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Original Research Article

Screening for autonomic neuropathy using validated non-invasive scale among diabetes patients treated in the selected primary health centres of Puducherry, India: an operational research

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ABSTRACT

Background: Diabetes autonomic neuropathy (DAN) is a complication of diabetes which has direct implications on the mortality of diabetes patients. American Diabetes Association (ADA-2017) guidelines recommend early recognition and treatment of DAN. In this regard, we conducted a study among diabetic patients treated in the selected PHCs of Puducherry to determine the proportion with DAN and to assess the factors associated with DAN.
Methods: A cross-sectional analytical study was conducted among diabetics and information on socio-demographic details, morbidity and behavioural risk factors were elicited using semi-structured interview schedule. The COMPASS-31 questionnaire was administered to assess the autonomic neuropathy symptoms. The data was captured using EpiCollect mobile app and analysed using Stata 12.0 software. The proportion of DAN was expressed as percentage with 95% confidence interval. The association between independent factors and DAN was assessed using multivariate generalized linear models. The prevalence ratio with 95% CI was used to express the strength of association.
Results: Of the total 303 individuals with diabetes, 32 {10.6% (95% CI: 7.3%-14.6%)} were screened positive for autonomic neuropathy using COMPASS-31 scale. The number of individuals with diabetes who needed to be screened (NNS) for finding one with autonomic neuropathy was 10 (303/32).
Conclusions: One in ten individuals with diabetes was screened positive for autonomic neuropathy. With good yield, there is need for including autonomic neuropathy screening as a component in the comprehensive care provided to diabetes patients in the primary health centres.

Keywords: Diabetes, Autonomic neuropathy, Primary health centre, Non-communicable diseases

INTRODUCTION

Diabetes is an emerging pandemic with estimated 415 million individuals suffering from this disease. The International Diabetes Federation estimated that 69.2 million people had diabetes during the year 2015.[1] In India, diabetes with prevalence of 8.7% and need for extended years of care add on to the agony of the healthcare system.[1] Early diagnosis of diabetes and appropriate management are the mainstay of avoiding the untoward life threatening complications in diabetic patients. Appropriate management of the diabetes includes person centred individualized treatment, ensuring medication adherence and screening for early diagnosis of complications.[2]

Diabetic autonomic neuropathy (DAN) is one such complication of diabetes which involves adrenergic,

cholinergic, dopaminergic, autonomic fibers as well as peptidergic neurons. The sequela of DAN includes tachycardia, orthostatic hypotension, gastroparesis, bladder dysfunction and erectile dysfunction.[3-7] The Cardiac autonomic neuropathy can lead to heart block and mortality.[8-10] In this regard, American Diabetes Association (ADA-2017) guidelines recommend early recognition and treatment of DAN in order to improve symptoms, reduce sequelae, and improve quality of life.[11] Also, knowing the burden of autonomic neuropathy will help to advocate for including the same in routine screening for complications.

Due to non-availability of facilities for nerve conduction tests and heart rate monitoring devices there is no scope for screening of DAN at the primary health care setting where most of the patients are treated.[12,13]

Hence, the symptom based validated scale like Composite Autonomic Symptom Score-31 (COMPASS-31) can be tried as a feasible tool for screening.[14] But there are no published literature from India, on screening for DAN among diabetes patients using feasible scales like COMPASS-31. Hence, we planned the current study to assess the burden of autonomic neuropathy among individuals treated for diabetes in the primary care setting. Also we explored the factors associated with screening positive for autonomic neuropathy using COMPASS-31 scale.

METHODS

Study design and setting

A community based cross-sectional analytical study was carried out in the service area of selected PHCs (Kirumampakkam and Thavalakuppam) of Puducherry, South India.

Puducherry is a Union Territory located in Southern part of India, comprising of four districts namely Puducherry, Karaikal, Mahe and Yanam. As per 2011 Census, Puducherry district has a population of 0.9 million. Prevalence of type II diabetes ranges from 5.8% to 8.97% in Puducherry.[15-18] Apart from public health facilities, diabetes care is provided in the private sector as well. The study was carried out in two PHCs located at Kirumampakkam and Thavalakuppam areas of Puducherry. The PHCs functions round the clock and cater to approximately 20,000 to 30,000 populations.

