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Comparative Gall Bladder Volume and Contractility Index in Diabetics and Normoglyceamics in Jos University Teaching Hospital

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Abstract. Diabetes mellitus is a syndrome of chronic hyperglycemia due to relative insulin resistance, insulin deficiency or both. It is a non-communicable disease of growing health importance and is implicated in the aetiology of autonomic neuropathy, one of which eventually leads to gall bladder dysfunction. This leads to increased prevalence of gallstones, increased fasting gall bladder volume and impaired contractility and motility of the gall bladder.

This was a cross-sectional comparative study where 66 diabetics and 66 normoglycaemics patients and control subjects age and sex matched were recruited and examined in Jos University Teaching Hospital. All the subjects had their gall bladder evaluated with ultrasound machine fitted with a 3.5MHz curvilinear transducer. The findings were documented for both fasting state and following ingestion of fatty milk. The results were expressed as percentages and tests of significance were done using the chi-square and Student's *t*-test. A P-value of < 0.05 was considered statistically significant. The mean fasting gall bladder volume of diabetic and normoglycaemic was 37.3±11.7cm^3 and 28.2±8.9cm^3 respectively and was statistically significant (P<0.05). The mean average post-prandial volume of diabetic and normoglycaemic was 23.0±13.8cm^3 and 15.1±6.2cm^3 respectively and was statistically significant (P<0.05). The average gall bladder contractility index of diabetic and normoglycaemic was 42.6±11.4% and 49.9±10.0% respectively and was statistically significant (P<0.05).

The study revealed that diabetics have significantly higher gall bladder volumes (fasting and post-prandial) with impaired gall bladder motility due to poor contractility from autonomic neuropathy.

Keywords: Ultrasound, Gall Bladder Volume, Contractility Index, Diabetes Mellitus, Autonomic Neuropathy

Introduction

Diabetes mellitus (DM) is a syndrome of chronic hyperglycemia due to relative insulin resistance, insulin deficiency or both (Gale & Anderson, 2006). It affects more than 120 million people worldwide and it is estimated that it will affect 370 million people by the year 2030 (Stephens, 2004). The prevalence of diabetes has reached an epidemic proportion with the figure of 10.2% in West Pacific and 3.8% in Africa (Ekpenyong *et al.*, 2012). It is estimated that people living with diabetes in Nigeria are over 1.5 million and a study in Jos put the prevalence of diabetes in adult urban population at 3.1% (Puepet *et al.*, 2007). However, Africa is expected to see the largest increase overtime and with the least resources to deal with the scourge (Gale & Anderson, 2006). Diabetes mellitus is usually irreversible, although patients

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can have a reasonably normal life style, its late complications result in reduced life expectancy and major health concerns. These complications include macrovascular disease leading to an increased prevalence of coronary artery disease, peripheral vascular disease, stroke and microvascular damage causing diabetic nephropathy, retinopathy and neuropathy (Bener *et al*., 2002).

The risk factors for diabetes mellitus include previous family history, middle age, obesity, physical inactivity, increased waist-hip ratio, alcohol intake and ethnicity (Alberti, 2001). There is an asymptomatic period of hyperglycaemia, being on an average 5-7 years. Many individuals tend to have complication at the time of diagnosis, which are micro and macrovascular (Rodrigues & Motta, 2012).

Among the various types of neuropathy, autonomic neuropathy (AN), although a well-recognized complication, is given less attention. In addition to manifestation in many other systems, autonomic neuropathy gives varied manifestations in gastrointestinal tracts i.e. gastroparesis, nocturnal diarrhoea, oesophageal dysmotility, constipation and gall bladder dysfunction, being consequences of vagal neuropathy leading to reduced gastrointestinal motility (Huang *et al*., 2010). Autonomic neuropathy leads to increased or large gall bladder volume and impaired gall bladder motility which are predictors of biliary stasis and the formation of biliary sludge and/or gallstones. Gall bladder involvement in diabetic neuropathy results in high incidence of gallstones, significant increase in gall bladder volume and poor contractility or motility of the gall bladder (Shakil, Church, & Rao, 2008).

