Original Article

Prevalence and concomitance of diabetic peripheral sensory neuropathy and lower limb peripheral arterial disease in type II diabetics and its correlation with obesity

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Abstract

Introduction: Among type 2 diabetics (T2D), macrovascular complication lower limb Peripheral Arterial Disease (PAD) and microvascular complication Diabetic Peripheral Sensory Neuropathy (DPSN) have scarcely studied concordance and their association with obesity. Qualitative and general body fat parameters give a complete picture of obesity. We studied the association of vibration perception threshold (VPT)-based DSPN and ankle brachial pressure index (ABPI))-based PAD, and the effect of obesity on them, in T2Ds. **Methods:** A cross-sectional study was done on 152 under-treatment T2Ds. Bio-esthesiometer-based VPT from the sole of each foot and VersaDop-based ABPI from all limbs were assessed. Prevalence of DSPN (VPT ≥25) and PAD (ABPI ≤0.9) was measured and compared for concomitance. The odds ratio was used for testing association and multiple linear regressions were accomplished for predictors of VPT and ABPI taking *P* value < 0.05 as statistically significant. **Results:** T2Ds had a mean age of 53 years, a mean duration of 67 months, and 48% glycemic control. The prevalence of abnormal VPT and ABPI was 64% and 23%, respectively. VPT-based subgroups do not defer significantly from ABPI and vice versa. Obesity was associated with only abnormal ABPI (visceral > general). Odd's ratio for neuropathy with vasculopathy was insignificant while VPT and ABPI had differences in significant predictors. **Conclusion:** T2Ds having 64% neuropathy and 23% vasculopathy had one-third concomitance but lack of association and different predictors for each. Vasculopathy not neuropathy was associated with obesity; visceral more than general; suggesting scope for its rectification. It suggests different progression of these complications, despite some cross-talk between them.

Keywords: Ankle-brachial index, diabetic neuropathy, diabetic vascular disease, obesity, peripheral artery disease, type 2 diabetes mellitus

Introduction

Type II diabetics (T2Ds) suffer from many aftermaths as vascular complications. Diabetic Peripheral Sensory Neuropathy (DPSN) is the most common microvascular complication with a prevalence

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of 38% in our population.[1] Similarly, lower limb peripheral arterial disease (PAD) is a common macrovascular complication as reported previously with a 46% prevalence.[2] DPN can be measured by Vibration Perception Threshold (VPT)[3] and PAD can be measured by Ankle-Brachial Pressure Index (ABPI).[4] Both VPT and ABPI offer qualitative and quantitative inferences to screen T2Ds with vascular complications. The crosstalk between microvascular complications like DPN and macrovascular complications like PAD[5] has an unknown status. It will be interesting to know the exact relationship between the two, in chronic T2Ds. With this background, we set out to study the prevalence, association, and concordance of DPN and PAD in a sample population of T2Ds by a cross-sectional study.

Materials and Methods

Study design and setup

A cross-sectional field study was conducted in a sample population of under-treatment T2Ds, attending the outdoor patient department of the Medicine department of a tertiary care hospital of a government medical college. Prior approval for taken from the IRB committee of our institution, and it was approved by the IRB board with EC approval number: 1134/2022, Department number 92/2022 dated 28/06/2022. For our current study setup (population of the city with type 2 Diabetes prevalence of 9.6%), we came to find the adequate sample size of 134 patients, using Raosoft (free online sample size calculator software of USA), getting 95% confidence interval and 5% error margin. Data was collected from April 2023 to October 2023, and further analysis was carried out.

Criteria for selection of participants

We included under-treatment T2Ds (at least 6 months of regular treatment), of age 40-60 years, of either gender, not addicted to alcohol or any form of smoking, and having recent glycemic control report. Of potential participants, we excluded T2Ds 1) with concomitant neuropathy and/or vasculopathy (other than due to diabetes), 2) with Diabetic foot/amputated limb 3) having previous neurological or cardiovascular intervention and patients taking neurotoxic drugs (like AKT), insulin, vasodilators and/or steroids. Post-assessment, 12 participants were excluded from potential candidates of study, due to ABPI being >1.4 (suggestive of atherosclerotic changes of vessels).

