https://africanjournalofbiomedicalresearch.com/index.php/AJBR
Afr. J. Biomed. Res. Vol. 27(4s) (November 2024); 4056-4063
Research Article

Correlation between Fasting Blood Glucose, Serum Ferritin and Glycated Haemoglobin (Hba1c) Level in Patients of Type 2 Diabetes Mellitus

Razook Fareedh J[1], Suresh K[1], Prabhu G[1], Ilandevan K[1*]

[1*]Department of General Medicine, Sri Venkateshwaraa Medical College Hospital and Research Centre, Puducherry, India.

[*]**Corresponding Author:** Ilandevan K
Email ID: ilandeva92@gmail.com

Abstract:
The study was undertaken to evaluate the correlation of serum ferritin with fasting blood sugar and HbA1c in diabetes mellitus and to assess the possible relation between them to have better understanding of the disease process. Fasting blood sugar, serum ferritin and HbA1c were assayed in type 2 diabetic patients. Hyperglycemia was observed in all the diabetic patients. Serum ferritin levels in diabetic cases were significantly higher and also statistically significant.

Persistent hyperglycemia in uncontrolled diabetics can cause damage via increased production of free radicals especially ROS, from glucose auto-oxidation and inflammation. Elevated levels of serum ferritin are triggered by inflammation, independent of iron stores. Low- grade inflammation plays a predominant role in the pathogenesis of diabetes mellitus. Reactive oxygen species interfere with insulin signaling and may be the main mechanism for insulin resistance resulting in hyperglycemia.

Increased glucotoxicity contributes to oxidative stress and increased predisposition to inflammation consequently resulting in elevated serum ferritin levels.

Due to hyperglycemia, there is enhanced oxidative stress sequentially leading to increased inflammation and endothelial dysfunction. Elevated levels of inflammation predisposes to decline in sensitivity to insulin further triggering the cyclical process and resulting in detrimental effects in diabetes mellitus. The pathological sequence for type 2 diabetes is complex and entails many different elements that act in concert in the progression of the disease. Thus, a focus on reducing glycemia alone is inadequate to diminish the damaging effects in diabetes, highlighting the need for aggressive treatment of other risk factors.

Keywords: Type 2 diabetes mellitus, hyperglycemia, fasting blood sugar, serum ferritin, HbA1c, and inflammation.

***Author for correspondence: Email:** *ilandeva92@gmail.com*

Received 19/11/2024, Acceptance 25/11/2024

DOI: https://doi.org/10.53555/AJBR.v27i4S.4349

Introduction:
Diabetes mellitus (DM) is one of the most common diseases of current era which is characterized by hyperglycemia either due to insulin deficiency or insulin resistance. Type2 DM is also leading cause of coronary artery disease, peripheral artery disease, end-stage renal disease (ESRD) and adult blindness. With an increasing incidence worldwide, DM will be a

leading cause of mortality and morbidity [1]. The explosive increase of Diabetic population worldwide is a major public health concern both in developing and developed countries. Metabolic syndrome is also on an increasing trend. The metabolic syndrome is closely linked to insulin resistance and numerous studies indicate a link to iron overload. Increased serum ferritin, reflecting body iron overload, is often associated with measures of insulin resistance, such as elevated blood glucose and insulin levels [2].

Serum ferritin is an acute phase reactant and is a marker of iron stores in the body [3]. Iron is a transitional metal that can easily become oxidised and thus act as an oxidant [4]. Recent studies have shown that serum ferritin was proportional to serum glucose concentration, diastolic blood pressure, HDL cholesterol and insulin resistance. In fact, the higher the ferritin levels the higher the incidence of Type 2 Diabetes [5]. Hence our study was aimed to establish a correlation between serum ferritin with glycated Hemoglobin level in patients with type 2 diabetes mellitus.

Materials and Method:

The present study was carried out in Sri Venkateshwaraa Medical College Hospital and Research Centre which is a 750 bedded Multi Disciplinary Centre serving the rural population. The study was carried out in the department of General Medicine in association with diabetology clinic.

Type of Study: Cross-sectional study

Period of study: From NOV 2017 to MAY 2019

Study Population: Patients with Type 2 Diabetes Mellitus selected by random sampling from those admitted in medical wards and those who present to Medicine OPD.

