible and may finally be disabling. We determined the nerve conduction defects in asymptomatic diabetic patients.

Our study results are in agreement with the results of EL-Salem et al which showed a correlation between elevated glycosylated hemoglobin and subclinical neuropathy in neurologically asymptomatic diabetic patients and the authors recommended that therapies for diabetic neuropathy should target the early stages of the disease[29].

Karsidag et al reported that there is a correlation between HbA_{1c} levels and nerve conduction velocity in posterior tibial and peroneal nerves. However, upper extremity nerve conduction dysfunction was not correlated with HbA1c value[45]. Neither the duration of disease nor the age of the subject correlated with the nerve dysfunction, and that group reported that the percentages of abnormal electrophysiological parameters in different motor and sensory nerves were 86.7% in sural nerve, 83.3% in peroneal motor nerve, 73.3% in posterior tibial motor nerve, 66.7% in median motor nerve, 63.3% in ulnar motor nerve, 60% in median sensory nerve, and 46.7% in ulnar sensory nerve. While distal motor latency, F conduction time, and minimum F latency were the most frequent abnormal parameters in the upper extremity electrophysiological study; conduction velocity, minimum and mean F latencies, F conduction time were the most frequent abnormal parameters in the lower extremity and in all sensory nerve conduction studies,

the most frequent abnormal parameter was the onset latency.

Baba M, and Ozaki I, 2001 the prevalence of subclinical diabetic polyneuropathy in the United Arab of Emirates UAE, and they found close association between neurological deficit score and abnormalities in NCS[46]. Among various parameter of systemic nerve conduction studies in subclinical patients, prolonged F-wave latency seems the commonest abnormality suggesting morphological changes in subclinical diabetic nerves.

Conclusion

In conclusion, neuropathy was diagnosed in 79% of our diabetic patients by a combination of clinical findings and electrophysiological studies (EPS). This is a worrying prevalence, especially as it was picked up in 44% of asymptomatic patients by (EPS). This should be emphasized in the care of our diabetics. Further studies needed to confirm these findings.

References

1. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. **Diab Care 1998**; 21(9): 1414-1431.
2. Al-Nozha MM, Al-Matouq MA, et al. Diabetes Mellitus In Kingdom of Saudi Arabia. **Saud Med J 2004**; 25(11): 1603-1610.
3. Alqurashi KA, Aljabri KS, Bokhari SA. Prevalence of diabetes mellitus in a Saudi community. **Ann Saudi Med 2011**; 31(1): 19-23.
4. Poncelet AN, Diabetic polyneuropathy risk factors, patterns of presentation, diagnosis and treatment (Review). **Geriatr 2003;** 58: 16-18, 24-25, 30.
5. Davies M, Brophy S, Williams R, Taylor A. The prevalence, severity, and impact of painful diabetic peripheral neuropathy in type 2 diabetes. **Diab Care 2006;** 29(7): 1518-1522.
6. Tkac I, Bril V. Glycemic control is related to the electrophysiologic severity of diabetic peripheral sensorimotor polyneuropathy. **Diab Care 1998**; 21: 1749-1752
7. World Health Organization: Definition, Diagnosis, and Classification of Diabetes Mellitus and Its Complications: Report of a WHO Consultation. Part 1: Diagnosis and Classification of Diabetes Mellitus. Geneva, **World Health Organ 1999**.
8. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Follow-up report on the diagnosis of diabetes mellitus. **Diab Care 2003**; 26: 3160–3167.
9. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. **Diab Care 2004**; 27(1): 5-10.
10. American Diabetes Association. Standards of medical care in diabetes. **Diab Care 2008**; 31: 12-54.
11. kimura J. (editor). Principle and variations of nerve conduction studies. In Electrodiagnosis in Diseases of Nerve and Muscle, Principles and Practice, edition 3. **Oxford Univ Press 2001**; 91-129.
12. Mesrati F, Vecchierini M.F. F-waves neurophysiology and clinical value. **Neurophysiol Clin 2004**; 34: 217–243.
13. Karsidag S, Moral S, Sargın M, Salman S, Karsidag K, US O. The electrophysiological findings of subclinical neuropathy in patients with recently diagnosed type 1 diabetes mellitus. **Diab Res Clin Pract 2005**; 67: 211–219.
14. Papanas N, Dan Ziegler. New diagnostic tests for diabetic distal symmetric polyneuropathy. **J Diab Complicat 2011;** 25(1): 44-51.
15. Kohara N, Kimura J, Kaji R, Goto Y, Ischii J, Takiguchi M, F-wave latency serves as the most reproducible measure in nerve conduction studies of diabetic polyneuropathy, multicentre analysis in healthy subjects and patients with diabetic polyneuropathy. **Diabetologia 2000**; 43: 915–921.
16. Meijer J, Lange F, Links P, van der Hoeven H. Muscle fiber conduction abnormalities in early diabetic polyneuropathy. **Clin Neurophysiol 2008;** 119: 1379–1384.