Initial assessment and risk factor assessment

After general data collection and medical history evaluation, neuropathy and vasculopathy risk factor assessment was done with pre-validated questionnaires. The assessment included personal demographic and epidemiological data, diabetes history, drug (oral hypoglycemics and concomitant) history, addiction and other personal history and relevant laboratory investigations.

Dichotomous outcome was noted for the following risk factors, for each participant; hypertension, hyperlipidemia, cardiovascular diseases like valvular heart disease, family history of neuropathy and/or vasculopathy, asymptomatic neuropathy, male gender, poor glycemic control, and physical inactivity.

Vibration Perception Threshold (VPT) measurement

VPT measurement is as per our previous work.[1] Bio-esthesiometer, calibrated and validated by the company Diabetic Food Care, Chennai, India was used. Vibration perception was measured in each participant's pressure points of each foot, on the following sites; great toe, ball of great toe, and heel. The vibration was increased from 0 to 50 Hz until the threshold was achieved. The average of the results of pressure points was considered as a result of the VPT assessment.

Ankle Brachial Pressure Index (ABPI) measurement

ABPI measurement is as per our previous work.[2] Instrument VersaDop, vascular Doppler, working on the principle of photo-plethysmography was used for ABPI measurement. The cuff was applied on the following application sites; arm: aid-arm (bilaterally), Ankle: above level of malleoli (bilaterally). For the manual method, a doppler was applied to sites of the brachial and dorsalis pedis artery. After inflating the cuff 20–30 mm Hg above the last heard sound, pressure was slowly released. The first heart sound heard was recorded as the systolic pressure at that site. The order of measurement of the four sites was followed according of AHA guidelines.

Obesity parameters

A digital and portable non-invasive Omron Karada Scan (Omron Karada Scan HBF-375 Body Fat Analyzer, Omron Health Care Pvt Ltd. China), working on the principle of tetra polar BIA, was used that passes an electric current of 500 μA at 5 kHz frequency to scan the whole body.[6] It derived measures of body composition like total body fat, visceral fat, and BMI, and also measured the waist-to-hip ratio of each participant.

Defining the norms

- Glycemic control[7]:
  1. FPG ≥126 mg% fasting is defined as no caloric intake for at least 8 hr. or
  2. 2 hr PG ≥200 mg% during or
  3. HbA1c ≥6.5% or
  4. In a patient with classic symptoms of hyperglycemia or hyperglycaemic crisis, and random plasma glucose ≥200 mg%
- ABPI grading of PAD[8]:
  1. Normal: 0.9–1.4
  2. High: ≥ 1.4, typically indicative of vessel stiffening
  3. Low: ≤ 0.9, narrowing of vessels
  4. Nonmeasurable: unable to occlude blood vessels at 300 mm Hg of pressure application.
- VPT grading of DPSN[9]:
  1. Normal: <15 V
  2. Mild neuropathy: 15–20 V
  3. Moderate neuropathy: 20–25 V
  4. Severe neuropathy: >25 V

- Cut-off for ABPI-based PAD:
  1. ≤ 0.9 = Abnormal
  2. 0.9–1.4 = Normal
- Cut-off for VPT-based DPSN:
  1. <15 V = Normal
  2. ≥15 V = Abnormal

Statistical analysis

The collected data was entered and sorted on an Excel spreadsheet and used Graphpad-InStat software for analysis of data. Data were expressed as the mean ± standard deviation for continuous data and as a number or percentage for categorical data. A normality test was run to check the distribution of data and depending on it, parametric or nonparametric statistical tests were applied. Groups were compared by *t*-test, Mann–Whitney U test or ANOVA for continuous data, and Chi-square or Normality test for categorical data. For the contingency table of exposure to the outcome, odds ratios were calculated by a 95% confidence interval. Multiple linear regressions were performed to find significant predictors of VPT or ABPI from independent parameters. For all tests, the *P* value cut-off was 0.05 to take statistical significance.

Ethical aspects

After preliminary presentation and approval from the Department of Physiology, the proposal was scrutinized by the institutional Scientific Review Committee and Institutional Ethics Committee and approval was given as EC approval no. 1134/2022, Department no 92/2022, dated 28/06/2022. Later it was prospectively registered in the Controlled Trial Registry of India (CTRI), numbered CTRI/2017/01/007692. In-principal approval was taken from department of Physiology to make use of necessary instruments for the study and from the Department of Medicine, for the recruitment of study participants. Written informed consent form in vernacular language was sought from each potential participant, before assessment. he procedures in the study follow the guidelines laid down in the Declaration of Helsinki (2013).