Study population

All the individuals with diabetes registered and availing treatment from chronic disease clinic of the selected primary health centres of Puducherry was selected. The patient details like address and contact number were extracted from the NCD register maintained at the selected PHCs. The patients were traced back to their respective houses and were approached to participate in the study at their residence.

Exclusion criteria

Those eligible individuals whom the investigator failed to meet and interview even after making two visits to house were excluded from the study.

Sample size

We calculated minimum sample size of 293 individuals with diabetes assuming prevalence of autonomic neuropathy among diabetes patients to be 22%, absolute precision of 5%, 10% non-response rate and 95% confidence interval (5% alpha error).[3] However we extracted the address details of all the diabetes patients registered in the selected PHCs. We tried approaching all the patients in their respective residence for interview.

Data variables and study tools

The following information was obtained from the participant during the interview using pre-tested, semi-structured, self-designed questionnaire.

Socio-demographic characteristics

Age, gender, education, occupation, marital status, and monthly income.

Morbidity related characteristics

Duration of disease, duration of treatment, presence of hypertension (Y/N), presence of other co-morbidities (Y/N).

Behavioural risk factors

Information on physical inactivity (Y/N), high salt intake (Y/N), low fruit intake (Y/N), alcohol use in last one year (Y/N) and tobacco use in last one year (Y/N).

Anthropometric measurements

Like height and weight was measured as per STEPS guideline.

Autonomic neuropathy

The COMPASS-31 scale was used to screen the diabetes patients for autonomic neuropathy. The composite score was calculated by summing up the weighted scores of the each domain. The individuals with score of more than or equal to 16 were considered to have autonomic neuropathy. The domain components and weightage for each domain is shown below (Table 1).

Table 1: Domain components and weightage for each domain among individuals with diabetes.

Domains	Items (questions)	Weightage	Total score
Orthostatic intolerance	1-4	4.0	40
Vasomotor	5-7	0.8333333	5
Secretomotor	8-11	2.1428571	15
Gastrointestinal	12-23	0.8928571	25
Bladder	24-26	1.1111111	10
Pupillomotor	27-31	0.3333333	5
Total	1-31		100

Brief procedure

The current study was conducted during May to September, 2017. The study had two parts.

Part-1: Language validation of COMPASS-31 scale

The original version of the COMPASS-31 questionnaire was in English language. Linguistic validation of COMPASS-31 questionnaire was done by translating the questionnaire into Tamil language by two bi-linguistic persons separately and back translating it into English by two other bi-linguistic individuals. Both the original and back translated English versions were compared by a team of bi-linguistic persons and the Tamil version was finalized after correcting the mismatching words/sentences. All the bi-linguistic persons included in the language validation were well versed in both English and Tamil language. The final Tamil version of COMPASS-31questionnaire was used to assess the autonomic neuropathy among study participants.

Part-2: Screening for autonomic neuropathy

The address of the houses of all registered diabetic patients was obtained from the NCD (chronic disease) clinic register maintained at the selected PHCs. The individuals with diabetes were contacted in person at their residence. The study procedure, benefits and risks of the study were explained to eligible participants. After obtaining informed written consent the diabetes patient were interviewed using a pre-tested, semi-structured questionnaire. The individuals with diabetes were approached in their respective house to avoid disturbance to the routine care if the same interview was conducted in the premises of PHCs.

All the interviews were conducted in the premises of the participant's house after ensuring privacy. Information on socio-demographic characteristics and behavioural risk factors were collected by interviewing the study participant. The anthropometric measurements like height using wall mounted height measuring tape, weight using bathroom weighing scale were measured in accordance with WHO STEPS survey guidelines.

A language validated COMPASS-31 scale was used to assess the autonomic neuropathy among the study participants. The list of the participants screened positive for autonomic neuropathy was prepared and given to respective PHCs for further management.

Statistical analysis

Data was captured using EpiCollect mobile application. All the independent variables were converted into categorical variables and summarized as percentages. The proportion of study participants with autonomic neuropathy was summarized as percentage. The 95% confidence interval was used as an inferential measure. Number needed to screen (NNS) to a new case of autonomic was calculated by taking the inverse of yield (total number of eligible screened by number of individuals detected with autonomic neuropathy).

The reliability of the scale was measured using Cronbach's alpha for each of the domain of the COMPASS-31 scale. The domain specific items were pooled together and Cronbach's alpha was calculated.