17. Famuyiwa OO, Sulimani RA, Laajam MA, Al-Jasser SJ, Mekki MO. Diabetes mellitus in Kingdom of Saudi Arabia: the clinical pattern and complications in 1000 patients. **Ann Saudi Med 1992**; 12: 140-151.
18. Olaleye D, Perkins BA, Bril V. Evaluation of three screening tests and a risk assessment model for diagnosing peripheral neuropathy in the diabetes clinic. **Diab Res Clin Pract 2001**; 54: 115–128.
19. Shaw JE, Zimmet PZ. The epidemiology of diabetic neuropathy. **Diab Rev 1999**; 7: 245-252.
20. Rith-Najarian SJ, Stolusky T, Gohdes DM. Identifying diabetic patients at high risk for lower-extremity amputation in a primary health care setting. A prospective evaluation of simple screening criteria. **Diab Care 1992;** 15: 1386–1389.
21. Boulton AJ, et al. Diabetic neuropathies a statement by the American Diabetes Association. **Diab Care 2005**; 28(4): 956-962.
22. Várkonyi T, Kempler P. Diabetic neuropathy: new strategies for treatment. **Diab Obes Metab 2008**; 10(2): 99-108.
23. Boulton AJ. Management of Diabetic Peripheral Neuropathy. **Clin Diab 2005**; 23(1): 9-15.
24. Perkins BA, Olaleye D, Zinman B, Bril V. Simple screening tests for peripheral neuropathy in the diabetes clinic. **Diab Care 2001;** 24: 250–256.
25. American Diabetes Association American Academy of Neurology. Consensus statement. Report and recommendations of the San Antonio conference on diabetic neuropathy. **Diab Care 1988;** 11: 592-597
26. Vinik AI, Park TS, Stansberry KB et al. Diabetic neuropathies. **Diabetologia 2000**; 43: 957-973.
27. Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. **N Engl J Med 1993**; 329: 977–986.
28. Wiggin TD, Sullivan KA, Pop-Busui R, Amato A, Sima AA, Feldman EL. Elevated triglycerides correlate with progression of diabetic neuropathy. **Diab 2009**; 58(7): 1634-1640.
29. El-Salem K, Ammari F, Khader Y, Dhaimat O. Elevated glycosylated hemoglobin is associated with subclinical neuropathy in neurologically asymptomatic diabetic patients: a prospective study. **J Clin Neurophysiol 2009**; 26(1): 50-53.
30. Dorsey RR, Eberhardt MS, Gregg EW, Geiss LS. Control of risk factors among people with diagnosed diabetes, by lower extremity disease status. **Prev Chronic Dis 2009**; 6(4): 114.
31. Al-Shehri AM. Blood pressure control among type 2 diabetics. **Saudi Med J 2008**; 29(5): 718-722.
32. Neutzling MB, Taddei JA, Rodrigues EM, Sigulem DM. Overweight and obesity in Brazilian adolescents. **Int J Obes Relat Metab Disord 2000**; 24(7): 869-874.
33. Almajwal AM, Al-Baghli NA, Batterham MJ, Williams PG, Al-Turki KA, Al-Ghamdi AJ. Performance of body mass index in predicting diabetes and hypertension in the Eastern Province of Kingdom of Saudi Arabia. **Ann Saudi Med 2009**; 29(6): 437-445.
34. Bajaj M, Jialal I. Type 2 diabetes treatment and macrovascular complications--fat and sugar make a dangerous soufflé. **Metab Syndr Relat Disord 2009**; 7(2):79-81.
35. DCCT Research Group. Factors in development of diabetic neuropathy. Baseline analysis of neuropathy in feasibility phase of diabetes control and complications trial (DCCT). **Diabetologia 1988;** 37: 476-489.
36. Implications of the United Kingdom Prospective Diabetes Study. **Diab Care 2002;** 25: 28-32.
37. Booya F, Bandarian F, Larijani B, Pajouhi M, Nooraei M, Lotfi J. Potential risk factors for diabetic neuropathy: a