Results

The mean age and duration of diabetes were 53 years and 67 months, with equal males and females having predominantly urban domicile. Two-thirds had hypertension, half had glycaemic control and SRPA, and one-third had hyperlipidemia. The mean ABPI was 1.2 with a one-fourth prevalence of ABPI ≤ 0.9. The mean VPT was 20 with one-fourth prevalence of VPT ≥25. [Table 1]

On stratifying groups based on ABPI (cut-off = 0.9) values, VPT did not significantly differ between groups. On stratifying groups based on VPT (cut-off = 15), there is an insignificant difference in ABPI values. [Table 2] ABPI values did not significantly differ in 3 subgroups based on VPT value-based grades. [Table 3] Qualitative ABPI and VPT did not significantly differ in subgroups based on BMI stratification (cut-off = 22.9). There was a significant difference in ABPI qualitative distribution in groups based on visceral fat, but it was not evident for VPT distribution. [Table 4]

Gender and total body fat were predictors for both VPT and ABPI. Age, hypertension, and SRPA were other predictors for VPT while hyperlipidemia and BMI were other predictors for ABPI. [Table 5]

Taking VPT cut-off 25 and ABPI cut-off 0.9, there were 15 T2Ds with both DSPN, and PAD; 24 with only DSPN; 20 with only PAD, and 93 had neither DSPN nor PAD [Figure 1].

Discussion

Among chronic T2Ds, VPT-based DPSN and ABPI-based PAD were evaluated, keeping in focus the cross-talk between two complications affecting vessels of a different calibre. Diabetic neuropathy is the most common form of neuropathy worldwide,[9] and one of the serious and crippling microvascular complications, which needs prompt treatment, extensive care, and preventive strategies. Based on reviews of major studies of diabetic neuropathy in the last four decades, the global prevalence of clinical DSPN varies between 20% and 30% for type 2 diabetes, with significant variability between studies and geographical regions.[10] With VPT cut-off 15 and 25, our study revealed a point prevalence of 64.47% and 25.65%, respectively, of DSPN in known T2Ds. In another study[1] done in similar T2Ds using similar eligibility criteria, the prevalence of abnormal VPT (cut-off >25) reported is 38%. Such high prevalence in our population can be due to the private setup, poor glycaemic control, high mean age, high prevalence of obesity, and high mean disease duration. Such changes are due to underlying nerve barrier disruption, inflammation advanced glycation end products,

Table 1: Distribution of study parameters in study population; male, female and total

Variables	Male (79)	Female (73)	*P*	Total (152)
Age, years	54.6±5.6	51.1±6.6	***<0.001***	53.2±6.1
Domicile (rural/urban)	61/18	57/16	0.90	118/24
Disease duration, months	79.6±56	59.5±45.2	***0.016***	66.8±51.1
Glycemic control, number	40	33	0.61	73
Hypertension, number	52	52	0.59	104
Hyperlipidemia, number	26	23	0.99	49
SRPA, number	41	31	0.32	72
ABPI	1.2±0.12	1.2±0.12	0.84	1.2±0.14
ABPI <0.9, number	20	15		35
VPT (mean±SD)	20.1±9.6	20.1±10.9	0.99	20.1±10.1
VPT, number				
• Normal	29	25		54
• Mild	19	23	χ^2=1.54, *P*-0.67	42
• Moderate	10	6		16
• Severe	20	19		39
VPT ≥25, number	20/58	19/54	0.96	39/112

dyslipidemia, and many other mechanisms.[11] Most participants had mild-to-moderate DSPN without symptoms of same that calls for prompt treatment, early diagnosis, and better health literacy among type 2 diabetics. It can delay the disease progression to prevent dreadful aftermaths like neuropathic pain, ulceration, and ultimately spontaneous amputations.[12] All study participants were asymptomatic with respect to any neurological symptoms or signs, and therefore prevalence of ~64%, suggests potential possible early detection of manifest diabetic neuropathy. Another notable finding in our study was a significant increase in patients having abnormal VPT, concomitant with increased duration of diabetes (6.5 years and more); in line with the literature.[13] PAD is one of the most debilitating chronic complications of the diabetic spectrum, being either asymptomatic or intermittent claudication as the typical presenting symptom. The prevalence of PAD in diabetes is approximately 42%, globally.[13] ABPI is a non-invasive, symptom-independent tool to estimate the effect of PAD. A previous study from our population,[2] reveals abnormal ABPI in around 35% of the total sample population. Our study estimates a prevalence of abnormal ABPI of about 23%, owing to a relatively narrower range of age, for the selection of participants. Such low prevalence of abnormal ABPI can be due to age, use of hypolipidemics, use of anti-hypertensives, exclusion of smokers, and prevalent self-reported physical activity.[14]

