



Original Research Article

A comparative study of autonomic nervous system dysfunction in post menopausal women with diabetes and without diabetes as a predictor of cardiovascular events

Rohini N S^{1,*}, Bhanupriya², Anusuya S K¹, Ravishankar S N³, Akshay S Atre⁴, Pooja Shettannavar⁴, Rakshith N R⁵

¹Dept. of Obstetrics and Gynecology, Akash Institute of Medical Sciences and Research Center, Bangalore, Karnataka, India

²Dept. of Physiology, Akash Institute of Medical Sciences and Research Center, Bangalore, Karnataka, India

³Dept. of Internal Medicine, Akash Institute of Medical Sciences and Research Center, Bangalore, Karnataka, India

⁴Akash Institute of Medical Sciences and Research Center, Bangalore, Karnataka, India

⁵JSS Medical College, Mysuru, Karnataka, India



ARTICLE INFO

Article history:

Received 06-12-2019

Accepted 09-02-2020

Available online 15-06-2020

Keywords:

Post-menopausal women

Diabetes

Autonomic function tests

Cardiovascular disease

ABSTRACT

Introduction: Cardiovascular diseases (CVDs) are one of the leading causes of death in women across the globe. CVD is more prevalent in women after menopause due to the lack of estrogens which have a cardioprotective effect. Menopause and diabetes mellitus are individually high risk for cardiovascular autonomic neuropathy which in turn results in CV accidents and deaths.

Aims and Objectives: The aim of this study was to evaluate the Autonomic Nervous System dysfunctions in post menopausal women with diabetes mellitus, to grade the severity of dysfunctions and to compare the severity of the ANS dysfunction with age matched healthy controls.

Materials and Methods: This observational study was conducted in the department of Obstetrics and Gynecology, Akash Institute of Medical Sciences & Research Centre, Devanahalli, Bengaluru, Karnataka, India. A total of 120 postmenopausal women were examined for the study. They were divided into two equal groups (60 women in each group) as menopausal women with diabetes and without diabetes. The ANS dysfunctions were evaluated based on symptoms and also specific tests like heart rate response to Valsalva maneuver, heart rate response to standing up from supine position, blood pressure response to sustained handgrip, blood pressure response to standing up from supine position. The ANS dysfunctions were categorized into mild, moderate and severe dysfunctions.

Results: Of the 60 postmenopausal women without diabetes, 20 women had symptoms of autonomic dysfunction in the form of hot flushes, giddiness and palpitations, (33%) and they also tested positive for ANS dysfunction. Though the remaining 40 women did not have any symptoms, they tested positive for ANS dysfunction. 40 women had mild ANS dysfunctions, 12 had moderate dysfunctions and 8 had severe dysfunctions. In the other group of postmenopausal women with diabetes, 30 women had symptoms of ANS dysfunction (50%) and also tested positive for ANS dysfunction. The remaining 30 women, though did not have any symptoms, they also tested positive for ANS dysfunctions. 30 of them had mild dysfunctions, 18 had moderate dysfunctions and 12 had severe dysfunctions.

Conclusion: Our study has broadly shown that postmenopausal women suffer from autonomic derangements, and degree and severity of such derangements are much higher in post menopausal women with diabetes mellitus and are possibly at an increased risk of developing heart disease. Hence early detection, good control of diabetes and early detection of autonomic dysfunction and management is important in these women.

© 2020 Published by Innovative Publication. This is an open access article under the CC BY-NC license (<https://creativecommons.org/licenses/by-nc/4.0/>)

1. Introduction

Menopause has become a growing cause of concern as obesity, and metabolic syndrome (hypertension, diabetes

* Corresponding author.

E-mail address: dr.rohini.ns@gmail.com (Rohini N S).

mellitus and hyperlipidemia) are common during this period. Genetic, hormonal, and exogenous factors are responsible for changes in body composition during menopause.^{1,2} A decline in the levels of estrogens during menopause is responsible for these changes. Autonomic functions affecting the heart are disturbed in the postmenopausal period. Measurement of cardiac autonomic functions may prove to be a useful tool for diagnosing heart diseases in postmenopausal women.