The bivariate logistic regression was used to find the unadjusted association between the individual level characteristics and having screened positive for autonomic neuropathy. The unadjusted prevalence ratio with 95% CI was used as measure of association during bivariate logistic regression. The multivariate generalized linear model with Poisson family and log link function was used to get independent association of the individual level characteristics. All the characteristics with p value less than 0.10 in the bivariate logistic regression was included in the multivariate generalized linear models. The adjusted prevalence ratio with 95% confidence interval was reported for all the variables included in the multivariate model after adjusting for clustering at PHC level.

RESULTS

Socio-demographic, morbidity and behavioural risk profile

During the study period, we recruited 303 individuals with diabetes availing treatment from two selected primary health centres of Puducherry. Of the total 303 participants, 168 (55.5) were from Kirumampakkam PHC and the rest from Thavalakuppam PHC. The mean (SD) age of the study participants was 49.1 (10.5) years and 57 (18.8%) were aged above sixty years. Majority (51.5%) of the study participants were females. Highest percentage (48.8%) of the study participants belonged to Class III socio-economic status according to modified BG Prasad's classification. The socio-demographic profile of the study participants is presented in Table 2.

The morbidity profile of the study participants is presented in Table 3. The median (range) of the duration

of diabetes was 7 (1-39) years among the study participants. Of the total 303 participants, 57 (18.8%) had diabetes for more than ten years as on the day of the interview. Of the total, only 77 (25.4%) of the diabetes patients had their blood sugars controlled as per ADA standard. Hypertension was present in 50 (16.5%) of the individuals with diabetes included in the study. Any other comorbidity was present in 26 (8.6%) of the study participants.

Table 2: Socio-demographic characteristics of patients.

Characteristics	Frequency	%
Age (in years)		
Less than 45	114	37.6
45-59	132	43.6
60 and above	57	18.8
Gender		
Male	147	48.5
Female	156	51.5
Education status		
No formal education	59	19.5
Primary	127	41.9
Secondary	52	17.2
Higher secondary	44	14.5
Intermediate/diploma	6	2.0
Graduate	15	5.0
Occupation status		
Unemployed	119	39.3
Unskilled	90	29.7
Semi-skilled	71	23.4
Skilled	8	2.6
Semi-professional	12	4.0
Professional	3	1.0
Marital status		
Currently married	293	96.7
Widow/widower	10	3.3
Socio-economic status		
Class I	6	2.0
Class II	111	36.6
Class III	148	48.8
Class IV	38	12.5

The distribution of selected behavioural risk factor among the study participants is depicted in Figure 1. About 269 (88.8%) were not doing adequate leisure time physical activity and 234 (77.2%) were not consuming recommended amount of fruits. Alcohol use and tobacco use was present among 25.8% and 17.5% respectively.

Domain wise score and reliability of the scale

The distribution of weighted domain wise scores of COMPASS-31 scale among study participants is depicted in the Figure 2. The Cronbach's alpha calculated including items of each domain; orthostatic intolerance, vasomotor and pupillomotor domains had values more than 0.8 confirming the reliability of the items in the scale. The Cronbach's alpha after including all the items was 0.856.

Table 3: Morbidity related characteristics of individuals with diabetes.

Characteristics	Frequency	%
Duration of diabetes (years)		
Less than 5	114	37.6
5-10	132	43.6
More than 10	57	18.8
Blood sugar status		
Controlled	77	25.4
Uncontrolled	226	74.6
Hypertension	50	16.5
Any comorbidity	26	8.6
Ischaemic heart disease	7	2.3
Chronic kidney disease (CKD)	4	1.3
Foot ulcer	9	3.0
Body mass index		
Underweight (<18.5)	11	3.6
Normal (18.5-24.9)	263	86.8
Overweight (25-29.9)	27	8.9
Obese (30 and above)	2	0.7

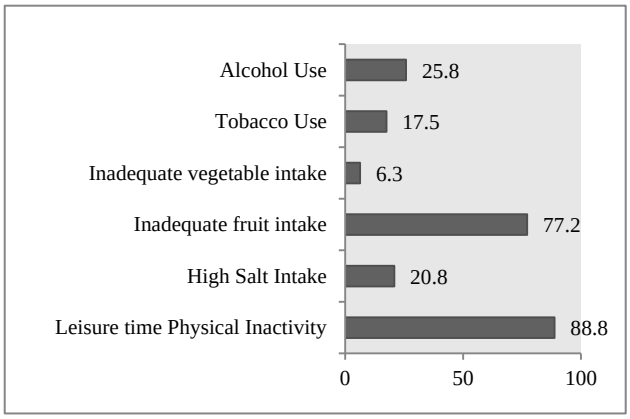

Figure 1: Behavioural risk factors among individuals with diabetes.

