



RESTLESS LEG SYNDROME AND DIABETIC NEUROPATHY: A CASE-CONTROL STUDY AMONG DIABETIC PATIENTS IN TABUK, KSA

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ABSTRACT

Diabetic Peripheral Neuropathy (DPN) and restless leg syndrome are common among patients with diabetes and might complicate each other's deleterious consequences. The study assessed the rates of peripheral neuropathy and restless leg syndrome in diabetes mellitus. This study is a case-control carried out in King Fahad specialist hospital and primary healthcare centers in Tabuk city, Saudi Arabia during the period from September to December 2020. 132 diabetic patients were selected as cases, and 132 as controls. A structured, self-administered questionnaire based on the International Restless Leg Syndrome Study Group consensus criteria and Michigan peripheral neuropathy assessment questionnaire were used to obtain information from the participants. Moreover, the Statistical Package for Social Sciences (SPSS) software was used for data analysis. Out of 264 participants with a mean age (46 ± 14 years), males' dominance was obvious (73.5% and 75.0% in patients and the control group, respectively). Peripheral neuropathy was evident in 18.2% of patients and 2.3% of the control group, P -value < 0.001 . Ninety-one of the participants in both of the study groups had restless leg syndrome, out of which 53.9% were from the diabetes mellitus group. No significant association was found between having restless leg syndrome with neither peripheral neuropathy nor diabetes mellitus, p values: 0.524, and 0.822, respectively. Peripheral neuropathy and restless leg syndrome were common among patients with diabetes, however, no significant association was found between restless leg syndrome with neither diabetes nor peripheral neuropathy; So, raising the awareness of the public and clinicians is highly needed.

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Introduction

Diabetic Peripheral Neuropathy (DPN) is a common complication of diabetes, which characterizes by many clinical manifestations and can lead to foot ulcers, amputations, and mortality among patients, it is defined as "the presence of symptoms and/or signs of peripheral nerve dysfunction in patients with diabetes after the exclusion of other causes", however, it can be present asymptotically [1, 2]. Even though half of DPN patients are asymptomatic, some of them have a progressive sensory impairment, which leads to burning feet sensation that responds poorly to analgesics. Additionally, it is associated with a reduction in patients' quality of life and a huge economic burden on the individual and the community [3-5].

The cause of Diabetic Peripheral Neuropathy (DPN) is multifactorial, peripheral nerve damage is due to the long-standing hyperglycemia and diabetes-related microvascular complications resulting in a decrease in nutrition especially to the distal nerve axons of the feet. In addition to nutritional deprivation, distal nerve axons also suffer from hypoxic damage due to decreased vascular supply. Exaggerated oxidative stress and excessive release of cytokines also play a role in DPN [6]. Although it is difficult to draw accurate estimates about the prevalence of DPN, it is estimated that 10-90% of diabetes patients suffer from DPN, and 15% of them have painful DPN, and it is a leading cause of "non-traumatic" leg amputations globally [7].

Restless Leg Syndrome (RLS) characterizes by a tendency to move the limbs with unpleasant sensations increasing at night and improved by rest. The diagnosis is usually clinical; the association of restless leg syndrome with diabetic neuropathy is

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controversial [8]. RLS as a common sleep disorder is treatable; however, it may mimic diabetic neuropathy leading to treatment delay [9].

The dramatic change in diet and lifestyle in Gulf countries including Saudi Arabia has made diabetes mellitus a growing health problem in these countries, increased prevalence of diabetes mellitus has been associated with high-energy consumption and Gross Domestic Product (GDP), Saudi Arabia has one of the highest adult diabetes prevalence (31.6%) [10]. Moreover, several studies have reported a high prevalence of DPN among the diabetic population in Saudi Arabia ranging from (19%) – (35%) [11-13]. Despite this, there is a huge knowledge gap to cover to compact DPN in the Saudi population and assess its relation to RLS. Thus, this study has aimed to assess the prevalence of peripheral neuropathy in diabetes mellitus patients in Tabuk city, Saudi Arabia.

