Section: Radiodiagnosis

Original Research Article

ROLE OF ULTRASONOGRAPHY IN EARLY DETECTION OF GASTROINTESTIONAL AUTONOMIC NEUROPATHY IN DIABETICS

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ABSTRACT

Background: Gastrointestinal autonomic neuropathy 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. There is no test to assess gastrointestinal autonomic nerve damage directly in humans at present. **Aim:** To evaluate the role of ultrasound for detecting the complications like autonomic neuropathy in patients with chronic diabetes at an earlier stage thereby preventing further progression of disease which helps to increase the quality of life

Materials and Methods: This is a Prospective observational study comparing the vagus nerve cross sectional area (CSA), Gall bladder volume in fasting and 45 minutes postprandial by real time ultrasonography and calculating Gall bladder contractility index (GBCI) in healthy controls and diabetics with and without autonomic neuropathy

Results: Our study showed significantly reduced GBCI with increased fasting and postprandial gall bladder volumes suggesting impaired gall bladder contractility in Diabetic patients with autonomic neuropathy compared to those without autonomic neuropathy and controls. Vagal nerve cross sectional area was also significantly reduced, indicating vagal nerve atrophy, in Diabetic patients with autonomic neuropathy compared to those without autonomic neuropathy and controls with no significant interside differences of Vagus nerve CSA in our study.

Conclusion: Ultrasonography is a simple, non-invasive, cost effective and easily available imaging modality which can be used as a screening tool in patients with chronic diabetes to detect complications like autonomic neuropathy at an earlier stage by calculating the gall bladder contractility index and Vagal nerve cross sectional area.

Keywords: Diabetic Gastrointestinal autonomic neuropathy, Ultrasonography, Gall bladder contractility index, Vagal nerve atrophy

INTRODUCTION

The prevalence of diabetes is continuously rising in India due to spread of modern life style and hence its associated complications are also increasing. Among various complications related to diabetes, diabetic neuropathy is the most common and serious complication. Diabetic gastrointestinal autonomic neuropathy (DGAN) is a complication of diabetes where nerve damage (neuropathy) affects the autonomic nervous system's control over the digestive system, leading to various gastrointestinal issues. This dysfunction can affect any part of the digestive tract, from the esophagus to the anus, and significantly impacts a patient's quality of life.[1,2]

The autonomic nervous system, especially the vagus nerve, plays a crucial role in regulating gastrointestinal function. Damage to these nerves in diabetes disrupts this regulation, impacting gastrointestinal motility and contributing to DGAN.[3] Gastrointestinal autonomic neuropathy 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.[4] There is no test to assess gastrointestinal autonomic nerve damage directly in humans at present. Hence, a trial had been made in this study to detect the autonomic neuropathy in diabetics earlier by using Ultrasonography which is a simple, non-invasive, cost effective and easily available imaging modality as a screening tool.

Aim

To evaluate the role of ultrasound for detecting the complications like autonomic neuropathy in patients with chronic diabetes at an earlier stage thereby preventing further progression of disease which helps to increase the quality of life

Objectives

The objective of this study is to detect autonomic neuropathy by assessing the changes in vagus nerve, GB volume and contraction index (GBCI) in diabetic patients either with or without autonomic manifestations as compared with controls.

MATERIALS AND METHODS

Study design: Prospective observational study comparing the vagus nerve cross sectional area (CSA), GB volume in fasting and 45 minutes postprandial by real time ultrasonography and calculating GBCI in healthy controls and diabetics with and without autonomic neuropathy.

Study tool: Ultrasonography of the abdomen and neck were performed on cases and controls on Esoate Mylab 7 ultrasound machine using curvilinear and linear transducers respectively.

Study population: 100-out of which 50 were cases having diabetics since more than 5 years and 50 were age matched controls without Diabetics.

Study period: One year (May 2024- April 2025).

Inclusion Criteria

- Randomly selected known cases of diabetes mellitus (diagnosed by the WHO criteria) from all the outpatient and inpatient departments of Rangaraya Medical College, GGH, Kakinada.
- The controls would include age matched non diabetics.

Exclusion Criteria

- Pregnant women.
- Patients with focal abnormalities of the gallbladder such as cholecystitis, cholelithiasis, choledocholithiasis and gallbladder inflammatory diseases and neoplasms.
- Extremely obese patients.
- Chronic alcoholics
- Those diagnosed with Parkinsonism disease
- Patients who have undergone truncal vagotomy.

Human participants protection

- The study was approved by the Institutional Ethics Committee of Rangaraya Medical College, reference number IEC/RMC/2025/1393.
- All methods were performed in accordance with the relevant guidelines and regulations as per the Declaration of Helsinki and other applicable ethical standards.
- Informed consent was obtained from each patient in their mother tongue.