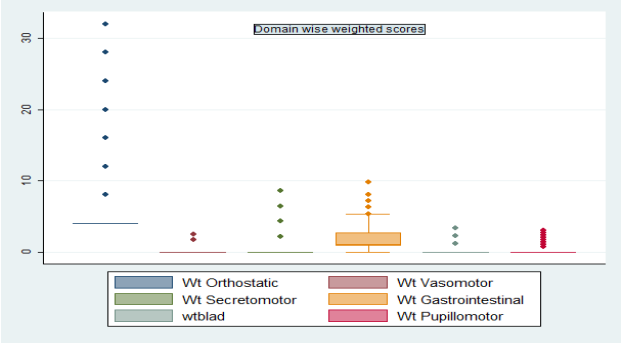

Figure 2: Distribution of domain wise scores among the study participants (n=303).

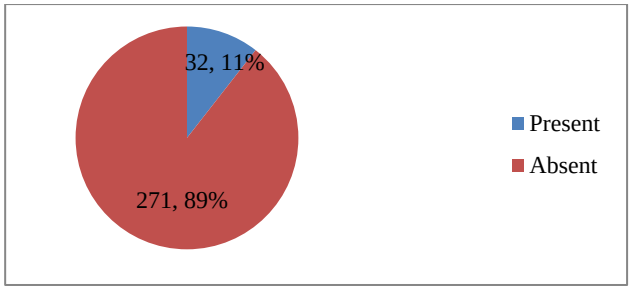

Figure 3: Distribution of autonomic neuropathy among individuals with diabetes.

Proportion of autonomic neuropathy and number needed to screen using COMPASS-31 scale

Of the total 303 individuals with diabetes, 32 {10.6% (*95% CI:* 7.3%-14.6%)} were screened positive for autonomic neuropathy using COMPASS-31 scale. The number of individuals with diabetes who needs to screened (NNS) for finding one with autonomic neuropathy was 10 (303/32). The distribution of autonomic neuropathy among study participants is depicted in Figure 3.

Table 4: Association of socio-demographic characteristics with autonomic neuropathy among individuals with diabetes.

Characteristics	Total	Autonomic neuropathy N (%)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)
Total	303			
Age (in years)				
Less than 45	114	0 (0)	-	-
45-59	132	10 (7.6)	1	1
60 and above	57	22 (38.6)	5.1 (2.6-10.1)	1.8 (0.3-9.4)
Gender				
Male	147	3 (2.0)	1	1
Female	156	29 (18.6)	9.1 (2.8-29.3)	10.6 (5.2-21.8)
Education status				
Less than primary	186	32 (17.2)	-	-
More than primary	117	0 (0)		
Occupation status				
Unemployed	119	29 (24.4)	14.9 (4.6-48.0)	3.0 (1.8-5.0)
Employed	184	3 (1.6)	1	1
Marital status				
Currently married	293	26 (8.9)	6.8 (3.6-12.6)	1.0 (0.4-2.7)
Widow/widower	10	6 (60.0)	1	1
Socio-economic status (BG Prasad's)				
Class I	6	0 (0)	-	-
Class II	111	8 (7.2)	1	1
Class III	148	15 (10.1)	1.4 (0.6-3.2)	0.9 (0.9-0.9)
Class IV	38	9 (23.7)	3.3 (1.4-7.9)	1.3 (1.2-1.3)

Table 5: Association of morbidity related characteristics with autonomic neuropathy among individuals with diabetes.

Characteristics	Total	Autonomic neuropathy N (%)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)
Total	303			
Duration of diabetes				
Less than 5	114	5 (4.4)	1	1
5-10	132	6 (5.0)	1.2 (0.4-3.7)	0.8 (0.6-1.0)
More than 10	57	21 (30.4)	7.0 (2.8-17.7)	1.3 (1.1-1.5)
Blood sugar status				
Controlled	77	8 (10.4)	1.0 (0.5-2.1)	-
Uncontrolled	226	24 (10.6)	1	
Hypertension				
Yes	50	17 (34.0)	5.7 (3.1-10.7)	2.2 (1.1-4.6)
No	253	15 (5.9)	1	1

Continued.

