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*Full Length Research Paper*

# Frequency and clinical pattern of autonomic neuropathy in adult diabetic Sudanese patients

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**Diabetic autonomic neuropathy can cause cardiac, gastrointestinal, genitourinary and metabolic disorders. Strict glycemic control can slow the onset of diabetic autonomic neuropathy and sometimes reverse it. The study was aimed at investigating the presence of diabetic autonomic neuropathy in a group of Sudanese diabetic patients. This is a descriptive prospective cross-sectional study. It was conducted at Herra medical center and Alnoor specialized center in Omdurman. One hundred diabetic patients were studied using standardized questionnaire, including history, clinical examination and investigations. Female to male ratio was 1.7:1. Most of the patients had Type 1 Diabetes mellitus (DM). Common age group affected was >51 years and common duration of DM was < 10 years. Diabetic autonomic neuropathy was diagnosed in 71% of the patients. The majority of the patients had early stage diabetic autonomic neuropathy. Diabetic autonomic neuropathy is a very common problem among our studied group (all the patients were adult diabetic Sudanese). Diabetic autonomic neuropathy can occur at any age and at any time, even at early diagnosis of diabetes but poor glycemic control is the main implicating factor. All diabetic patients have to do annual expiration/inspiration ratio to detect early stages of diabetic autonomic neuropathy.**

**Key words:** Autonomic neuropathy, Diabetic Sudanese Patients.

## INTRODUCTION

Diabetic neuropathy is a heterogeneous disorder that encompasses a wide range of abnormalities affecting both proximal and distal peripheral sensory and motor nerves, as well as the autonomic nervous system (Silink, 2005). Diabetic autonomic neuropathy is one of the more frequent, common and troublesome complication of diabetes mellitus. It is among the least recognized and understood complications of diabetes, despite its significant negative impact on survival and quality of life in people with diabetes. Factors in the pathogenesis of these complications are altered metabolism, vascular insufficiency, loss of growth factor trophism, and autoimmune destruction of nerves in a visceral and cutenous distribution (Susan and Helseth, 1997; Defronzo, 1997; Alberti and Zimmet, 1997). Diabetic autonomic neuropathy affects the nerves that control the heart, regulate the blood pressure and control blood glucose level. It also affects other internal organs, causing problems with digestion, respiratory function, urination, sexual response, and vision.

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In addition, the system that restores blood glucose levels to normal after a hypoglycemic episode may be affected, resulting in loss of the warning signs of hypoglycemia, such as sweating and palpitations (Bennett and Hadden, 1980; Jennifer, 1985; Mc Cance et al., 1997). Complications of diabetic autonomic neuropathy contribute greatly to morbidity, mortality, and reduced quality of life of the patients with diabetes and are the major source of increased costs of caring of the diabetic patients (Rosenbloom, 1999; Gerich, 1998). To compound the awareness problem, diabetic autonomic neuropathy has a slow and insidious onset and many patients may suffer from the condition unknowingly for many years. Early detection, diagnosing, and intervention are the prime importance in heading of the potentially serious consequences of diabetic autonomic neuropathy (Mc Cance and Hanson, 1995; James and David, 2005).

The study was aimed at investigating the presence and clinical pattern of diabetic autonomic neuropathy in a group of adult diabetic Sudanese patients, seen in the period between January to June 2008.

## METHODOLGY

This is a descriptive, prospective, cross-sectional hospital based study. It was conducted at Hera and Alnoor tertiary referral medical center in Omdurman. Study population: 100 adult diabetic Sudanese patients were included in the study. The study population includes Type 1 and 2 diabetic patients referred to the two centers over a period of six months, from January to June 2008. Inclusion criteria; all the patients were adult diabetic Sudanese. All of them gave their verbal consent to participate in the study. Data was collected by the authors using questionnaire retrieving information from patients. The informers were either the patients or close relatives.

A full detailed history was taken from each patient, the history included personal data such as age, sex, origin, type and duration of diabetes, symptoms related to central nervous system involvement (disturbance of high cerebral function, neck pain numbness, cranial nerves involvement ,upper and lower limbs weakness, sphincter defects,), symptoms of autonomic neuropathy involvement such as light headiness, palpitations, gastrointestinal symptoms such as constipation, nausea and vomiting, diarrhea, loss of taste, discomfort in swallowing, fecal incontinence, nocturnal diarrhea, sweating disturbances, dizziness, impotence, failure of erection and ejaculation, difficulty in intercourse, urine incontinence, difficult beginning of urination, incomplete emptying, excessive sweating, gustatory sweating, reduced sweating and symptoms of feet involvement (burning sensation of feet , cold feet).