Radiological investigation of gall bladder and biliary tree has evolved from cholecystography to more modern modalities such as dynamic ultrasound, dynamic cholescintigraphy, computed tomography scan, magnetic resonance cholangio-pancreatography and endoscopic retrograde cholangio-pancreatography. However most of these modalities have become less popular due to use of ionizing radiation, contrast media, cost and duration of performing the study (Shakil, Church, & Rao, 2008).

This study aimed at determining and comparing fasting gall bladder volume and contractility index (GBCI) in adult diabetics and normoglycaemic controls.

Materials and Methods

The study was carried out over a period of 13 months in the Department of Radiology, Jos University Teaching Hospital, Jos-North Central Nigeria in which 66 diabetic patients were recruited from medical endocrinology clinic while 66 normoglycaemic controls were recruited from General Outpatients Department (GOPD). The main inclusion criteria for diabetics were uncontrolled glycaemic level (FBS$\geq$ 7mmol/L) and age$\geq$ 18 years and who were on treatment irrespective of sex and/or duration of disease while inclusion criteria for normoglycaemics were FBS < 7.0mmol/L and age greater 18 years.

A non-probability convenience sampling method was used in recruiting eligible participants consecutively from the endocrinology clinic and general out-patient clinic until the sample size of 132 was reached.

Ethical approval was obtained from the Research and Ethnical committee of Jos University Teaching Hospital and Informed consent was obtained from the subjects before enrollment into the study.

Evaluation of the Gall Bladder

The weights of the subjects were measured on a bathroom scale and the height (meter) measured on a calibrated vertical wall. The body mass index (BMI) was obtained as weight (Kg)/ height (m^2).

Real time gray scale abdominal ultrasound examination was performed using General Electric (GE) Logic V5 Series S/W Functions, China, 2017, ultrasound machine fitted with a

3.5MHz curvilinear transducer in the privacy of the ultrasound suite after 8 hours or overnight fast.

The transducer was placed on the right subcostal area to obtain the long-axis view by varying the obliquity of the transducer until visualization of the maximal gall bladder longitudinal outline was seen, where the length and maximal antero-posterior diameter (height) were taken in arrested respiration with calipers crossing each other at 90^0. Subsequently the transducer was rotated through 90^0 to obtain the maximal transverse dimension and the width was measured in arrested respiration.

Three serial ultrasound scans of the gall bladder in the supine position were carried out for each subject as follows:

- fasting state;
- ten minutes after ingesting 200 mls of milk;
- twenty minutes after ingesting 200 mls of milk.

This enabled the variations of gall bladder volume to be studied as well as the contractility index i.e. ejection fraction to be obtained.

Gall bladder volume was obtained using the formula for a prolate ellipsoid (Pallotta *et al.*, 1994).

Volume (cm^3)=0.523x length (cm) x width (cm) x height (cm).

The average values were calculated following three serial measurements.

GBCI is defined as the percentage decrement of post-prandial size from initial size and calculated using the following formula (Ugwu, Eteudu, & Njoku, 2007).

Ejection Fraction (EF) % =

$$\frac{\text{Fasting gall bladder volume} - \text{Postprandial gall bladder volume}}{\text{Fasting gall bladder volume}} \text{ X } 100$$

In determination of contractility index, the measurements were performed at 10 and 20 minutes following milk ingestion. These time frames are in keeping with gall bladder emptying rate following fatty meal and the gall bladder contractility index was obtained at 10 and 20 minutes using fasting and post-prandial gall bladder volumes. The mean of the two values of GBCI was adopted as the actual GBCI.

Data Analysis

The data acquired was analyzed using the Statistical Package for Social Science SPSS (Version 23.0 by SPSS incorporation, Chicago, Illinois, USA, 2017). The continuous variables were expressed as means and standard deviation (SD). Further analysis with student's t-test for comparison between the diabetics and normoglycaemics was used. The correlation between fasting gall bladder volume and contractility index in diabetics and parameters such as age, body mass index, and duration of disease were determined using the Pearson correlation co-efficient. Chi – square test was also used to compute for association between variables. The results were documented in the form of tables and charts as appropriate. Statistical level of significance was set at $p \leq 0.05$.