Materials and Methods

Study Settings

This study was a case-control, hospital-based study, carried out in king Fahad specialist hospital and primary healthcare centers in Tabuk city, Saudi Arabia in the period from June to December 2020.

Sampling and Participants' Selection

This study was conducted among diabetes mellitus patients in Tabuk city, Saudi Arabia, with 132 diabetic patients selected as cases, and 132 as controls. The study was conducted during the period from September to December 2020. The sample size for this study was obtained using the formula: $Z^2 P-Q/d$, where $Z=$ 95% confidence (1.96), $P =$ the prevalence of peripheral neuropathy in diabetes mellitus patients in Tabuk city, Saudi Arabia, $d=$ and the margin of error = 0.05. The inclusion criteria for the cases were: adults more than 18 years old, living in Tabuk city, and diagnosed with diabetes mellitus, and the exclusion criteria were age less than 18 years old, and not living in Tabuk city.

Data Collection

A structured, self-administered questionnaire was used to obtain information from the participants. The questionnaire was composed of two sections. The first one was about the socio-demographic characteristics of the study participants and including age, gender, place of residence, and the participant's medical history with diabetes mellitus. The second section contained the International Restless Leg Syndrome Study Group consensus criteria (a validated 4-items for RLS diagnosis, the desire to move the limbs, worsen by rest, improved with movement, and more during the night [14, 15]) and Michigan diabetic neuropathy questionnaire, a reliable 15-items tool for the diagnosis of peripheral neuropathy [16]. The questionnaire inquiries about numbness, burning pain, and prickling sensations in legs and feet, muscle cramps, too sensitivity to touch, and feeling weak or the legs hurt when walking. Besides, the questionnaire asks about being diagnosed with neuropathy or had a previous amputation. Besides, if sensing the feet while walking, dryness of the skin and cracked skin are observed. A score >two indicated peripheral neuropathy [17].

Statistical Analysis

Statistical Package for Social Sciences (SPSS) software version 22.0 was used for data entry and analysis. Categorical data were presented as frequencies and percentages, while contentions data as means and standard deviations. Analytical statistics were conducted using Chi-Square tests (χ^2) to test for the association and/or the difference between two categorical variables. P-value equal to or less than 0.05 was considered statistically significant.

Ethical Considerations

This study conserved the participants' confidentiality; personal information (e.g. name, contact information, ID number) was not collected in our data to protect the privacy of the participants. We also ensure that the investigators are responsible to protect the participant's privacy. Informed consent was obtained from the participants before collecting the data. Ethical clearance was obtained from the Faculty of Medicine, University of Tabuk institutional review board (Ref. READ, 0103, dated 22/7/220).

Results and Discussion

Two hundred and sixty-four participants were included in this study, with 132 (50%) being cases of diabetes mellitus, while the other half were in the control group. The mean age for the participants in the case group was 46 ± 14 years, compared to 32 ± 10 years in the control, and the most common age group was (46-60 years) in the cases group, and (15-30 years) in the control. The majority of participants in both the case and control groups were males, with 97 (73.5%), and 99 (75.0%) males, respectively. Besides, the most common type of diabetes reported in the case group was type 2 diabetes with 81 patients (61.4%), and the mean duration for diabetes in years was 10 ± 8 years. The most common medication that was used by diabetic patients in this study was oral medications in 62 patients (47%). **Table 1** demonstrates the characteristics of the study participants.

Table 1. Characteristics of the Study Participants

		Study Group						p (X ²)
		Case		Control		Total		
		Count	%	Count	%	Count	%	
Gender	Male	97	73.5%	99	75.0%	196	74.2%	0.778 (0.079)
	Female	35	26.5%	33	25.0%	68	25.8%	
Age Range	15-30	23	17.4%	68	51.5%	91	34.5%	< 0.001* (70.13)
	31-45	31	23.5%	48	36.4%	79	29.9%	
	46-60	56	42.4%	16	12.1%	72	27.3%	
	61-80	22	16.7%	0	0.0%	22	8.3%	
Peripheral Neuropathy Assessment	Normal	108	81.8%	129	97.7%	237	89.8%	< 0.001* (18.19)
	Abnormal	24	18.2%	3	2.3%	27	10.2%	

In the present study, 73.3% of patients suffered from type 2 diabetes, the majority were on oral hypoglycemic drugs and insulin (89.3%), while 10.6% were not on medications **Table 2**.