DSPN - a microvascular and PAD a macrovascular diabetic complication have different pathways but not without a cross-talk. DSPN was more prevalent than PAD indicating more prevalence of microangiopathy than macroangiopathy in type 2 diabetics, in accordance with literature[15,16] Both these complications have in common interplay of metabolic dysregulation, inflammation, oxidative stress, and endothelial dysfunction as basic pathophysiology.[16] But there are differences in pathways, disease course, and risk factors also. So, we associated VPT-based DSPN with ABPI-based PAD both quantitatively and qualitatively among T2Ds. DSPN was not significantly associated with prevalent PAD and vice versa. Among those having PAD or severe DSPN, one-third had both concomitant; while the rest one-third had either PAD or DSPN. ABPI was not associated with the severity of VPT grades and there was an insignificant odds ratio for PAD with DSPN. Both have different predictors also except body fat and gender which are known in the literature.[17-19] This lack of association between the two can be due to: 1) the different nature of blood vessels in which complications are being studied[16]; 2) treated rather than newly diagnosed diabetics, 3) the difference in methods of assessment of DSPN and PAD, 4) high mean age and mean duration[20] 5) poor glycaemic control and lack of availability of HbA1c based glycaemic variability that is better than HbA1c *per se*[21]; 6) difference in pathway for progression of both complications[16] 7)

Table 2: Quantitative & Qualitative comparison of ABPI distribution in sub-groups stratified by VPT cut-off 15 and VPT distributions in sub-groups stratified by ABPI cut-off 0.9

	ABPI <0.9	ABPI ≥0.9	*P*
VPT (mean±SD)	19.8±10.8	20.2±10.1	0.84
	VPT >15	**VPT ≤15**	***P***
ABPI (mean±SD)	1.15±0.23	1.12±0.23	0.45
ABPI <0.9*, number	15	20	χ^2=1.06,
ABPI ≥0.9, number	38	76	*P*-0.30

*Odds risk=1.5 (95% C.I. -0.69, 3.25)

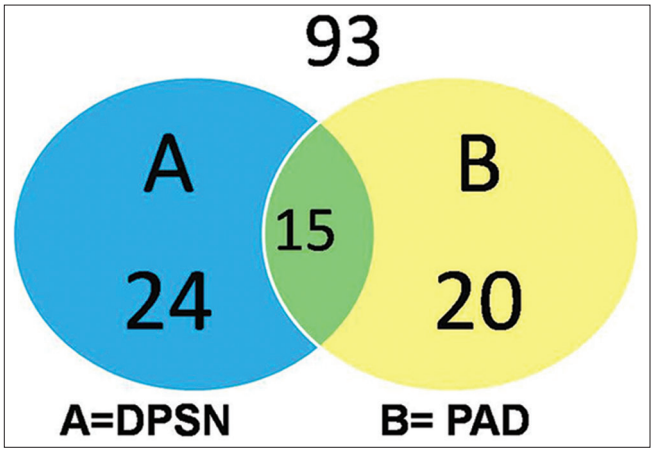

Figure 1: Prevalence and concomitance of DSPN and CAD in study participants

Table 3: Comparison of ABPI parameters among 3 subgroups stratified by DPSN grading

Parameters	Group 1 (VPT <15)	Group 2 (VPT 15-25)	Group 3 (VPT >25)	*P*	*Post-hoc* test
AP (mean±SD)	161.44±56.02	171.06±29.91	170.07±36.25	0.97	NA
BP (mean±SD)	143.88±21.60	143.23±21.75	142.50±30.46	0.96	NA
ABPI (mean±SD)	1.09±0.23	1.17±0.20	1.05±0.31	0.09	NA

Table 4: Comparison of the qualitative distribution of ABPI (cut-off 0.9) and VPT (cut-off 15) in subgroups stratified by BMI, visceral, and waist-to-hip ratio