Results

The mean age for male and female diabetics were 50.7±10.9 years and 48.3±9.5 years respectively while the mean age for male and female normoglycaemics were 41.0±14.5 years and 41.3±13.3 years respectively (Table 1).

Table 1. Age and sex matched distribution of subjects

	Diabetic				Normoglycaemic			
Age group of participants (years)	Male	%	Female	%	Male	%	Female	%
18-27	1	4.2	1	2.4	4	16.7	5	11.9
28-37	2	8.3	5	11.9	5	20.8	11	26.2
38-47	5	20.8	12	28.6	6	25.0	8	19.0
48-57	8	33.3	19	45.2	5	20.8	14	33.3
58-67	7	29.2	4	9.5	2	8.3	2	4.8
68-77	1	4.2	1	2.4	2	8.3	2	4.8
Total	24	100.0	42	100.0	24	100.0	42	100.0
Mean±SD	50.7± 10.9		48.3± 9.5		41.0± 14.5		41.3± 13.3	

The mean BMI for the diabetic and normoglycaemic were 27.5±4.8 kg/m^2 and 25.1 ±5.1 kg/m^2 respectively. This was statistically significant (P<0.05; Table 2).

Table 2. Relationship between mean age and BMI of subjects

Variables	Overall Mean±SD	Diabetic subject Mean±SD	Normoglycaemic subject Mean±SD	t	P-value
Age (years)	45.2±11.8	49.2±10.0	41.2±13.6	3.819	0.001*
BMI (Kg/m^2)	26.33±5.1	27.5±4.8	25.1±5.1	2.776	0.006*

The average fasting gall bladder volumes (FGBV) were 37.3± 11.7cm^3 and 28.2±8.9cm^3 for diabetics and normoglycaemic respectively. This was statistically significant (*P*= 0.001; Table 3).

The average fasting blood sugar levels (FBS) were 9.0 ±3.9 mmol/L and 3.6±0.5 mmol/L for diabetics and normoglycaemic respectively. This was statistically significant (*P*= 0.05; Table 3)

Table 3. Relationship between the means of FGBV and FBS in the subjects

Variables	Overall Mean±SD	Diabetic subject Mean±SD	Normoglycaemic subject Mean±SD	t	P-value
FGBV (cm^3)	32.8±10.3	37.3±11.7	28.2±8.9	5.018	0.001*
FBS (mmol/l)	6.3±2.3	9.0±4.1	3.6±0.5	10.619	0.001*

Note: * = significance at P ≤ 0.05 level

The mean FGBV for male diabetic and normoglycaemic were 36.9±9.8 cm^3 and 27.2 ± 5.2 cm^3 respectively. This was statistically significant (*P*<0.05), while for female diabetic and normoglycaemics were 37.5±12.8cm^3 and 28.7 ±10.5cm^3 respectively. This was also statistically significant (*P*<0.05; Table 4).

Table 4. Relationship between sex and average FGBV in the subjects

FGBV (cm^3)	Diabetic subject (Mean±SD)	Normoglycaemics (Mean±SD)	t	P-value
Male	36.9±9.8	27.2±5.2	4.290	0.001*
Female	37.5±12.8	28.7±10.5	3.429	0.001*

Note: * = significance at P ≤ 0.05 level

There was statistically significant relationship between average FGBV and age of subjects and BMI (*P*<0.05 and *P*<0.05) respectively, however there was no statistically significant relationship with duration of disease (*P*>0.05). There was positive linear correlation between fasting gall bladder volume (FGBV) with age of subjects, BMI and duration of disease (r=0.391, r=0.405, and r=0.150 respectively, Figure 1).