Table 2. Disease Information Related to Diabetics Included in the Study

		Count	%
Type of Diabetes	1	31	27.7%
	2	81	73.3%
Duration of Diabetes	1 year or less	17	13.3%
	Between 1 to 5	31	24.2%
	between 6 to 15	50	39.1%
	15 or more	30	23.4%
Treatment is Taken to Control Diabetes	Oral Drugs	62	46.9%
	Insulin Injection	56	42.4%
	No Medication	14	10.6%

Compared with the case group, 119 (90.2%) of the control group said that their feet are too sensitive to touch. Additionally, the majority of the cases (83 participants, 62.9%) reported that they have prickling feelings in their legs or feet, and 90 (68.2%) said that they feel weak all over most of the time. Moreover, more than half of the participants in the case group (72 participants, 54.5%) reported that the skin on their feet is so dry that it cracks open. **Table 3** shows the participants' responses to diabetic neuropathy assessment questions. According to peripheral neuropathy assessment, 24 (18.2%) of the cases were considered abnormal, while 3 (2.3%) of the control group were considered abnormal, and peripheral neuropathy was significantly associated with the cases group (p-value < 0.001).

Regarding Restless Leg Syndrome, 91 of the participants in both of the study groups had Restless Leg Syndrome, 49 (53.9%) participants were from the diabetes mellitus group, and the rest were from the control group. Additionally, 11 (12.1%) of them had abnormal assessment results for peripheral neuropathy. No significant association was found between having Restless Leg Syndrome with neither peripheral neuropathy nor diabetes mellitus, p values: 0.524, and 0.822, respectively. 51 (56.0%) of Restless Leg Syndrome patients reported that their symptoms get worse during the night, and 64 (70.3%) said that they get better with movements, **Tables 4 and 5** shows respondents answers to Restless Leg Syndrome questions and their association with peripheral neuropathy and diabetes mellitus.

Table 3. Participants Responses to Diabetic Neuropathy Assessment Questions

		Study Group						p (X ²)
		Case		Control		Total		
		Count	%	Count	%	Count	%	
1. Are your Legs and/or Feet Numb?	No	55	41.7%	92	69.7%	147	55.7%	< 0.001* (21.01)
	Yes	77	58.3%	40	30.3%	117	44.3%	
2. Do you ever have any burning pain in your legs and/or feet?	No	63	47.7%	97	73.5%	160	60.6%	< 0.001* (18.34)
	Yes	69	52.3%	35	26.5%	104	39.4%	
3. Are your feet too sensitive to touch?	No	15	11.4%	13	9.8%	28	10.6%	0.689 (0.16)
	Yes	117	88.6%	119	90.2%	236	89.4%	
4. Do you get muscle cramps in your legs and/or feet?	No	61	46.2%	65	49.2%	126	47.7%	0.622 (0.24)
	Yes	71	53.8%	67	50.8%	138	52.3%	
5. Do you ever have any prickling feelings in your legs or feet?	No	49	37.1%	86	65.2%	135	51.1%	< 0.001* (20.75)
	Yes	83	62.9%	46	34.8%	129	48.9%	