	BMI ≥22.9	BMI <22.9	Statistic	VF ≥10	VF <10	Statistic	WHR High	WHR Normal	Statistic
ABPI abnormal	103	13	OR=0.72, 95% CI	99	17	OR=2.73, 95% CI,	90	15	OR=4.06, 95% CI
ABPI Normal	33	3	(0.19,2.68), *P*=0.63	32	15	(1.23,6.08), ***P=0.014***	31	21	(1.87,8.85), ***P=<0.001***
VPT abnormal	86	12	OR=0.57, 95% CI	83	15	OR=0.69, 95% CI,	75	23	OR=1.55, 95% CI
VPT normal	50	4	(0.18,1.87), *P*=0.35	48	6	(0.25,1.90), *P*=0.47	40	19	(0.75,3.18), *P*=0.23

Table 5: Predictors of ABPI or VPT by multiple linear regressions

Predictors (*X*)	*Y*1=VPT		*Y*2=ABPI	
	β	*P*	β	*P*
Age	0.18	***0.018***	0.03	0.69
Sex	−0.29	***<0.001***	−0.16	***0.04***
Glycemic control	0.02	0.79	0.07	0.32
Hypertension	0.21	***0.021***	0.10	0.23
Hyperlipidemia	−0.12	0.14	−0.45	***<0.001***
SRPA	0.26	***<0.001***	−0.05	0.53
WHR	0.37	***<0.001***	−0.11	0.15
Total Body Fat	−0.39	***<0.001***	−0.60	***<0.001***
Visceral Fat	0.25	0.10	−0.16	0.26
BMI	−0.05	0.72	0.57	***<0.001***

cut-offs of VPT and ABPI used that affect disease classification 8) varying prevalence of both complications at the onset of disease that cannot be ascertained by cross-sectional nature of study[22] 9) subjective nature of VPT against objective nature of ABPI assessment, 10) Asian ethnicity,[23] 11) presence of other confounders that affects both complications differently. This lack of total agreement between the prevalence of these two also hints at and reiterates the use of both together for better monitoring of disease progression and suggests intervention for the same.

Obesity is known to be associated with vascular complications in diabetes as evidenced by a recent large multi-ancestry genome-wide study.[24] We found a lack of association between obesity and VPT indicating a lack of prevalent association between body adiposity and microangiopathy in chronic diabetics with lack of glycaemic control. This is in contrast to literature citing obesity as a metabolic driver for neuropathy.[25] Contrastingly, ABPI was associated with obesity, visceral more than general, in our diabetics, in line with previous molecular evidence cited[26] but in the context of our chronic diabetics who are far from the glycaemic target. The association of obesity with macro, not microvascular complication, is in line with a current study[27] revealing that bariatric surgery in people with obesity can lead to a reduction in the incidence of macrovascular complications with the impact of bariatric surgery on microvascular complications staying less clear. Irrespective of its association with complications of diabetes, obesity especially central must be controlled for better disease control especially in light of poor glycaemic control in our diabetics.

Even the predictors were not the same for VPT and ABPI in our diabetics. Gender and total body fat were significant predictors for both these complications in line with previous works[1,2] on our population but done on different sets of diabetics. HbA1c value was not a significant predictor of any of the two possibly owing to lack of HbA1c control in most diabetics. Visceral fat was alike an insignificant predictor of any of the two outcomes indicating it to be not a predictor despite its association with both complications. Age, prevalent hypertension, physical activity, and waist-to-hip ratio were exclusive predictors of VPT; while hyperlipidemia and BMI were exclusive predictors of ABPI. This differential pattern of predictors further ascertains the difference between DSPN and PAD in diabetics.

Lack of co-existence, lack of association, different prevalence, and non-overlap of predictors were found between neuropathy and vasculopathy in a sample population of our diabetics with high HbA1c and mean high duration of disease. A global study showed that both the prevalence and three-year incidence of vascular complications were high in type 2 diabetics with relatively short duration, highlighting the need for early risk-factor modification.[28] Similarly, the lack of HbA1c in most T2Ds gives a false glycaemic status that is used more than the gold standard in the Indian context and can give false values of disease control. Post-COVID, the diabetic situation has gotten even worse[29] as reported recently. In diabetes microvascular complication like proteinuria is monitored but retinopathy and neuropathy are not used optimally. Similarly, macrovascular complications are not used for screening in the Indian context, and with the fact that it can be present in the absence of microvascular complications as seen in our study.