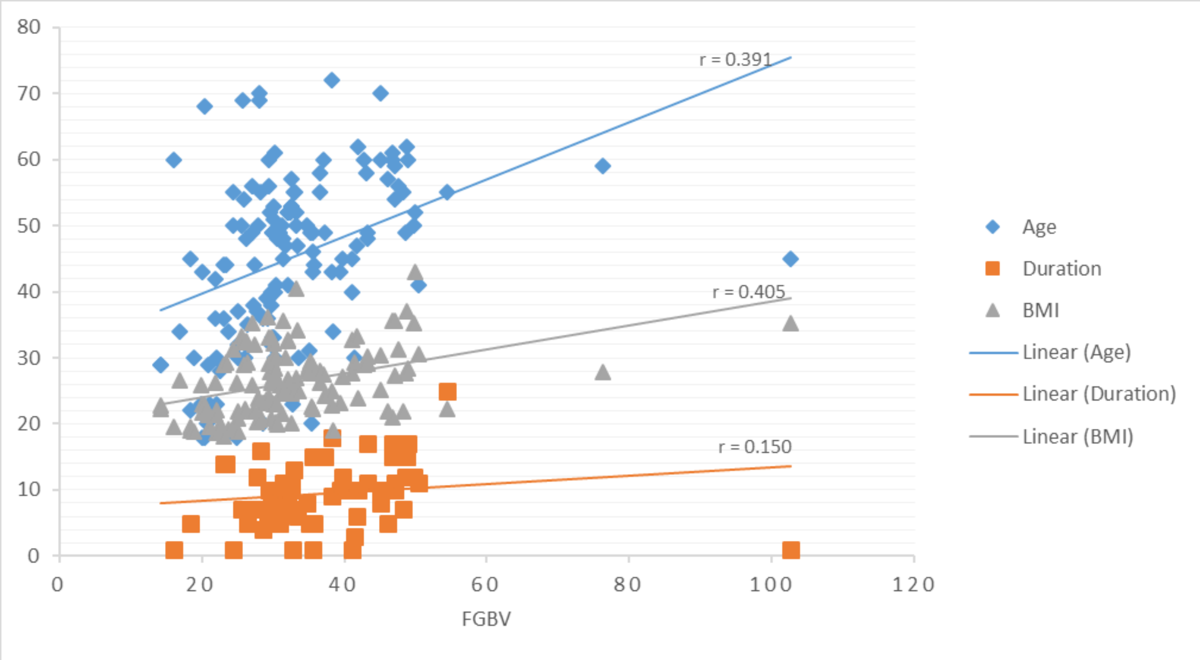

Figure 1. Scatter diagram showing relationship between FGBV and age, BMI & duration of disease

The post-prandial volume (PPV) at 10 minutes for the diabetic and normoglycaemic were 25.2±9.9cm^3 and 17.1±7.0cm^3 respectively. This was statistically significant (*P*<0.05).

At 20 minutes, the PPV for diabetics and normoglycaemic were 20.9±22.5cm^3 and 11.2 ±5.3cm^3 respectively. This was statistically significant (*P*<0.05).

The average PPV for diabetics and normoglycaemics were 23.0±13.8 cm^{3}and 15.1±6.2 cm^3 respectively. This was statistically significant (*P*<0.05; Table 5).

Table 5. PPV parameters and relationship in subjects

Variables	Overall subjects Mean±SD	Diabetic subject Mean±SD	Normoglycaemic subject Mean±SD	t	P-value
10 mins PPV (cm^3)	21.2±8.5	25.2±9.9	17.1±7.0	5.794	0.001*
20 mins PPV (cm^3)	16.1±13.9	20.9±22.5	11.2±5.3	3.147	0.002*
Average PPV (cm^3)	19.1±10.0	23.0±13.8	15.1±6.2	4.765	0.001*

Note: * = significance at P ≤ 0.05 level; PPV=Post-prandial volume

The mean PPV for male diabetics and normoglycaemics were 24.1±18.8 cm^3 and 15.4±3.9 cm^3 respectively. This was statistically significant (*P*<0.05) while the mean PPV for female diabetics and normoglycaemics were 22.4±10.2 cm^3 and 15.0±7.3 cm^3 respectively. This was also statistically significant (*P*<0.05; Table 6).

Table 6. Relationship between sex and PPV in the subjects

Variables	Diabetic subject (Mean±SD)	Normoglycaemics (Mean±SD)	t	P-value
PPV (cm^3)				
Male	24.1±18.8	15.4±3.9	2.227	0.031
Female	22.4±10.2	15.0±7.3	3.838	0.001

Note: * = significance at P ≤ 0.05 level; PPV=Post-prandial volume

There was statistically significant relationship between average PPV and Age of diabetics as well as the BMI (*P*<0.05 and *P*<0.05) respectively with a positive linear correlation between them (r=0.230 and r=0.287) respectively. However, no statistical significant relationship with the duration of disease (*P*>0.05) though a positive linear correlation with the duration of the disease was seen (r=0.088; Figure 2).