case control study. **BMC Neurol 2005**; 10: 5-24.
38. Barbosa AP, Medina JL, Ramos EP, Barros HP. Prevalence and risk factors of clinical diabetic polyneuropathy in a Portuguese primary health care population. **Diab Metab 2001**; 27(4): 496-502.
39. Ashok S, Ramu M, Deepa R et al. Prevalence of neuropathy in type 2 diabetes patients attending diabetes center in South India. **J Assoc Phys India 2002**. 50: 546–550.
40. Cho DY, Mold JW, Roberts M. Further investigation of the negative association between hypertension and peripheral neuropathy in the elderly: an Oklahoma Physicians Resource/Research Network (OKPRN) Study. **J Am Board Fam Med 2006**; 19(3): 240-250.
41. Eliasson B: Cigarette smoking and diabetes. **Prog Cardiovasc Dis 2003;** 45: 405-413.
42. Wiggin TD, Sullivan KA, Pop-Busui R, Amato A, Sima AA, Feldman EL. Elevated triglycerides correlate with progression of diabetic neuropathy. **Diab 2009**; 58(7): 1634-1640.
43. Rahman M, Griffin SJ, Rathmann W, Wareham NJ. How should peripheral neuropathy be assessed in people with diabetes in primary care? A population-based comparison of four measures. **Diab Med 2003**; 20(5): 368-374
44. Tesfaye S et al. Vascular Risk Factors and Diabetic Neuropathy. **N Engl J Med 2005;** 352: 341-350.
45. Karsidag S, Moral S, Sargın M, Salman S, Karsidag K, US O. The electrophysiological findings of subclinical neuropathy in patients with recently diagnosed type 1 diabetes mellitus. **Diab Res and Clin Prac 2005;** 211–219.
46. Baba M, Ozaki I. Electrophysiological changes in diabetic neuropathy: from subclinical alterations to disabling abnormalities. **Arch Physiol Biochem 2001**; 109(3): 234-240.

Appendix 1: Physical Assessment (To be completed by health professional).

APPEARANCE OF FEET	**RIGHT**			**LEFT**		
Normal	**Yes (0), If no, check all that apply:**			**Yes (0), If no, check all that apply:**		
Deformities	Yes (0)	No (1)		Yes (0)	No (1)	
Dry skin, callus	Yes (0)	No (1)		Yes (0)	No (1)	
Infection	Yes (0)	No (1)		Yes (0)	No (1)	
Fissure	Yes (0)	No (1)		Yes (0)	No (1)	
Ulceration	Present (0)	Absent (1)		Present (0)	Absent (1)	
Other - specify:						
Ankle Reflexes	Present (0)	Reinforcement (0.5)	Absent (1)	Present (0)	Reinforcement (0.5)	Absent (1)
Vibration perception at great toe	Present (0)	Decreased (0.5)	Absent (1)	Present (0)	Decreased (0.5)	Absent (1)
Monofilament	Normal (0)	Reduced (0.5)	Absent (1)	Normal (0)	Reduced (0.5)	Absent (1)
Total Score _____/10 Points						

Appendix 2: Michigan Neuropathy Screening Instrument.

History (To be completed by the person with diabetes)		**Yes**	**No**
1.	Are you legs and/or feet numb?	1	2

2.	Do you ever have any burning pain in your legs and/or feet?	1	2
3.	Are your feet too sensitive to touch?	1	2
4.	Do you get muscle cramps in your legs and/or feet?	1	2
5.	Do you ever have any prickling feelings in your legs or feet?	1	2
6.	Does it hurt when the bed covers touch your skin?	1	2
7.	When you get into the tub or shower, are you able to tell the hot water from the cold water?	1	2
8.	Have you ever had an open sore on your foot?	1	2
9.	Has your doctor ever told you that you have diabetic neuropathy?	1	2
10.	Do you feel weak all over most of the time?	1	2
11.	Are your symptoms worse at night?	1	2
12.	Do your legs hurt when you walk?	1	2
13.	Are you able to sense your feet when you walk?	1	2
14.	Is the skin on your feet so dry that it cracks open?	1	2
15.	Have you ever had an amputation?	1	2
Total score:			