6. Does it hurt when the bed covers touch your skin?	No	114	86.4%	124	93.9%	238	90.2%	0.039* (4.27)
	Yes	18	13.6%	8	6.1%	26	9.8%	
7. When you get into the tub or shower, are you able to tell the hot water from the cold water?	No	6	4.5%	5	3.8%	11	4.2%	0.758 (0.095)
	Yes	126	95.5%	127	96.2%	253	95.8%	
8. Have you ever had an open sore on your foot?	No	91	68.9%	118	89.4%	209	79.2%	< 0.001* (16.74)
	Yes	41	31.1%	14	10.6%	55	20.8%	
9. Has your doctor ever told you that you have diabetic neuropathy?	No	121	91.7%	130	98.5%	251	95.1%	0.01* (6.55)
	Yes	11	8.3%	2	1.5%	13	4.9%	
10. Do you feel weak all over most of the time?	No	42	31.8%	79	59.8%	121	45.8%	< 0.001* (20.89)
	Yes	90	68.2%	53	40.2%	143	54.2%	
11. Are your symptoms worse at night?	No	94	71.2%	116	90.6%	210	80.8%	< 0.001* (15.77)
	Yes	38	28.8%	12	9.4%	50	19.2%	
12. Do your legs hurt when you walk?	No	75	56.8%	99	75.0%	174	65.9%	0.002* (9.71)
	Yes	57	43.2%	33	25.0%	90	34.1%	
13. Are you able to sense your feet when you walk?	No	20	15.2%	7	5.3%	27	10.2%	0.008* (6.97)
	Yes	112	84.8%	125	94.7%	237	89.8%	
14. Is the skin on your feet so dry that it cracks open?	No	60	45.5%	101	76.5%	161	61.0%	< 0.001* (26.76)
	Yes	72	54.5%	31	23.5%	103	39.0%	
15. Have you ever had an amputation?	No	124	93.9%	132	100.0%	256	97.0%	0.004* (8.25)
	Yes	8	6.1%	0	0.0%	8	3.0%	

Table 4. Respondents' Answers to Restless Leg Syndrome Questions

	Yes		No		Total	
	Count	%	Count	%	Count	%
Restless Leg Syndrome	91	34.5%	173	65.5%	264	100.0%
Are symptoms of RLS worse during the night?	51	56.0%	40	44.0%	91	100.0%
Are symptoms of RLS better with movement?	64	70.3%	27	29.7%	91	100.0%
Are symptoms of RLS worse with immobilization	48	52.7%	43	47.3%	91	100.0%
A desire to move the legs	3	3.3%	88	96.7%	91	100.0%

Table 5. Association between Restless Leg Syndrome, Peripheral Neuropathy, and Diabetes Mellitus

		Restless Leg Syndrome					
		Yes		No		Total	
		Count	%	Count	%	Count	%
Peripheral Neuropathy	Normal	80	33.8%	157	66.2%	237	100.0%
	Abnormal	11	40.7%	16	59.3%	27	100.0%
Diabetes Mellitus	No	42	31.8%	90	68.2%	132	100.0%
	Yes	49	37.1%	83	62.9%	132	100.0%

Diabetes Mellitus is a major health issue in the Arab region especially and the world in general. Peripheral neuropathy as a complication of diabetes is considered a burden on both the patients and society [18]. This study investigated the prevalence of Peripheral Diabetic Neuropathy and Restless Leg Syndrome among the Saudi population in Tabuk city. According to the findings, the prevalence was found to be 18.2%, which is considered low when compared to the other studies conducted in Saudi Arabia. A cross-nation study conducted among 1039 patients revealed that 65.3% of them had Diabetic Peripheral Neuropathy, which was considered very high compared to the global prevalence of 15% at that time [19, 20]. Moreover, another study was conducted among diabetic patients in Jeddah Governance, Saudi Arabia, and the prevalence of DPN was 19.9% [11]. A recent study was performed among Hospitalized Diabetic Patients in Riyadh, Saudi Arabia and they found that only 3.5% of them had DPN. It is noticed that the reported prevalence of DPN is decreasing throughout the years; this might be due to the increase in the awareness of patients about glycemic control, which is a crucial factor in delaying the rate of development of DPN [21]. However, this disparity in prevalence could be due to the difference in populations and the methods of data collection since some studies have used clinically based methods for the diagnosis, while others like this one have used questionnaire-based methods.

Compared with the gulf region, the prevalence of DPN in this study was lower than in the United Arab Emirates (39%) [22]. Various studies from different countries reported a wide range of DPN prevalence, from 61.3% in Egypt, to 14% in Turkey [23, 24]. This difference in prevalence is most probably due to many factors including different populations and sociodemographic, different prevalence of diabetes, and the difference in defining the criteria of DPN diagnosis. All of these differences highlight the importance of a multinational study that addresses the issue of DPN prevalence difference.