Sample size: Sample size was calculated for correlation between HbA1c and serum ferritin in type 2 diabetes mellitus based on previous studies which showed that correlation coefficient (r) between HbA1c and Serum Ferritin was 0.66, assuming α error of 1% and β error of 10%. Sample size was calculated to be 27. So 50 diabetic and 50 non diabetic subjects will be included in the study.

Group-I-Control; Group-II-TYPE 2DM

Inclusion criteria:

- Age between 35 to 70 years of both gender with type 2 diabetes mellitus

Exclusion criteria:

- Age <35 and >70 years
- Chronic kidney disease
- Severe Anemia
- Liver disease / malignancy
- Patients of iron supplements
- Diabetics with history or evidence of conditions leading to iron loss like gastro intestinal blood loss, history of blood transfusion or donation in past 3 months.
- Subjects with chronic infection
- Patient on corticosteroid

Method of data collection:

All type 2 diabetic patients attending to medical and diabetology department in Sri Venkateshwaraa Medical College Hospital and Research Centre were included in the study after obtaining informed concern and description of the procedure. After documenting the demographic data of the patients, details of clinical history and diabetes was obtained from the patients. A thorough general physical examination and a detailed systemic examination was obtained and documented as in Performa.

Interventions/Investigations needed:

Sample collection: After all the required procedures the patients were subjected for investigations. The investigations done were HbA1c, fasting blood sugar and serum ferritin levels.

5 mL of fasting blood sample will be collected and centrifuged for serum/plasma separation. Sample will be analysed for the measurement of plasma glucose by glucose oxidase-peroxidase method, whole blood will be taken in EDTA vial for HbA1c and serum ferritin will be assessed by ELISA method by commercially available kit.

Measurement of fasting blood glucose: Serum concentration of glucose was estimated by using analytical kits from Erba Diagnostics Mannheim GmbH in semi-autoanaylzer (CHEM-5 Plus V2, Erba Mannheim).

Measurement of testing HbA1c: Glycated hemoglobin was estimated by Nephelometry kits from Agappe in MISPA-i card reader.

Measurement of testing serum ferritin: Serum concentrations of ferritin, was estimated by Chemiluminiscence immunoassay (CLIA) kits from Acculite Monobind in Lumax CLIA strip reader.

Normal Value:

Men: 20-350 µg/ml; Women: 10-200µg/ml.

Statistical Analysis: Statistical analysis was done by using SPSS version 23.0.

Results and Discussion:

In the present study we had evaluated 100 subjects including 50 controls and 50 type 2 diabetic subjects. Of the 50 type 2 diabetic subjects, 34 were males and 16 were females and among controls, 38 were males and 12 were females.

In our study it was found that maximum patients affected were male group under the age of 51-60 years (20 patients), followed by the age group of >60 years (19 patients), and the age group of 41-50 years (11 patients) (**Table-1, Fig.1**). This is similar to various other studies in our country some was done by Ramesh

Chandra Thanna *et al*. [6]. The mean age of the study group was 54.5±8.5 years, study done by Poonam Arora *et al*. [7] mean age of diabetic patients was 52.37± 7.98 years.

In our study we conclude that male patients dominated the both study and the control group. Male: female ratio was 68%:32% (**Table-2, Fig.2**). This is similar to other studies form our country, study done by Ramesh Chandra Thanna [6] showed M:F - 64:36.

The mean ± SDs of BMI in controls and type 2 diabetic subjects were in the range of 22.60±2.60 mg/dL and 26.34±2.31 mg/dL respectively. The mean value of BMI was higher in type 2 diabetic subjects compared to controls (**Table-3, Fig.3**). Various other studies done in our country demonstrated BMI among diabetic respectively; mean BMI was 24.85kg/m2 in Ramesh Chandra Thanna [6] and mean BMI was 23.95 ± 3.15 kg/m2 in a study done by L. S. Patil *et al*. [8].

The mean ± SDs of fasting serum glucose in controls and type 2 diabetic subjects were in the range of 90.93 ± 6.27 mg/dL and 188.20 ± 58.89 mg/dL, respectively. The mean value of fasting serum glucose was higher in type 2 diabetic subjects compared to controls (**Table-4, Fig.8**). The increase is found to be statistically highly significant ($p < 0.001$) which is in accordance with Mahajan A *et al*. [9] 4.92 (4.50–5.31) (mmol/liter) and 7.67 (6.33–10.28) (mmol/liter) & Meshram A *et al*. [10] 82 ± 6.2 mg/dL and 140 ± 5.1 mg/dL.