DM can affect many different organs and over time, can lead to serious complications, both microvascular (include neuropathy, nephropathy and retinopathy) and macrovascular (include cardiovascular disease, stroke, and peripheral vascular disease).^{3,4} Diabetic autonomic neuropathy (DAN) is one of the most common complications of DM. Clinical symptoms include orthostatic hypotension, resting tachycardia, exercise intolerance, pseudomotor dysfunction, constipation, and gastroparesis. The prevalence of DAN may increase to 65% with increasing age and DM duration.³⁻⁵ Menopause and diabetes mellitus are individually high risk for cardiovascular autonomic neuropathy which in turn results in CV accidents and deaths. So menopausal women with diabetes are at a much higher risk for cardiovascular related events than menopausal women without diabetes.⁶ Any autonomic dysfunction, if detected early, would enable early interventions to prevent heart diseases. Hence, measuring the autonomic activity in postmenopausal women would provide strong evidence of a potential target for existing as well as future heart disease in these women. Very few studies in this field are available from the Indian subcontinent, particularly, South India, and hence, this study was taken up with the following objectives:

1. To evaluate the ANS dysfunctions based on both symptoms and clinical tests in post menopausal women with diabetes compared with post menopausal women without diabetes.
2. To grade the severity of ANS dysfunctions into Mild, Moderate and Severe dysfunctions.
3. To compare the severity of ANS dysfunctions between the two groups.

2. Materials and Methods

The present study was conducted at Akash Institute of Medical Sciences & Research Center, Devanahalli and was carried out on 120 menopausal women in Department of Medicine and Department of Obstetrics and gynecology wards from July 2018 to July 2019. A detailed clinical history and clinical examination was done for all the study subjects. All patients were explained about the nature of the study and informed consent was obtained from all the patients. All postmenopausal women who have attained menopause before the age of 65 years were included in this study. Postmenopausal women with obesity, on hormone

replacement therapy, on lipid-lowering drugs, history of hormonal imbalance or hormonal disorder were excluded from the study.

The ANS dysfunction was evaluated based on symptoms like hot flushes, sweating, palpitations and giddiness. Also specific tests like Heart rate response to Valsalva maneuver, Heart rate response to standing up from supine position, Blood pressure response to sustained handgrip, Blood pressure response to standing up from supine position were done.

1. Heart rate response to Valsalva maneuver - The Valsalva ratio, that is, the ratio of longest R-R interval after 20 beats of end of maneuver to the shortest R-R interval during the maneuver was calculated. The result was taken as three successive readings. A ratio of 1.1 or lower was taken abnormal.⁷⁻¹⁰
2. Heart rate response to standing up from supine position – The ratio of longest R-R interval around 30th beat after standing. To the shortest R-R interval, around 15th beat after standing was calculated. A ratio <1 was taken as abnormal.⁷⁻¹⁰
3. Blood pressure response to sustained handgrip – A <10 mmHg increase in diastolic pressure before and 3 min after sustained handgrip was taken as abnormal.⁷⁻¹⁰ (Figure 1)

Blood pressure response to standing up from supine position - It was measured while the participant was lying supine and again 1 min after standing up and the difference was noted. In normal participant, the systolic blood pressure should not decrease by more than 10 mmHg, in patients with autonomic dysfunction, the systolic blood pressure falls more than 30 mmHg.⁷⁻¹⁰ (Figure 2)



Fig. 1: Sustained hand grip test being done in a patient

Autonomic dysfunction was classified using criteria of Ewing and Clarke as follows:

1. Normal: All five tests normal
2. Early involvement: One of the three heart rate tests abnormal
3. Definite involvement: Two or more of the heart rate tests abnormal



Fig. 2: Blood pressure response to Valsalva maneuver being done on a patient

4. Severe involvement: Two or more of the heart rate tests abnormal plus one or both of the blood pressure tests abnormal
5. Atypical pattern: Any other combination of abnormal tests

2.1. Statistical analysis

Results were expressed in percentages using SPSS version 21.0.

3. Results

Out of the sixty healthy non diabetic postmenopausal women included in the study group, all of them had autonomic dysfunction either symptomatically in the form of hot flushes, giddiness, palpitations or tested positive for ANS dysfunctions. 33% were symptomatically positive while 67% were clinically positive for autonomic dysfunction. This distribution is as illustrated in Table 1.

Table 1: Autonomic dysfunction wise distribution of non diabetic postmenopausal women

Autonomic Dysfunction	No of non diabetic postmenopausal women	Percentage (%)
Symptoms and signs	20	33.33
Only Signs	40	66.67
Total	60	100

When the severity of the ANS dysfunctions were categorized, 40 of them had mild ANS dysfunctions, 12 had moderate and only 8 had severe dysfunctions as illustrated in Figure 3.