Data collection method

For calculating Gall bladder contractility index

- The first reading was taken when the patient was fasting for 8 to 12 hours. After 45 mins of standard meal, repeat scan was performed and the gallbladder volume was recorded.[5]
- The examination was done in supine position.
- After visualization of the maximal gallbladder longitudinal outline, the measurements were taken on arrested respiration, with calipers crossing each other at 90 degree.
- Subsequently, the probe is rotated through 90 degree to obtain the maximal transverse dimension and the width was measured on arrested respiration.
- The volume of the gallbladder was taken by using these three measurements, that is the length, height and width of the gallbladder. The volume of the gallbladder is calculated using the ellipsoid formula.[6]

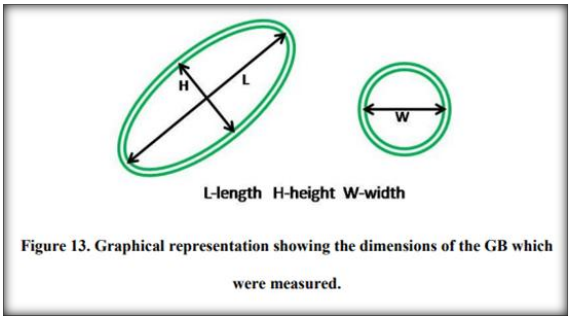


Figure 13. Graphical representation showing the dimensions of the GB which were measured.

$$= \frac{\pi \times L \times W \times H}{6}$$

- The gall bladder contraction index is the percentage decrement in gallbladder volume post ingestion of a meal.
- Gallbladder contraction index= [(fasting gallbladder volume–post meal gallbladder volume)/(Fasting gallbladder volume)] x 100

Vagus nerve imaging

- Participant position : Supine
- Head turned to the side opposite to the investigated site.
- Axial view was obtained at the level of the thyroid lobe.

- Both the carotid artery and internal jugular vein served as anatomical landmarks.
- The Vagus nerve was identified as a small rounded hypoechoic/or honeycomb structure wedged deep to the Carotid artery and Jugular vein.
- The cross-sectional area (CSA) of the Vagus nerve was measured by following the contour of the nerve just inside the hyperechoic rim with the probe exactly orthogonal to the nerve and with the least pressure applied.[7]

RESULTS

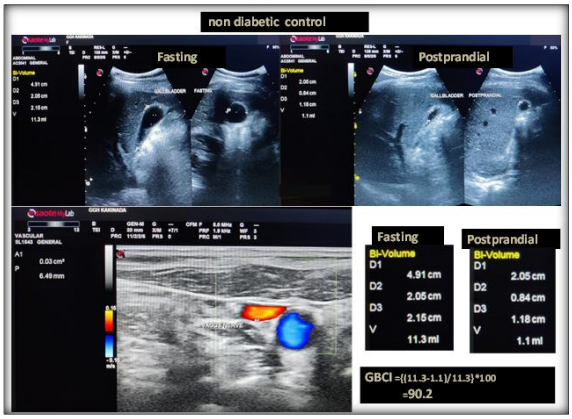
The study population consisting of 50 cases and 50 controls were in the age group of 25 to 60 years, out of which 54 were males and 46 females. Out of 50 cases 12 patient were clinically diagnosed to have autonomic neuropathy.

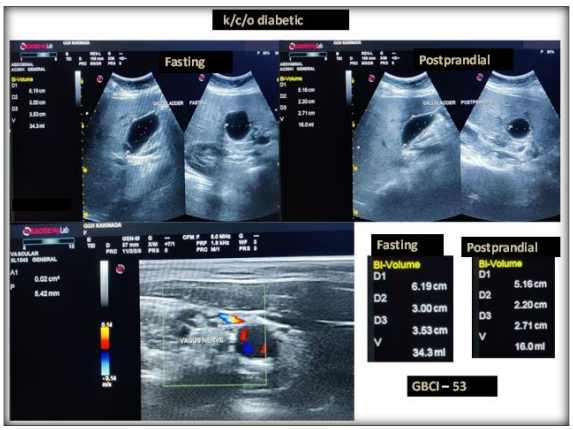
Fasting and postprandial gall bladder volume: The mean fasting gall bladder volumes (FGBV), were 17.56 ml, 24.50 ml, 34 ml and the mean postprandial gall bladder volumes (PPGV) were 10.24 ml, 18.93 ml, 27.8 ml in non diabetics, Diabetics without autonomic neuropathy and Diabetic patients with autonomic neuropathy respectively. The mean fasting and postprandial gall bladder volumes were significantly more in Diabetic patients with autonomic neuropathy compared to those without autonomic neuropathy and control group.