In the current study, 37.1% of diabetes mellitus patients were considered to have Restless Leg Syndrome. A previous study conducted among Koreans showed that the prevalence of Restless Leg Syndrome was 22%, which is considered low compared to this study. Other studies were conducted in Saudi Arabia, and the prevalence of Restless Leg Syndrome was only 5.2% in one study, which has been conducted among Saudi adults attending primary health care centers, and 42% in another study conducted among type 2 diabetes patients [25-27]. In contrast to this study, in which no significant association was found between peripheral neuropathy and Restless Leg Syndrome, a study performed by Merlino *et al.* confirmed that neuropathy is a risk factor for Restless Leg Syndrome [28]. The contradiction between the studies could be explained by the different methods of assessment.

Although 18.2% of the participants had DPN, only 1.5% said that their doctor told them that you have diabetic neuropathy. This might be because the doctors were not aware of the DPN or they have considered it as part of the regular progression and the natural history of diabetes and not as a complication, this might indicate a lack of awareness among doctors about DPN, which will require serious intervention to raise their awareness about this issue. One of the limitations of this study is that it did not investigate the presence of risk factors for DPN among the participants, risk factors such as BMI, poor glycemic control, and other comorbidities (dyslipidemia, peripheral vascular disease, hypertension, and chronic kidney disease), have been significantly associated with DPN [21]. Another limitation is that only a questionnaire-based assessment for DPN was made and was not combined with clinical assessment.

Conclusion

Diabetic Peripheral Neuropathy and Restless Leg Syndrome were common among patients with type 2 diabetes in Tabuk City, Saudi Arabia. However, no significant association was found between Restless Leg Syndrome neither diabetes nor Peripheral Neuropathy. More interventions ought to be planned and implemented to raise the awareness of the public and clinicians about the issue of Diabetic Peripheral Neuropathy.

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Conflict of interest: None

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Ethics statement: All the participants gave verbal consent before responding to the questionnaire, the institutional review board of the Faculty of Medicine, University of Tabuk, Saudi Arabia approved the research (Ref. READ, 0103, dated 22/7/220).

References

1. Hicks CW, Selvin E. Epidemiology of peripheral neuropathy and lower extremity disease in diabetes. *Curr Diab Rep.* 2019;19(10):86. DOI: DOI:10.1007/s11892-019-1212-8.
2. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. *Diabetes Care.* 2020;43(Suppl 1):S14-31. DOI: 10.2337/dc20-S002. PMID: 31862745.
3. Ebata-Kogure N, Nozawa K, Murakami A, Toyoda T. Clinical, and economic burdens experienced by patients with painful Diabetic Peripheral Neuropathy: an observational study using a Japanese claims database. *PLoS One.* 2017;12(10):e0187250. DOI:10.1371/journal.pone.0187250.
4. Selvarajah D, Kar D, Khunti K, Davies MJ, Scott AR, Walker J, et al. Diabetic peripheral neuropathy: advances in diagnosis and strategies for screening and early intervention. *Lancet Diabetes Endocrinol.* 2019 Dec;7(12):938-948. DOI: 10.1016/S2213-8587(19)30081-6.
5. Ugwu E, Adeleye O, Ezeani I. Predictors of lower extremity amputation in patients with diabetic foot ulcer: findings from MEDFUN, a multi-center observational study. *J Foot Ankle Res.* 2019;12(1):34. DOI: 10.1186/s13047-019-0345-y.
6. Dewanjee S, Das S, Das AK, Bhattacharjee N, Dihingia A, Dua TK, et al. Molecular mechanism of diabetic neuropathy and its pharmacotherapeutic targets. *Eur J Pharmacol.* 2018 Aug 15;833:472-523. DOI: 10.1016/j.ejphar.2018.06.034. Epub 2018 Jun 30. PMID: 29966615.
7. Hall GC, Morant SV, Carroll D, Gabriel ZL, McQuay HJ. An observational descriptive study of the epidemiology and treatment of neuropathic pain in a UK general population. *BMC Fam Pract.* 2013;14(1):28. DOI: 10.1186/1471-2296-14-28. PMID: 23442783; PMCID: PMC3599764.
8. Mirghani H. Restless leg syndrome among Sudanese patients with type 2 diabetes mellitus: a case-control study. *Cureus.* 2020;12(8):e9635. DOI: 10.7759/cureus.9635. PMID: 32923236; PMCID: PMC7480782.
9. Kalra S, Gupta A. Diabetic painful Neuropathy and restless leg syndrome in diabetes. *Diabetes Ther.* 2018;9(2):441-7. DOI: 10.1007/s13300-018-0376-6. Epub 2018 Feb 9. PMID: 29427229; PMCID: PMC6104281.