Diabetes has a threatening future prediction for India with anticipation of a heavy load on health are system.[30] Family physicians working at the primary care level will be the backbone of diabetes, better to be said as diabesity. Our study suggests early diagnosis of diabetes, optimum screening for both micro and macrovascular complications, and better glycaemic control as per HbA1c that is lacking in diabetics even at private setup. It hints use of screening for vasculopathy, neuropathy, and visceral obesity at the family physician level. It also calls for a study on newly diagnosed diabetics to study the prevalence of these complications and to monitor how they progress to further clarify the cross-talk in question.

Conclusion

Type 2 Diabetics, with poor glycemic control, 64% prevalent peripheral sensory neuropathy, and 23% prevalent lower limb vasculopathy, had their one-third concomitance but with lack of association and difference of predictors for each. Both complications are associated with obesity; visceral more than general; suggesting scope for rectification of same. It suggests different progression of these microvascular and macrovascular complications, despite of cross-talk between them.

Data availability

The authors of this manuscript are willing to share the data supporting the results of this manuscript upon request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Solanki J, Doshi R, Virani N, Sheth N, Dhamecha J, Shah C. Prevalence and correlates of vibration perception threshold based diabetic peripheral neuropathy in Gujarati urban population: A cross sectional study. J Fam Med Prim Care 2022;11:7055-9.
2. Solanki J, Makwana A, Mehta H, Gokhale P, Shah C. A study of prevalence and association of risk factors for diabetic vasculopathy in an urban area of Gujarat. J Fam Med Prim Care 2013;2:360-4.
3. Silas A, Kavitha KV, Tiwari S, Unnikrishnan AG. Diabetic Peripheral Neuropathy in India and the United States: Clinical Insights from a Comparative Review. Chronic Diabetes Res Pract 2024;3:33-41.
4. Poredos P, Stanek A, Catalano M, Boc V. Ankle-brachial index: Diagnostic tool of peripheral arterial disease and predictor of cardiovascular risk—An update of current knowledge. Angiology 2024:00033197241226512.
5. Climie RE, van Sloten TT, Bruno RM, Taddei S, Empana JP, Stehouwer CD, *et al.* Macrovasculature and microvasculature at the crossroads between type 2 diabetes mellitus and hypertension. Hypertens 2019;73:1138-49.
6. Omron Instruction Manual. Full Body Sensor Body Composition Monitor and Scale Model HBF-510 2008 China Omron Healthcare.
7. ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, *et al.* 6. Glycemic targets: Standards of care in diabetes—2023. Diabetes Care 2023;46:S97-110.
8. Weragoda J, Seneviratne R, Weerasinghe MC, Wijeyaratne SM. ABPI against colour duplex scan: A screening tool for detection of peripheral arterial disease in low resource setting approach to validation. Int J Vasc Med 2016:2016:1390475.
9. Papachristou S, Pafili K, Trypsianis G, Papazoglou D, Vadikolias K, Papanas N. Skin advanced glycation end products among subjects with type 2 diabetes mellitus with or without distal sensorimotor polyneuropathy. J Diabetes Res 2021;2021:6045677.
10. Hansen CS, Määttä LL, Andersen ST, Charles MH. The epidemiology of diabetic neuropathy. In Diabetic Neuropathy: Advances in Pathophysiology and Clinical Management. Cham: Springer International Publishing; 2023. p. 5-36
11. Galiero R, Caturano A, Vetrano E, Beccia D, Brin C, Alfano M, *et al.* Peripheral neuropathy in diabetes mellitus: Pathogenetic mechanisms and diagnostic options. Int J Mol Sci 2023;24:3554.
12. Quiroz-Aldave J, Durand-Vásquez M, Gamarra-Osorio E, Suárez-Rojas J, Roseboom PJ, Alcalá-Mendoza R, *et al.* Diabetic neuropathy: Past, present, and future. Caspian J Intern Med 2023;14:153.