### Symptoms of autonomic neuropathy

1. Constipation
2. Nausea and vomiting
3. Nocturnal diarrhea
4. Discomfort in swallowing
5. Fecal incontinence
6. Loss of taste
7. Palpitations
8. Fainting
9. Light headiness
10. Failure of erection and ejaculation
11. Urine incontinence
12. Excessive sweating, gustatory sweating reduced sweating,
13. Blurring of vision, light sensitivity, difficult focusing, reduced lacrimation
14. Burning sensation of feet
15. Cold feet

Symptoms related to other systems were included. Past medical history (similar illness, infectious disease, and autoimmune disease), drugs history, family history (similar illness, neurological illness, autoimmune disease) and social history were included. Clinical examination was done for all patients including general examination (temperature, pupil, mouth and skin), pulse rate, measurement of blood pressure in supine and standing position looking for postural hypotension, resting tachycardia and fixed heart rate, in response to sitting and standing position. Also examination of the central nervous system was done for all patients looking for evidence of peripheral neuropathy and autonomic nervous system involvement. The following investigations were done for each patient: RBS, HbA1c, CBC, urine analysis, RFT, lipid profile. Then all of the patients were connected to ECG machine, rhythm strip lead 2 was done looking for:

1. Beat to beat heart rate variation during inspiration and expiration with the patient at rest and supine, breathing 6 breaths/min, a difference in heart rate of >15 beat/min is normal and <10 beat/min is abnormal, R-R inspiration/R-R expiration >1.17 is normal and abnormal if less (Ziegler et al., 1992).
2. Heart rate response to standing during continuous ECG monitoring. The R-R interval is measured at beats 15 and 30 after standing. Normally, a tachycardia is followed by reflex bradycardia. The 30:15 ratio is normally >1.03 and abnormal if less (Noronha et al., 1981)
3. Heart rate response to Valsalva maneuver, during which the patient forcibly exhales into the mouthpiece of a manometer to 40 mmHg for 15 s during ECG monitoring. Healthy subjects develop tachycardia and peripheral vasoconstriction during strain, and an overshoot bradycardia and rise in blood pressure with release. The ratio of longest R-R to shortest R-R should be >1.2 and abnormal if less (Bhatia et al., 1976). Data was introduced into the computer from a master sheet recording, using software program. It was entered and analyzed and then the results were expressed in form of tables, figures and graphs using Statistical Package for Social Science.

## RESULTS

The study showed that 61% of the patients had Type 1 DM and 39% had Type 2 DM. 64% of the patients were females and 36% were males, with female to male ratio of 1.7:1. According to age distribution, 1% of the patients below 20 years, 0% between 21 to 30 years, 10% between 31 to 40 years, 26% between 41 to 50 years and 63% above 51 years. 51% of the patients had DM for < 10 years duration, 33% had DM duration between 11 to 20 years and 16% had DM for > 21 years. Evidence of DAN present in 70% of the patients. According to age groups, DAN occurs 100% in patients age <20 years and this is because those patients have been diabetics since childhood, and in patients between 31 to 40 years. It represents 84% in patients between 41 to 50% and 93% in patients >51 years. Feet are the most affected part of the body by DAN (78%), followed by disorders of sweating

(67%) and vision (67%). The most affected system by DAN was the gastrointestinal system (70%), followed by cardiovascular system (59%), and genitourinary system represents the least affected system (22%). Constipation and nausea were the commonest gastrointestinal symptoms of DAN, (55 and 30%) respectively, followed by early satiety (20%), diarrhea occur in 11% of the patients, loss of taste occur in 7%, discomfort in swallowing in 6%,vomiting of undigested food occur in 4% and fecal incontinence occur in 4% .