Characteristics	Total	Autonomic neuropathy N (%)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)
Any comorbidity				
Yes	26	8 (30.8)	3.6 (1.8-7.1)	-
No	277	24 (8.7)	1	
Body mass index*				
Underweight (<18.5)	11	5 (45.5)	6.6 (1.5-29.1)	2.8 (1.6-4.8)
Normal (18.5-24.9)	263	25 (9.5)	1.4 (0.3-5.5)	1.5 (1.2-1.8)
Overweight/obese (>25)	29		1	1

*WHO classification of body mass index.

Table 6: Association of behavioural risk factors with autonomic neuropathy among individuals with diabetes.

Behavioural risk factors	Total	Autonomic neuropathy N (%)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)
Total	303			
Physical inactivity				
Yes	269	31 (11.5)	3.9 (0.5-27.8)	0.7 (0.3-2.0)
No	34	1 (3.0)	1	1
Inadequate fruit intake				
Yes	69	29 (12.4)	1	1
No	234	3 (4.4)	0.4 (0.1-1.1)	1.0 (0.4-2.2)
Inadequate vegetable intake				
Yes	284	28 (9.9)	1	1
No	19	4 (21.1)	2.1 (0.8-5.5)	0.7 (0.5-1.0)
High salt intake				
Yes	63	0 (0.0)	-	
No	240	32 (13.3)		
Alcohol use*				
Yes	78	4 (5.1)	0.4 (0.2-1.1)	5.0 (4.4-5.7)
No	225	28 (12.4)	1	1
Tobacco use*				
Yes	53	10 (18.9)	2.1 (1.1-4.3)	0.9 (0.6-1.4)
No	250	22 (8.8)	1	1

*Consumed at least once in past one year.

Factors associated with autonomic neuropathy

The Table 4 shows the association of socio-demographic factors with autonomic neuropathy among the study participants. The age of above 60 years {PR-5.1 (2.6-10.1)}, female gender {PR-9.1 (2.8-29.3)}, unemployed {PR-14.9 (4.6-48.0)}, living with spouse {PR-6.8 (3.6-12.6)} and Class IV SES {PR-3.3 (1.4-7.9)} were associated with autonomic neuropathy. However on adjusting for all the variables (including morbidity profile and behavioural risk factors) and clustering at PHC level, female gender {PR-10.6 (5.2-21.8)}, being unemployed {PR-3.0 (1.8-5.0)} and class IV SES {PR-1.3 (1.2-1.3)} were independently associated with autonomic neuropathy.

The Tables 5 and 6 shows the association of morbidity related characteristics and selected behavioural risk factors with autonomic neuropathy among the study participants.

DISCUSSION

A community based cross-sectional analytical study was conducted among 303 individuals with diabetes in the selected areas of Puducherry, South India. The study was aimed to determine the prevalence of diabetic autonomic neuropathy among the diabetes patients and also to assess the factors associated with diabetes. The study used non-invasive, validated symptom based questionnaire to assess the autonomic neuropathy among the study participants. The reliability of the scale was assessed during the study and the scale showed high internal consistency. The autonomic neuropathy was present in 10.6% (95% CI: 7.3%-14.6%) of the study population. The female gender, being unemployed, class IV SES, duration of disease for more than ten years, having hypertension and having BMI in underweight range and alcohol use were independently associated with individual screening positive for autonomic neuropathy using COMPASS-31 scale.

In the current study, the COMPASS-31 scale had good internal consistency in three out of six domains. The orthostatic intolerance, vasomotor and pupillomotor domains showed a Cronbach's alpha of more than 0.8. Similar consistency statistics have been reported in the previous studies with these three domains having Cronbach's alpha of more than 0.8. As in other studies, even in the current study the three domains; gastrointestinal, secretomotor and bladder had lower Cronbach's alpha. This high consistency of the scale even in the current study setting proves it to be beneficial tool for screening.[19-20]

Compared to previous studies the current study had relatively lower prevalence of the autonomic neuropathy among diabetes patients. The studies in the past had reported the prevalence of the autonomic neuropathy among diabetes patients to be ranging from 17 to 73%. However, in the current study it was found that only 11% of the diabetic patients werehaving DAN. This difference in the prevalence may be due to the fact that the previous studies were mostly from western countries with different phenotyping. The previous studies also included patients who were on insulin, whereas the current study included only those diabetes patients on oral hypoglycaemic drugs. Being on insulin is a proxy for uncontrolled diabetes status requiring higher degree of care with insulin.[21-22]