13. Azhar A, Basheer M, Abdelgawad MS, Roshdi H, Kamel MF. Prevalence of peripheral arterial disease in diabetic foot ulcer patients and its impact in limb salvage. Int J Low Extrem Wounds 2023;22:518-23.
14. Mandaglio-Collados D, Marín F, Rivera-Caravaca JM. Peripheral artery disease: Update on etiology, pathophysiology, diagnosis and treatment. Med Clín 2023;161:344-50.
15. Mather KJ, Bebu I, Baker C, Cohen RM, Crandall JP, DeSouza C, *et al.* Prevalence of microvascular and macrovascular disease in the Glycemia Reduction Approaches in Diabetes-A Comparative Effectiveness (GRADE) Study cohort. Diabetes Res Clin Pract 2020;165:108235.
16. Zakir M, Ahuja N, Surksha MA, Sachdev R, Kalariya Y, Nasir M, *et al.* Cardiovascular complications of diabetes: From microvascular to macrovascular pathways. Cureus 2023;15:e45835.
17. Park HS, Cho Y, Seo DH, Ahn SH, Hong S, Suh YJ, *et al.* Impact of diabetes distress on glycemic control and diabetic complications in type 2 diabetes mellitus. Sci Rep 2024;14:5568.
18. Lempesis IG, Varrias D, Sagris M, Attaran RR, Altin ES, Bakoyiannis C, *et al.* Obesity and peripheral artery disease: Current evidence and controversies. Curr Obes Rep 2023;12:264-79.
19. Chavan D, Lomte N, Bhattacharya M, Singh A, Sonavale R. Microvascular and macrovascular complications in non-obese/overweight and obese/overweight type 2 diabetes mellitus. Indian J Med Sci 2023;75:156-60.
20. Meir J, Huang L, Mahmood S, Whiteson H, Cohen S, Aronow WS. The vascular complications of diabetes: A review of their management, pathogenesis, and prevention. Expert Rev Endocrinol Metab 2024;19:11-20.
21. Sartore G, Ragazzi E, Caprino R, Lapolla A. Long-term HbA1c variability and macro-/micro-vascular complications in type 2 diabetes mellitus: A meta-analysis update. Acta Diabetol 2023;60:721-38.
22. Genç S, Evren B, Çankaya C, Tecellioğlu M, Bozbay A, Yavuz AÖ, *et al.* Vascular complications and associated comorbidities in newly diagnosed pre-diabetes: Is it the tip of the iceberg? European Rev Med Pharmacol Sci 2023;27:7557-68.
23. Hassan S, Gujral UP, Quarells RC, Rhodes EC, Shah MK, Obi J, *et al.* Disparities in diabetes prevalence and management by race and ethnicity in the USA: Defining a path forward. Lancet Diabetes Endocrinol 2023;11:509-24.
24. Suzuki K, Hatzikotoulas K, Southam L, Taylor HJ, Yin X, Lorenz KM, *et al.* Multi-ancestry genome-wide study in>2.5 million individuals reveals heterogeneity in mechanistic pathways of type 2 diabetes and complications. medRxiv 2023:2023.03.31.23287839. doi: 10.1101/2023.03.31.23287839.
25. Zhu J, Hu Z, Luo Y, Liu Y, Luo W, Du X, *et al.* Diabetic peripheral neuropathy: Pathogenetic mechanisms and treatment. Front Endocrinol 2024;14:1265372.
26. Jia G, Bai H, Mather B, Hill MA, Jia G, Sowers JR. Diabetic vasculopathy: Molecular mechanisms and clinical insights. Int J Mol Sci 2024;25:804.
27. Bashir B, Iqbal Z, Adam S, Ferdousi M, Chick W, Hussein HA, *et al.* Microvascular complications of obesity and diabetes—Role of bariatric surgery. Obes Rev 2023;24:e13602.
28. Arnold SV, Khunti K, Tang F, Chen H, Cid-Ruzafa J, Cooper A, *et al.* Incidence rates and predictors of microvascular and macrovascular complications in patients with type 2 diabetes: Results from the longitudinal global discover study. Am Heart J 2022;243:232-9.
29. Vashist K, Frediani JK, Weber MB, Ali MK, Narayan KV, Patel SA. Changes in diabetes care and management practices during the COVID-19 pandemic. Res Sq 2024:rs-3.rs-3849240. doi: 10.21203/rs. 3.rs-3849240/v1.
30. Kumar A, Gangwar R, Ahmad Zargar A, Kumar R, Sharma A. Prevalence of diabetes in India: A review of IDF diabetes atlas 10th edition. Curr Diabetes Rev 2024;20:105-14.