Hyperglycemia in DM is caused by both overproduction and underutilization of glucose. There is a relative excess of glucagon also. As a consequence, glucose production is increased rather than consumption by liver, and also there is drastic reduction of uptake of glucose into muscle and adipose tissue finally contributing to hyperglycemia [11].

In our present study, 10 patients only affected by Hypertension and 40 patients were in absence (**Table-5, Fig.5**).

The mean ± SDs of HbA1c in controls & type 2 diabetes were in the range of 5.42 ±0.47 & 8.59 ± 1.83 %, respectively (**Table-6**). The mean value of HbA1c was higher in type 2 diabetic subjects as compared to controls. The increase was statistically highly significant ($p < 0.001$). This is in accordance with Dalan R et al 4.42 ± 0.37 & 7.59 ± 1.43 % [12].

Glycated hemoglobin concentration represents the integrated values of glucose over preceding 6 to 8 weeks since the rate of formation of HbA1c is directly proportional to the concentration of glucose in blood.

It is currently considered as the best index of metabolic control for diabetic patients in clinical setting. It is as well a measure of risk for the development of micro and macrovascular complications [13, 14].

The most important factor governing the quantity of glycated hemoglobin formed is the prevailing plasma glucose concentration. As the plasma glucose concentration is increased in diabetic subjects, glycated hemoglobin also increased in diabetic subjects [15].

It represents the mean daily blood sugar concentration and degree of carbohydrate imbalance, better than fasting blood glucose concentrations or glucose tolerance test results. Hence it may provide a better index of control of diabetic patient without resorting to a glucose loading procedure [16].

The mean ± SDs of ferritin in controls and type 2 diabetic subjects were in the range of 101.55 ± 78.76 ng/mL and 263.34 ± 82.65 ng/mL respectively (**Table-7**). The mean value of ferritin in type 2 diabetic subjects was higher when compared to controls. The increase was found to be statistically highly significant ($p < 0.001$). This is in accordance with the Sharifi F *et al*. [45] & Abou-Shousha S.A [17].

In the present study we also found positive correlation existed between ferritin, BMI and HbA1c in type 2 a diabetic subject which was statistically significant (**Table-8**). This is in accordance with Shetty J.K *et al*. [18] & Kim N.H *et al.* [19].

Ferritin is one of the key proteins regulating iron homeostasis, is widely available clinical biomarker to evaluate iron status. However, growing evidence has shown that even moderately increased iron stores represented by high-normal ferritin concentrations are associated with diabetes [20].

At least three possible explanations may account for elevated ferritin concentrations in patients with diabetes.

1) Elevated ferritin concentrations may represent elevated body iron stores.

2) Ferritin is also an acute-phase reactant and elevated ferritin concentrations may reflectinflammation.

3) Delayed clearance of glycosylated ferritin in patients with diabetes may have led to the elevated ferritin concentrations [21].

Excess iron deposition in the liver may cause IR by interfering with theability of insulin to suppress hepatic glucose production. Iron is autoxidized to form highly reactive lipid soluble iron-oxygen complexes.

Conclusion

Chronic hyperglycemia predispose to inflammation in diabetes mellitus. Hyperglycemia itself can impair pancreatic beta cell function and exacerbate insulin resistance, leading to a vicious cycle of hyperglycemia causing a worsening metabolic state.

A significant increase in serum ferritin levels are observed in diabetes. This rise in ferritin levels are independent of iron stores, as haemoglobin levels are within reference range. This increase in serum ferritin levels which is indicators of inflammation. Inflammatory response may have a dual role in DM, either it can have a causal relationship leading to insulin resistance or the response can be intensified by the hyperglycaemic state ensuring in vascular complications. In conclusion, inflammatory pathways play a pivotal role in the development and progression of diabetic complications. Modulation of inflammatory processes in diabetes by therapeutic interventions will have beneficial actions on diabetes.