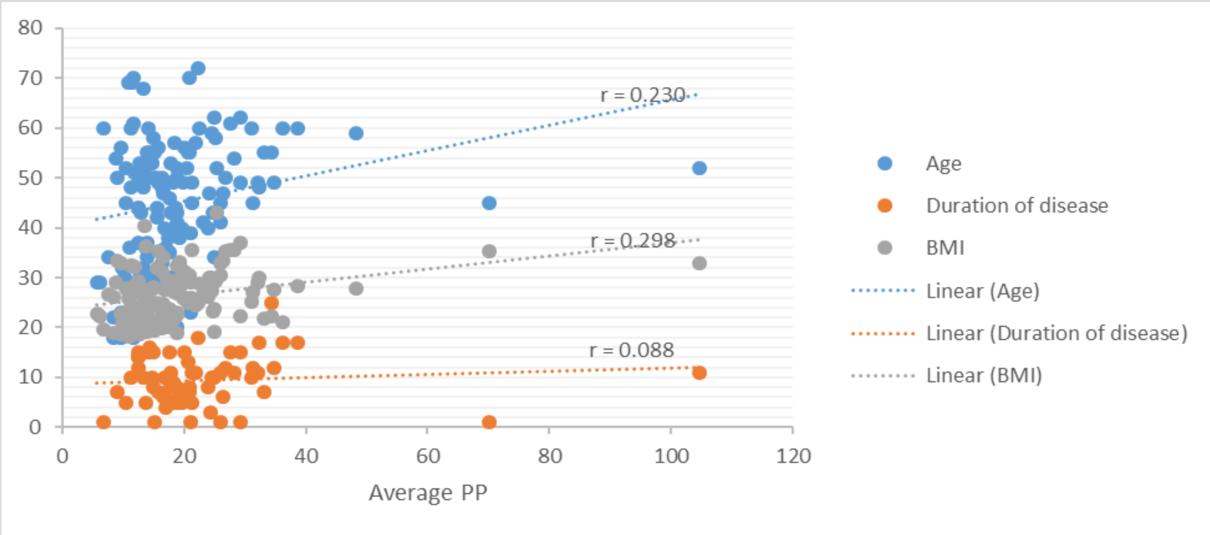

Figure 2. Scatter diagram showing relationship between average PP and age, BMI & duration of disease

The mean gall bladder contractility index (GBCI) at 10 minutes was 33.1 ±12.0% and 39.5±11.9% for diabetics and normoglycaemic respectively. This was statistically significant (*P*<0.05).

The mean GBCI at 20 minutes was 52.0±12.3% and 60.3±10.6% for diabetics and normoglycaemics respectively. This was statistically significant (*P*=0.001).

The average GBCI was 42.6±11.4% and 49.9±10.0% for diabetic and normoglycaemic respectively. This was statistically significant (*P*<0.05; Table 7).

Table 7. GBCI parameters and relationship in subjects

Variables	Overall $\bar{x}$±SD subjects	Diabetic subject $\bar{x}$±SD	Normoglycaemic subject $\bar{x}$±SD	t	P-value
GBCI (%) at 10 mins	36.3±12.0	33.1±12.0	39.5±11.9	-3.070	0.003*
GBCI (%) at 20 mins	56.2±11.5	52.0±12.3	60.3±10.6	-4.170	0.001*
Average GBCI (%)	46.3±10.7	42.6±11.4	49.9±10.0	-3.932	0.001*
Duration of DM	-	9.45±4.9			

* = significance at P ≤ 0.05 level

Discussion

Diabetes Mellitus affects people of all ages, but is most common in people 45–64 years of age in developing countries and >64 years of age in developed countries (Kramer & Molitch, 2005). The predominant age group amongst the diabetics was 48-57 years. This is in agreement with the work of Karmer and Molitch (2005) that showed that Diabetes Mellitus affects people 45-64 years of age in developing countries and that increasing age is a risk factor for development of gall bladder disease. The mean age groups of male and female diabetics in this study were 50.7±10.9 years and 48.3±9.5 years respectively. For the normoglycaemics, mean age group was 41.0±14.5 years for males and 41.3±13.3 years for females. This is in agreement with a study by Osawe *et al.* (2016) that documented mean age group for diabetic male and female as 46.7 years and 43.5 years respectively; for normoglycaemic male and female as 36.9 years and 31.6 years respectively.