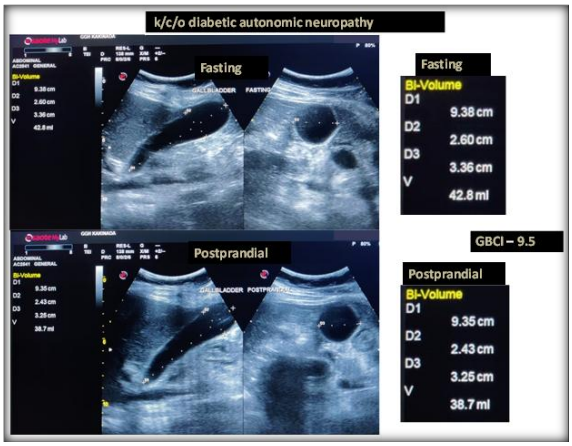
Gall bladder contractility index: The mean gall bladder contractility index was 43.09, 23.25 and 18.27 in non diabetics, Diabetics without autonomic neuropathy and Diabetic patients with autonomic neuropathy respectively. The gall bladder contractility index was significantly less in Diabetic patients with autonomic neuropathy compared to those without autonomic neuropathy and control group, indicating an impaired gall bladder contractility in Diabetic patients with autonomic neuropathy.

Vagal nerve cross sectional area: The mean vagal nerve cross sectional area in cm2 was 0.041, 0.031 and 0.018 cm2 in non diabetics, Diabetics without autonomic neuropathy and Diabetic patients with autonomic neuropathy respectively. The vagal nerve cross sectional area was significantly reduced in Diabetic patients with autonomic neuropathy compared to those without autonomic neuropathy and control group in our study, indicating an vagal nerve atrophy in Diabetic patients with autonomic neuropathy.

Side to side comparison of Vagus nerve CSA revealed no significant interside differences.[8]







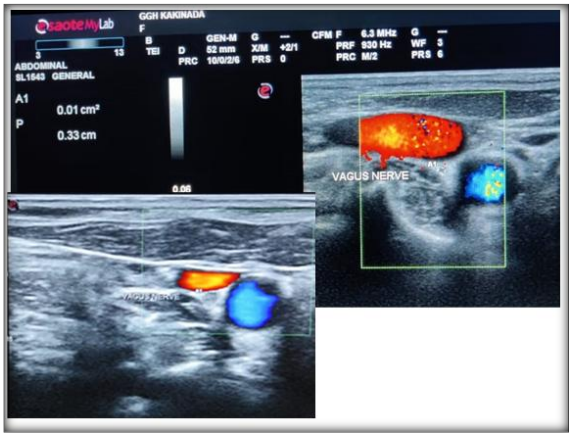


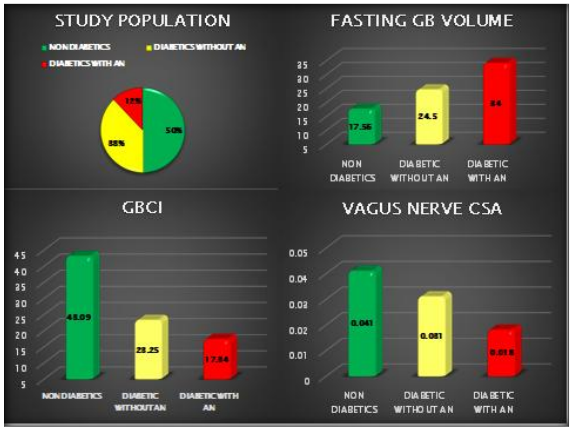
Table 1: Table showing maximum and minimum values, mean and standard deviation of different parameters used between controls and diabetics with and without autonomic neuropathy

Variable		Mean	Std deviation	Minimum	Maximum
Fasting GB volume (ml)	Non diabetic	17.56	4.18	3.1	26.5
	Diabetics without AN	24.5	4.4	17.4	34.3
	Diabetics with AN	34	5.4	25.8	42.2
GBCI	Non diabetic	43.09	12.05	18.3	90.2
	Diabetics without AN	23.25	6.94	8.5	40
	Diabetics with AN	18.27	6.33	5.4	27.5
Vagus Nerve CSA	Non diabetic	0.041	0.006	0.03	0.05
(cm^2)	Diabetics without AN	0.031	0.008	0.02	0.05
	Diabetics with AN	0.018	0.004	0.01	0.02

Table 2: Comparison Table of CSA, FGBV, PPGV and GBCI between controls and diabetics with and without autonomic neuropathy