In the other group of 60 post menopausal women with Diabetes, 30 women had symptoms of ANS dysfunctions and also tested positive while the remaining 30 women

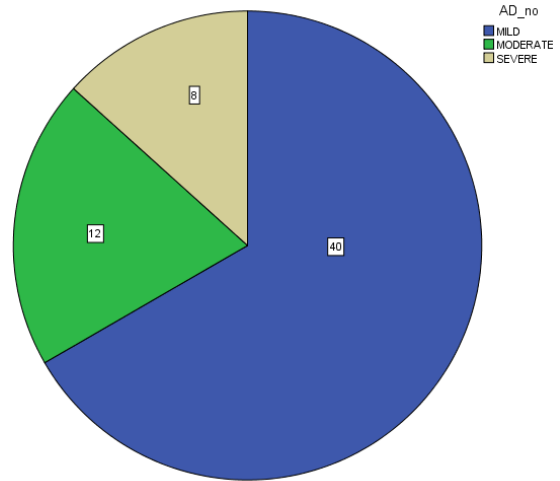


Fig. 3: Showing autonomic dysfunction among non diabetic postmenopausal women with clinically positive for ANS dysfunction- without diabetes

tested clinically positive though they did not have any symptoms. This distribution is as illustrated in Table ??.

When the severity of the ANS dysfunctions were categorized, 30 of them had mild ANS dysfunctions, 18 had moderate and 12 had severe dysfunctions as illustrated in Figure 4.

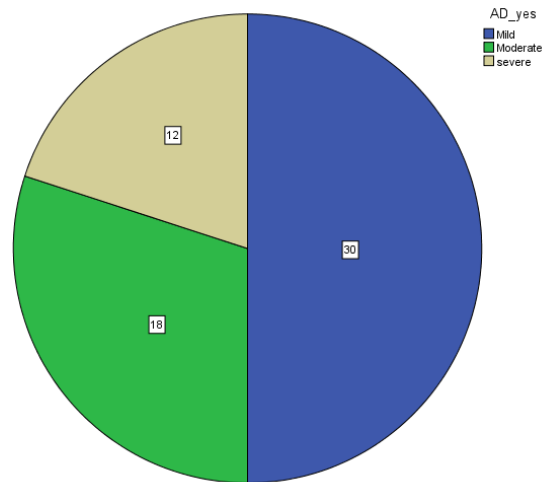


Fig. 4: Showing Autonomic dysfunction among Diabetic Postmenopausal women with clinically positive for ANS dysfunction: with diabetes

4. Discussion

Our study was carried out in 120 postmenopausal women out of which 60 were without diabetes and 60 were with diabetes. In our study, the largest group was in the age range

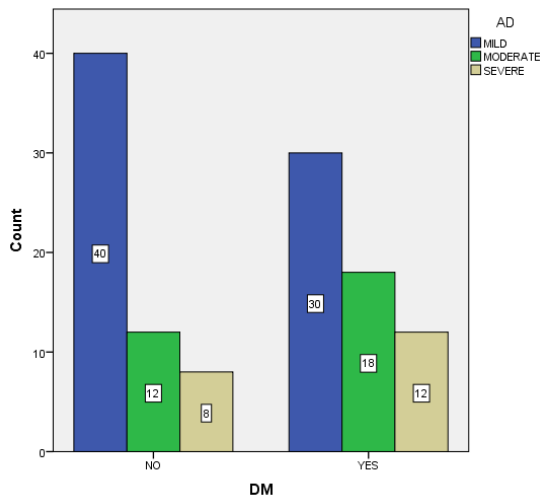


Fig. 5: Showing the autonomic nervous system dysfunction in post menopausal women with and without diabetes in relation to the severity of manifestations

of 55–60 years (50%) and the females of age range of 50–55 years was 20% and females of age range of 60–65 years was 30%.

In the present study, autonomic nervous system abnormality was seen in both the groups. Though all the patients in both the groups had ANS dysfunctions either symptomatically or clinically, the percentage of women who were symptomatic and the severity of ANS varied between the two groups. 33% of post menopausal women without diabetes had symptoms of ANS dysfunction like hot flushes, giddiness and palpitations while it was 50% in postmenopausal women with diabetes.

Also, when the severity of ANS derangements were compared between the two groups, the number of women with moderate and severe degree of ANS dysfunctions were higher in the post menopausal women with diabetes mellitus than those without diabetes mellitus.

Menopausal women are known to have some of the ANS function abnormalities in form of hot flushes, giddiness in relation to postural change and palpitations probably due to hormone imbalance. Our data correlate well with other studies like Virtanen et al. who performed autonomic nervous system tests in healthy postmenopausal women, which showed autonomic nervous function normal for age.¹¹ However, they have not taken the symptoms into consideration but in our study almost all patients have symptoms of ANS dysfunction.

In a study done by M Taranikatti et al, they have concluded that postmenopausal women with obesity suffer from autonomic derangements and are possibly at an increased risk of developing heart disease.¹² Arunima Chaudhuri et al., studied anatomic function and obesity in postmenopausal women, reported that decreased sympathovagal activity with obesity in postmenopausal

women.¹³ Our study shows that, there is a similar enhanced risk of CVDs in post menopausal women, all the more with greater risk in the patients having diabetes as there is an established relation between Autonomic nervous system dysfunction in the form of heart rate variability and postural variations in blood pressure and cardiovascular events which cause high degree morbidity and mortality. Hence, it is necessary that these derangements be identified early during menopause and appropriate intervention be given to stop or delay any potential heart disease.