Regarding the cardiovascular symptoms of DAN, most patients complained of light headiness (47%), and palpitations (40%). Fainting occur in 2% of patients. 7% of our patients complained of impotence, 2% had failure of erection and ejaculation, 3% complained of difficulty in intercourse, 14% of urine incontinence, 1% of difficulty in beginning urination, and 4% of incomplete emptying. It was found that, 61% of the patients had excessive sweating, 28% had gustatory sweating, and 4% had reduced sweating. It did appear that, 55% of the patients had blurring of vision, 33% had light sensitivity, 26% had difficulty in focusing and only 16% of our patients had reduced lacrimation. Burning sensation of feet and worsening of it at night was the commonest symptoms of feet involvement (76 and 50%) respectively, cold feet occurred in 30% of the patients, and 18% had pruritus. Systemic hypertension was present in 53% of the patients that participated in the study. Normal heart rate was observed in 88% of the patients, while 12% of them had resting tachycardia. 69% of the patients had fixed heart rate and 31% had variable heart rate. Postural hypotension occurred in 18% of the patients. Examination of the skin revealed that 19% of the patients had dry skin, 9% had loss of hair, 36% had dry skin and loss of hair and 36% of the patients had normal skin. Regarding body temperature, it was normal in 45% of the patients, (44%) of the patients had hypothermia, and hyperthermia was detected in 11% of the patients.

Clinical evidence of diabetic peripheral neuropathy was present in 71% of the patients. Diabetic retinopathy was observed in 59% of the patients. The majority of the diabetic patients who had evidence of autonomic neuropathy had impaired expiration/ inspiration ratio (90%), abnormal response of heart rate to standing was positive in 81% of our diabetic patients and abnormal heart rate response to Valsalva was found in 45% of the same studied patients (Figure 1). The majority of the patients included in this study had inadequate glycemic control (73%) and only 27% had good glycemic control as was evidenced by HB A1c. Impaired lipid profile was found in 41% of the patients and abnormal renal function test in 9% of the patients.

## DISCUSSION

The study showed that most of our patients had Type 1 DM. The mean age affected was found to be 50 years. Most of our patients showed an evidence of DAN (70%). This is comparable to the study done by Ziegler et al. (1992) and Noronha et al. (1981) but it differed from the study done by Bhatia et al. (1976) where they found that, only 29% of their patients were affected by this complication, also it differed from the study done by Dyck et al. (1993) and Neil et al. (1989) where they found that only 7% of their patients showed an evidence of DAN. This wide estimate of prevalence rates of DAN is most likely due to the fact that, most of the patients in our study had Type1 DM, also longer duration of DM, poor glycemic control, and late presentation of our patients can be blamed. Diabetic diarrhoea (DD) although troublesome, is not associated with evidence of malabsorption and can be self-limiting. Before considering DD as a diagnosis, we should exclude the more common parasitic causes of diarrhoea like giardiasis, viral and bacterial infections. Gastroparesis diabeticorum when symptomatic is distressing, difficult to treat, and may even impair the glycemic control, when the delayed gastric emptying causes alterations of meal absorption (Awad et al., 2001). Similar to what was mentioned in the literature, and like what was reported by Maleki et al. (1998) we found that the gastrointestinal system was the most involved one, but this was differed from what was reported by Vinik and Erbas (2001) and Maser et al. (1990).

The similarity to the result mentioned by Maleki and his colleagues is due to longer duration of DM and poor glycemic control. The difference from what was reported by Maser and his colleague is due to the fact that, their study was ascertained in a cohort of larger number of well controlled diabetic patients with definite duration of DM and in certain age group. As the majority of the DAN cases are asymptomatic, autonomic dysfunction can conveniently be detected by testing the cardiovascular responses to various stimuli. The prevalence of cardiovascular DAN among our studied group was similar to what was reported by Pappachan et al. (2008); Mehta et al. (2002); Raza et al. (2000) and Tentolouris et al. (1997). The increase incidence of symptomatology in favor of cardiovascular DAN, may be due to co-existence of other diseases like hypertension, ischemic heart disease and cardiomyopathy. It did appear that the prevalence of symptoms in favour of genitourinary system involvement, is less than what was mentioned in the literature (Tentolouris et al., 1997; Bacon et al., 2002; Richardson and Vinik, 2002). Erectile dysfunction(ED) is common among diabetic patients and often the only symptom of DAN. In our society, it seems that ED is far more common than the reported figures; this is due to embarrassment of patients and reluctance of doctors to discuss sexual matters with them (Awad et al., 2001). Bladder dysfunctions (including retention) are very rare. The study showed that, there is increased incidence of gustatory sweating and reduction of sweating; this is