Parameters		Non Diabetics (50)	Diabetics without Autonomic Neuropathy (38)	Diabetics with Autonomic Neuropathy (12)	Chi-square test	p value
Mean age		45.73 ± 3.19	42.35 ± 7.31	56.16 ± 8.85		
Sex	Male	27	19	8		
	Female	23	19	4		
CSA of Vagus nerve (cm^2)		0.041 ± 0.006	0.031 ±0.008	0.018 ± 0.004	41.026	<0.001*
Fasting Gallbladder volume (ml)		17.56± 4.18	24.50 ± 4.40	34 ± 5.40	38.828	<0.001*
Postprandial Gallbladder volume (ml)		10.24 ± 3.50	18.93 ± 4.41	27.8 ± 5.23	35.135	<0.001*
GBCI		43.09± 12.05	23.25 ± 6.94	18.27 ± 6.33	21.76	<0.001*

Comparison of CSA, FGBV, PPGV and GBCI between controls and diabetics with and without autonomic neuropathy



DISCUSSION

The prevalence of diabetes is continuously rising in India due to spread of modern life style so its associated complications are also increasing. Among various complications related to diabetes, diabetic neuropathy is the most common and serious complication. Diabetic Autonomic Neuropathy, a serious complication characterized by dysfunction of the autonomic nervous system, is among the least recognised and understood complications of diabetes despite having a significant negative impact on survival and quality of life in people with diabetes.[9]

In individuals with diabetes, autonomic neuropathy can significantly impact gallbladder function, leading to reduced gallbladder contractility, meaning the gallbladder doesn't empty as effectively after meals. This impaired contractility results in a larger gallbladder volume, both in the fasting state (before meals) and after meals, compared to individuals without diabetes.

In healthy individuals, during postprandial period there is an increase in the CCK levels favouring the gallbladder emptying time, whereas in diabetic patients with autonomic neuropathy the sensitivity of gallbladder to CCK is impaired and so the emptying time is delayed and invariably leading to increase in the gallbladder volume.[10,11]

As because both the fasting and postprandial gallbladder volume is high among the diabetic patients the gallbladder contraction index was found to be less in diabetic patients compared to non diabetic controls. In essence, the gallbladder's contractility index, which reflects its ability to empty, is significantly reduced in diabetics with autonomic neuropathy, making them more susceptible to gallbladder-related issues.[12,13,14]

Similarly in our study, the postprandial gallbladder volume was found to be significantly increased with significantly reduced gallbladder's contractility index among diabetic patients with autonomic neuropathy compared to diabetic patients without autonomic neuropathy and non diabetic controls. This was consistent with the studies done by KP Dhivya et al,[12] Kalyani DV et al,[13] and Doddamane K et al.[14]

The vagus nerve, a crucial component of the autonomic nervous system, is particularly vulnerable as it is the longest autonomic nerve and nerve damage in diabetes often starts with the longest nerves.

Studies using ultrasound have shown that the vagus nerve in diabetic patients exhibits a reduced cross-sectional area compared to healthy individuals. This indicates vagal nerve atrophy, which is associated with autonomic neuropathy.[15,16] Similarly in our study, the cross sectional area of vagus nerve was also found to be significantly decreased in diabetic patients with autonomic neuropathy compared to diabetic patients without autonomic neuropathy and non diabetic controls. This was consistent with the studies done by Tawfik EA et al,[15] and Kotb, Mamdouh Ali et al.[16]

In our study, both the fasting and postprandial gallbladder volumes were comparatively high among the diabetic patients without autonomic neuropathy and the gallbladder contraction index was found to be less in them compared to non diabetic controls, indicating the future risk of development of autonomic neuropathy in these people. Hence, showing that Ultrasonography is a simple, non-invasive, cost effective and easily available imaging modality which can be used as a screening tool in patients with chronic diabetes to detect complications like autonomic neuropathy at an earlier stage thereby preventing further progression of disease which helps to increase the quality of life.

CONCLUSION

- Diabetic patients had statistically significant larger fasting GB volume, lower GBCI and decreased vagal CSA. These values are highly significant amongst those with autonomic neuropathy.
- Impaired GB contraction was found amongst diabetics which is attributed to vagal neuropathy, therefore GB function should be routinely evaluated in such patients. This findings may have relevance in the diagnosis and treatment of diabetic neuropathy if further validated.
- Ultrasonography is a simple, non-invasive, cost effective and easily available imaging modality which can be used as a screening tool in patients with chronic diabetes to detect complications like autonomic neuropathy at an earlier stage thereby preventing further progression of disease which helps to increase the quality of life.

Limitations

- Correlation of gender or duration of diabetes with gallbladder volume and vagus nerve cross sectional area were not included in this study.
- Relatively small number of patients with severe parasympathetic involvement were enrolled in this study, future study with larger sample size are recommended.

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