10. Simo N, Kuate-Tegueu C, Ngankou-Tchankeu S, Doumbe J, Maiga Y, Cesari M, et al. Correlates of diabetic polyneuropathy of the elderly in Sub-Saharan Africa. *PLoS One*. 2020;15(10):e0240602. DOI: 10.1371/journal.pone.0240602. PMID: 33119646; PMCID: PMC7595408.
11. Wang DD, Bakhotmah BA, Hu FB, Alzahrani HA. Prevalence and correlates of diabetic peripheral Neuropathy in a Saudi Arabic population: a cross-sectional study. *PLoS ONE*. 2014;9(9):e106935. DOI:10.1371/journal.pone.0106935.
12. Algeffari MA. Painful diabetic peripheral Neuropathy among Saudi diabetic patients is common but under-recognized: multicenter cross-sectional study at primary health care setting. *J Family Community Med*. 2018;25(1):43-7. DOI: 10.4103/jfcm.JFCM_145_16. PMID: 29386961; PMCID: PMC5774042.
13. Sendi RA, Mahrus AM, Saeed RM, Mohammed MA, Al-Dubai SA. Diabetic Peripheral Neuropathy among Saudi diabetic patients: a multicenter cross-sectional study at primary health care setting. *J Family Med Prim Care*. 2020;9(1):197-201. DOI: 10.4103/jfmfc.jfmfc_927_19.
14. Hoffman DL, Sadosky A, Alvir J. Cross-national burden of painful Diabetic Peripheral Neuropathy in Asia, Latin America, and the Middle East. *Pain Pract*. 2009;9(1):35-42. DOI: 10.1111/j.1533-2500.2008.00249.x. Epub 2008 Oct 27. PMID: 19019046.
15. Allen RP, Picchiatti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J. Restless leg syndrome diagnosis and epidemiology workshop at the national institutes of health; international restless leg syndrome study group. restless leg syndrome: diagnostic criteria, special considerations, and epidemiology. a report from the restless leg syndrome diagnosis and epidemiology workshop at the national institutes of health. *Sleep Med*. 2003;4(2):101-19. DOI: 10.1016/s1389-9457(03)00010-8. PMID: 14592341.
16. Zografou I, Iliadis F, Sambanis C, Didangelos T. Validation of Neuropad in the Assessment of Peripheral Diabetic Neuropathy in Patients with Diabetes Mellitus Versus the Michigan Neuropathy Screening Instrument, 10g Monofilament Application and Biothesiometer Measurement. *Curr Vasc Pharmacol*. 2020;18(5):517-522. DOI: 10.2174/1570161117666190723155324. PMID: 31340739.
17. Aktar Reyhanioglu D, Adiyaman SC, Bektaş M, Bulut O, Özgen Saydam B, Bayraktar F, Kara B. Validity and reliability of the Turkish version of the Michigan Neuropathy Screening Instrument. *Turk J Med Sci*. 2020 Jun 23;50(4):789-797. DOI: 10.3906/sag-1906-63. PMID: 32178509; PMCID: PMC7379468.
18. Xiong Q, Lu B, Ye H, Wu X, Zhang T, Li Y. The diagnostic value of Neuropathy symptom and change score, Neuropathy impairment score, and Michigan Neuropathy screening instrument for diabetic peripheral neuropathy. *Eur Neurol*. 2015;74(5-6):323-7. DOI: 10.1159/000441449. Epub 2015 Dec 19. PMID: 26684759.