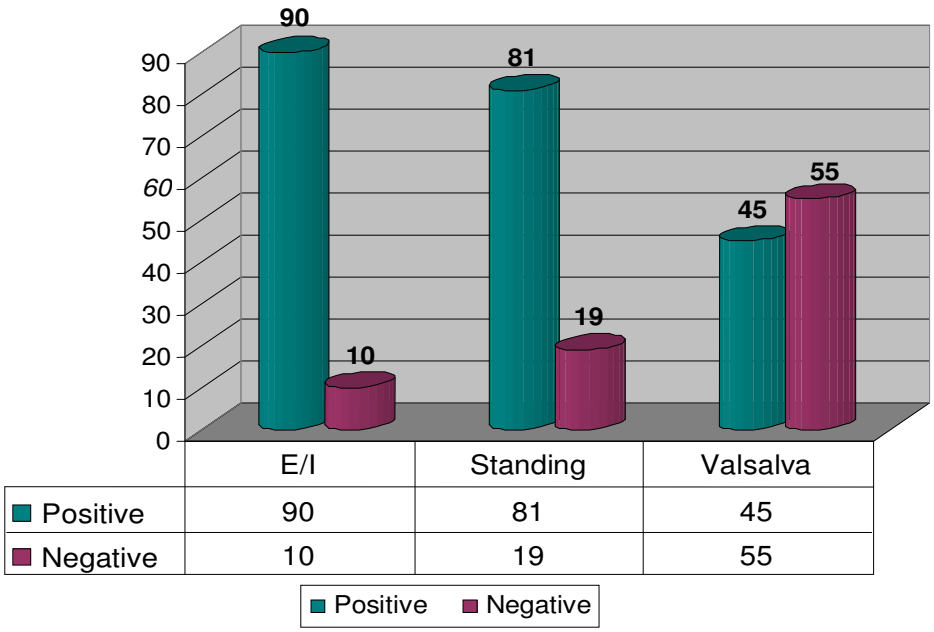


**Figure 1.** Percentage of positive E/I ratio, Valsalva maneuver and heart rate response to standing among 100 adult diabetic Sudanese patients in study carried in Al Noor and Herra Medical Centers in the period between January to June 2008.

differed from what was observed by Maser et al. (1990). Further studies were needed looking for the underlying causes like genetics, environmental and nutritional factors. A considerable number of our patients showed evidence of visual disturbances which can be a part of DAN or diabetic retinopathy. Also, abnormalities of the pupils in form of dilated, irregular and sluggish reaction to light were observed in a considerable number of the patients. A considerable number of our patients were hypertensive and this is similar to study conducted in Punjab (Raza et al., 2000). Symptoms of feet involvement were detected in a large number of patients (78%), most of them had poor glycemic control and they share features of both DAN and peripheral neuropathy.

Regarding examination of pupils for pallor and asymmetry, mouth for dental caries and dryness, skin for loss of hair, dryness and temperature and pulse rate for resting tachycardia and fixed heart rate, all of them are sings in favour of ANS involvement.

## Conclusion

1. Diabetic autonomic neuropathy is a very common problem among our studied group.
2. Neither age nor type of diabetes are limiting factors in its emergence, being found in young individuals with newly diagnosed Type 1 diabetes and older individuals newly diagnosed with Type 2 diabetes.
3. Poor glycemic control plays a central role in the development of DAN.

## RECOMMENDATIONS

Autonomic dysfunction is a prevalent and serious complication for individuals with diabetes. The clinical manifestations of autonomic dysfunction can affect daily activities (e.g., exercise), produce troubling symptoms (e.g., syncope), and cause lethal outcomes. The patient's history and physical examination are ineffective for early indications of autonomic nerve dysfunction, and thus recommendations for the use of non-invasive tests that have demonstrated efficacy are warranted. The economic impact of the recommendation to use autonomic function testing is minimal compared with the economic impact of the catastrophic events related to advanced cardiovascular, cerebrovascular, and renal complications. The relative cost of testing will always be less than the incremental costs of treating either a detected complication or the more catastrophic event that could eventually occur. Given the clinical and economic impact of this complication, testing of diabetic individuals for cardiovascular autonomic dysfunction should be part of their standard of care.

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