The previous studies employed more quantitative and bio-physical measures to assess the autonomic neuropathy among diabetes patients. Here in the current study, the COMPASS-31 scale used mainly symptom scale which might have led to under diagnoses. The symptoms are relatively late manifestation of the pathological changes which eventually disturbs the normal physiological state. Hence, the scale might have missed those cases with early pathological changes, which might not have manifested as a symptom.[23]

In all the previous studies the mean age of study participants was close to 60 years. In the current study mean age of the study participants was just close to 50 years. The lower age of the participants in the current study might have led to lower prevalence of the autonomic neuropathy. The age act as positive contributor to the disease in two ways; as seen in current study higher age has independent effect on the autonomic neuropathy. Also, as the age increases there is high chance that there will be increase in the duration of the diabetes. Duration of diabetes also has a positive association with screening positive for autonomic neuropathy. This difference in study groups might have led to varied result in the current study setting. Though there was relatively less burden of DAN in the current study population compared to previous studies, the number needed to screen was quite low. With NNS of 10, the autonomic neuropathy can be considered for regular screening among the diabetes patients.

In the current study female gender, being unemployed, class IV SES, duration of disease for more than ten years, having hypertension and having BMI in underweight range and alcohol use were independently associated with individual screening positive for autonomic neuropathy using COMPASS-31 scale. The studies in the past also reported duration of the disease to be independently associated with the DAN.[24] In the current study we also found female gender to be positively associated with autonomic neuropathy. Female gender being quoted to be having relatively higher prevalence of neurological problems in general, might have shown the positive association.

The lower BMI and having hypertension were associated with the DAN. However, the cause and effect relationship this association cannot be proved with the current study design. The lower BMI may be a sequelae of autonomic neuropathy which leads to gastroparesis and weight loss. Similarly, hypertension may be due to pathological changes in the heart caused due to cardiac autonomic neuropathy. However, this information is beneficial to prioritize the diabetes patients for elaborate screening of DAN.

The alcohol use was positively associated with autonomic neuropathy in the current study. No studies in the past had explored this relationship. It may be worth looking into this relationship as in general alcohol has proven to be associated with neuropathies. The synergistic action and pathways of destruction of neural fibres in diabetes patients with alcohol consumption needs to be assessed.

There are few strengths in the current study. First, the study was conducted using validated COMPASS-31 scale with high internal consistency. Second, single investigator conducted all the interviews and hence reducing the inter-observer bias. Third, we used mobile based data collection (EpiCollect) app which helped reducing the information loss due to data collection using paper based forms. Fourth, the internal consistency of the study tool (COMPASS-31) was assessed and has been reported. Fifth, the robust multivariate models adjusting for clustering at the PHC levels were used for assessing the independent association and strength of association was expressed as prevalence ratios. This has led to derive the precise estimates in the current study.

Limitations

There are few limitations in the study. First, the study had relatively low response rate during the recruitment of the participants. The investigator was not able to trace back all the patients. However, we made the second visit to house was made to ensure the participation. Second, the validity of the study tool was not assessed in the sub sample of the study participants. Hence, we failed to estimate the true prevalence of autonomic neuropathy. Third, we failed to objectively assess the diabetes control

status among study participants and depended on their previous blood sugar estimation, which was not standardized.

Recommendations

There are few implications and recommendation from this study. First, COMPASS-31 scale with high internal consistency can be validated and used as a screening tool for autonomic neuropathy. Second, the autonomic neuropathy can be considered in routine complication screening of diabetes patients as number needed to screen is as low as 10. Third, there is need to preferentially screen diabetes patients who are females, those who consume alcohol, those with lower BMI and those diagnosed with hypertension.

CONCLUSION

One in ten individuals with diabetes were screened positive for autonomic neuropathy using non-invasive, validated COMPASS-31 scale. On screening ten diabetes patients, one individual with autonomic neuropathy can be picked up. Diabetes patients with hypertension, longer duration of disease, alcohol use and lower BMI had significantly higher chance of screening positive for autonomic neuropathy. With good yield, there is need for including autonomic neuropathy screening as a component in the comprehensive care provided to diabetes patients in the primary health centres.

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