19. Jaiswal M, Divers J, Dabelea D, Isom S, Bell RA, Martin CL, et al. Prevalence of and risk factors for diabetic peripheral Neuropathy in youth with type 1 and type 2 diabetes: search for diabetes in youth study. *Diabetes Care*. 2017;40(9):1226-32. DOI: 10.2337/dc17-0179. Epub 2017 Jul 3. PMID: 28674076; PMCID: PMC5566278.
20. Halawa MR, Karawagh A, Zeidan A, Mahmoud AE, Sakr M, Hegazy A. Prevalence of painful Diabetic Peripheral Neuropathy among patients suffering from diabetes mellitus in Saudi Arabia. *Curr Med Res Opin*. 2010;26(2):337-43. DOI: 10.1185/03007990903471940. PMID: 19968592.
21. Aleidan FAS, Ahmad BA, Alotaibi FA, Aleesa DH, Alhefdhi NA, Badri M, et al. Prevalence and risk factors for diabetic peripheral Neuropathy among Saudi hospitalized diabetic patients: a nested case-control study. *Int J Gen Med*. 2020; 13:881-9. DOI: 10.2147/IJGM.S273807. PMID: 33116780; PMCID: PMC7584505.
22. Control T.D, Group C.D. R. The effect of intensive diabetes therapy on the development and progression of neuropathy. The diabetes control and complications trial research group. *Ann Intern Med*. 1995;122(8):561-8. DOI: 10.7326/0003-4819-122-8-199504150-00001. PMID: 7887548.
23. Al-Maskari F, El-Sadig M. Prevalence of risk factors for diabetic foot complications. *BMC Fam Pract*. 2007;8(1):59. DOI: 10.1186/1471-2296-8-59. PMID: 17927826; PMCID: PMC2174471.
24. Erbas T, Ertas M, Yucel A, Keskinaslan A, Senocak M. TURNEP Study Group. Prevalence of peripheral neuropathy and painful peripheral neuropathy in Turkish diabetic patients. *J Clin Neurophysiol*. 2011;28(1):51-5. DOI: 10.1097/WNP.0b013e3182051334. PMID: 21221008.
25. Cho YW, Na GY, Lim JG, Kim SH, Kim HS, Earley CJ, et al. Prevalence and clinical characteristics of Restless Leg Syndrome in Diabetic Peripheral Neuropathy: comparison with chronic osteoarthritis. *Sleep Med*. 2013;14(12):1387-92.
26. BaHammam A, Al-Shahrani K, Al-Zahrani S, Al-Shammari A, Al-Amri N, Sharif M. The prevalence of Restless Leg Syndrome in adult Saudis attending primary health care. *Gen Hosp Psychiatry*. 2011;33(2):102-6. DOI: 10.1016/j.genhosppsy.2011.01.005. Epub 2011 Feb 12. Erratum in: *Gen Hosp Psychiatry*. 2011 Jul-Aug;33(4):410. Al-sharani, Khalid [corrected to Al-shahrani, Khalid]; Al-amri, Nojowd [corrected to Al-amri, Nojoud]. PMID: 21596202.
27. Mirghani HO, Amirthalingam P, Mohammed OS. The effect of restless leg syndrome on diabetes control among type-2 diabetic patients in the Northwest region of Saudi Arabia. *J Diabetol*. 2016;7(3):3. <http://www.journalofdiabetology.org>. Accessed on Saturday, December 12, 2020, IP: 46.152.118.221]
28. Merlino G, Fratticci L, Valente M, Del Giudice A, Noacco C, Dolso P, et al. Association of restless leg syndrome in type 2 diabetes: a case-control study. *Sleep*. 2007;30(7):866-71. DOI: 10.1093/sleep/30.7.866. PMID: 17682657; PMCID: PMC1978361.