5. Conclusion

Our study has broadly shown that postmenopausal women suffer from autonomic derangements and the degree and severity of such derangements are much higher in post menopausal women with diabetes mellitus and are possibly at an increased risk of developing heart disease. It would be imperative to screen all post menopausal women to detect any such derangement using reliable and precise tests of autonomic functions to detect any abnormalities early. This information can help in better clinical interpretation to detect any hidden or undiagnosed heart condition and thereby the outcomes can be improved through early and timely interventions. The tests can be performed with ease in a clinical setup. These tests specifically determine changes pertaining to sympathetic and parasympathetic activities and so they will help to advise such women to take up lifestyle modifications such as yoga or meditation, walking and dietary changes and good glycemic control to overcome this increased risk of CVDs to a certain extent. However, this study still has some limitations due to the small sample size that can be increased to make it more robust and also by taking into consideration several other factors that can influence autonomic activity such as physical and mental activities and diet. Further studies on the subject can refine the findings to make it even more applicable in the clinical context.

6. Acknowledgement

We thankful to the authorities of Akash Institute of Medical Sciences & Research Centre, Devanahalli, Bengaluru, Karnataka, India.

7. Source of Funding

None.

8. Conflict of Interest

None.

References

- Garcia M, Mulvagh SL, Merz CN, Buring JE, Manson JE. Cardiovascular disease in women clinical perspectives. *Circ Res.*

- 2016;118(8):1273–93.
2. Mosca L, Barrett-Connor E, Wenger NK. Sex/Gender Differences in Cardiovascular Disease Prevention. *Circ*. 2011;124(19):2145–54.
 3. Vinik AI, Erbas T, Casellini CM. Diabetic cardiac autonomic neuropathy, inflammation and cardiovascular disease. *J Diabetes Investig*. 2013;4(1):4–18.
 4. Spallone V, Ziegler D, Freeman R, Bernardi L, Frontoni S, Pop-Busui R. Cardiovascular autonomic neuropathy in diabetes: clinical impact, assessment, diagnosis, and management. *Diabetes Metab Res Rev*. 2011;27:639–53.
 5. Karayannis G, Giamouzis G, Kokkinos DV, Skoularigis J, Triposkiadis F. Diabetic cardiovascular autonomic neuropathy: clinical implications. *Expert Rev Cardiovasc Ther*. 2012;10(6):747–65.
 6. Moodithaya S, Avadhany ST. Gender differences in age-related changes in cardiac autonomic nervous function. *J Aging Res*. 2012;2012:679345. doi:10.1155/2012/679345.
 7. Pal GK, Pal P. Textbook of Practical Physiology. 2nd ed. Orient Black Swan/Universities Press; 2005.
 8. Ewing DJ, Clarke BF. Diagnosis and management of diabetic autonomic neuropathy. *BMJ*. 1982;285:916–8.
 9. Torsvik M, Häggblom A, Eide GE, Schmutzhard E, Vetvik K, Winkler AS. Cardiovascular autonomic function tests in an African population. *BMC Endocr Disord*. 2008;8(1):19.
 10. Park K. Park's Textbook of Preventive and Social Medicine. Jabalpur, India: Bhanot; 2009.
 11. Virtanen I, Polo-Kantola P, Erkkola R, Polo O, Ekholm E. Climacteric vasomotor symptoms do not imply autonomic dysfunction. *Br J Obstet Gynaecol*. 1999;106(2):155–64.
 12. Taranikanti M, Dronamraju A, Bala S, Guntuka RK, Mudunuru AK. Autonomic Nervous System Derangement as a Predictor of Cardiovascular Disease in Obese Postmenopausal Women. *Indian J Cardiovasc Dis Women WINCARS*. 2019;04(01):008–014.
 13. Chaudhuri A, Borade N, Tirumalai J, Saldanha D, Ghosh B, Srivastava K. A study of autonomic functions and obesity in postmenopausal women. *Ind Psychiatry J*. 2012;21(1):39–43.

Author biography

Rohini N S Associate Professor

Bhanupriya Assistant Professor

Anusuya S K Associate Professor

Ravishankar S N Professor and HOD

Akshay S Atre Undergraduate Student

Pooja Shettannavar Undergraduate Student

Rakshith N R Undergraduate Student

Cite this article: Rohini N S , Bhanupriya , Anusuya S K , Ravishankar S N , Atre AS, Shettannavar P, Rakshith N R . A comparative study of autonomic nervous system dysfunction in post menopausal women with diabetes and without diabetes as a predictor of cardiovascular events. *Indian J Obstet Gynecol Res* 2020;7(2):182-186.