The mean FGBV was higher in diabetics (37.3±11.7 cm^3) than in normoglycaemics (28.2±8.9 cm^3). Similar findings have been observed by Rai *et al.* (2016), who documented 45.3 ±3.4cm^3 and 29.9±3.0cm^3 for diabetics and control respectively. The fasting blood sugar (FBS) was significantly higher in diabetics, which is expected ($P<0.05$) and implies that the higher the FBS, the higher the FGBV. The FGBV was also higher in female diabetics than in female normoglycaemics, which is of statistical significance and corroborated by similar studies (Osawe *et al*., 2016; Rai *et al*., 2016; Jain & Poranjape, 2013).

There is positive linear correlation between fasting gallbladder volume and BMI, age of patients and duration of disease in this study. This association is strong for BMI and the age of subjects. However, the relationship with the duration of disease is weak. This means that the higher the BMI, the age of subjects and the duration of disease, the higher the FGBV.

These findings are consistent with previous studies in which it was found that FGBV is higher in diabetics than in normoglycaemics (Olokoba *et al*., 2006; Chhabra *et al*., 2013; Agarwal *et al.*, 2004).

The Post-Prandial Volume (PPV) was also found to be higher in diabetics than in normoglycaemics at 10 minutes and 20 minutes. The average PPV was also higher (23.0±13.8 cm^3) in diabetics than in normoglycaemics (15.1±6.0cm^3). This was statistically significant, suggesting that PPV is raised in Diabetes Mellitus and is consistent with findings in similar studies in which it was found that patients with diabetes had statistically significant higher PPVs than those without; more significant in those with diabetic neuropathy (Kayacetin *et al.*, 2003, Gaur *et al.*, 2000).

The Gall Bladder Contractility Index (GBCI) was lower in diabetics than in normoglycaemics at both 10 minutes and 20 minutes. This was consistent with findings of Ugbaja *et al.* (2015) in where GBCI was lower in diabetics (without neuropathy 33.4± 13.6%; 39.6± 15.2% with neuropathy) than in control (47.7± 18.4%). Other studies also established a similar pattern among the diabetics and normoglycaemics which showed that decrease gall bladder tone is associated with long standing type II diabetes mellitus, was as a result of impairment in gall bladder ejection (Osawe *et al.*, 2016; He *et al.*, 2001; Singh *et al.*, 2006).

The Mean GBCI was slightly lower in female diabetics (41.1± 11.0%) than in male diabetics (45.0± 12.0%). This is at variance with the findings of Osawe *et al.* (2016) which showed that female diabetics had higher GBCI than males. It is however similar to findings in a study by Saxena, Sharma, and Dubey (2005) in which GBCI was lower in females, though this could have been because there was a high incidence of calculi in their population, which has a negative effect on contractility.

There was no statistically significant relationship between GBCI, BMI, Age and duration of disease. There was, however, a positive linear correlation of weak strength with duration of disease which is inconsistent with similar studies which made a negative correlation with duration of disease but only in those with neuropathy which was not assessed in this study (Ugbaja *et al.*, 2015; Parkman *et al*., 2010).

The negative relationship between gall bladder contractility index with duration of disease signifies that there has been enough time for the gall bladder complications to set in, therefore, the higher the duration of disease, the lower the GBCI. The higher the BMI, the lower the GBCI. The higher the age, the lower the GBCI. Similar study in the past alludes to this fact that gall bladder tone reduces with age (Jain & Poranjape, 2013).

Conclusion

This study revealed that diabetics have higher gall bladder volumes (fasting and post-prandial) with impaired gall bladder motility due to poor contractility consequent on autonomic neuropathy.

The study also revealed a statistically significant relationship between gall bladder volumes with age of diabetic subjects and body mass index with a positive correlation with age of patients, body mass index and duration of disease.

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