References

1. Fauci AS, Kasper DS, Longo DL, Braunwald E, Hauser SL, Jameson JL, et al. Harrison's Principles of internal medicine. United State, 18th Edition 2012
2. Jiang R, Manson JE, Meigs JB, Ma J, Rifai N, Hu FB. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. JAMA 2004; 291:711-7.
3. Koorts AM, Viljoen M. Acute phase proteins: Ferritin and ferritin isoforms. University of Petoria, South Africa 2011; 154-84
4. Forouhi NG, Harding AH, Allison M, Sandhu MS, Welch A, Luben Re et al. Elevated serum ferritin levels predict new-onset type 2 diabetes: results from the EPIC-Norfolk prospective study. Diabetologia 2007; 50: 949-56.
5. Wrede CE, Buettner R, Bollheimer LC, Scholmeirch J, PalitzschK-D and Hellerbrand C. Association between serum ferritin and the insulin resistance syndrome in a representative population. Eur J Endocr 2006; 154: 333-40.
6. Ramesh Chandra Thanna, Shreya Nigosker Level of Serum ferritin and Glycated hemoglobin (HbA1C) in type 2 diabetes mellitus. International Journal of Medical and Health Research. ISSN: 2454-9142.
7. Arora: Serum Ferritin in Type 2 Diabetes Mellitus Int J Cur Res Rev | Vol 9 • Issue 6 • March 2017.
8. L. S. Patil, Dr. Timmanna Giraddi, Dr. Deepak Chinagi, Dr. Prasad Ugaragol and Dr. Banashankari Kolluru, 2017. "A study on relation between serum ferritin and glycated hemoglobin in type 2 diabetes mellitus", International Journal of Current Research, 9,(08), 55849-55853
9. Mahajan A et al. High-Sensitivity C-reactive protein levels and type 2 diabetes in urban north Indians. J Clin Endocrinol Metab.2009;94(6):2123-127
10. Meshram A et al. HbA1c, hs-CRP and anthropometric parameters evaluation in the patients of diabetes mellitus of central rural india. Int J Med Sci Public Health2013;2(2):291-94
11. Puri D. Text book of medical biochemistry. 3rd ed. New Delhi:Elsevier;2011.p.324
12. Dalan R, Earnest A, Leow MKS. Ethnic variation in the correlation between fasting glucose concentration and glycated hemoglobin (HbA1c). Endocrine Practice 2013:1-16
13. Burtis CA, Ashwood ER, Bruns DE. Teitz textbook of clinical chemistry and molecular diagnostics, 4th ed. New Delhi; Saunders Harcourt: 2006.p.869-85
14. Makris K, Spanou L. Is there relationship between mean blood glucose and glycated hemoglobin. J Diabetes Sci Technol 2011;5(6):1572-583
15. Koeing RJ, Peterson CM, Kilocharles, Cerami Anthony, Williamson JR. Hemoglobin A1c as an indicator of degree of glucose intolerance in diabetes. Diabetes 1976;25(3):230-32
16. Sharifi F, Sazandeh Sh. Serum ferritin in type 2 diabetes mellitus and its relationship with HbA1c. Acta Medica Iranica 2004;42(2):142-45
17. Abou-Shousha SA, El-Megeed MHA, Sultan HK. Interleukin, ferritin and soluble transferrin receptors in type 2 diabetes mellitus. The Egyptian Journal of Immunology 2006;13(1):19-25
18. Shetty JK, Prakash M, Ibrahim MS. Relationship between free iron and glycated hemoglobin in uncontrolled type 2 diabetes patients associated with complications. Ind J Clin Bio 2008;23(1):67-70
19. Kim NH et al. Serum ferritin in healthy subjects and type 2 diabetic patients. Yonsei Med J 2000;41(3):387-92
20. Sun L et al. Ferritin concentrations, Metabolic syndrome, and type 2 diabetes in middleaged and elderly Chinese. J Clin Endocrinol Metab 2008, 93(12):4690-696
21. Ford ES, Cogswell ME. Diabetes and serum ferritin concentration among U.S adults. Diabetes Care 1999;22(12):1978-983

Tables and figures

Table: 1 Distribution of controls and diabetic cases as per age group

Age in years	**Cases**		**Controls**	
	N	**%**	**n**	**%**
31-40	-	-	02	04
41-50	11	22	26	52
51-60	20	40	15	30
>60	19	38	07	14
Total (n=)	50	100.0	50	100.0
Mean ± SD	45.5 ± 7.8		46.6 ± 6.7	

Figure: 1 Distribution of controls and diabetic cases as per age group

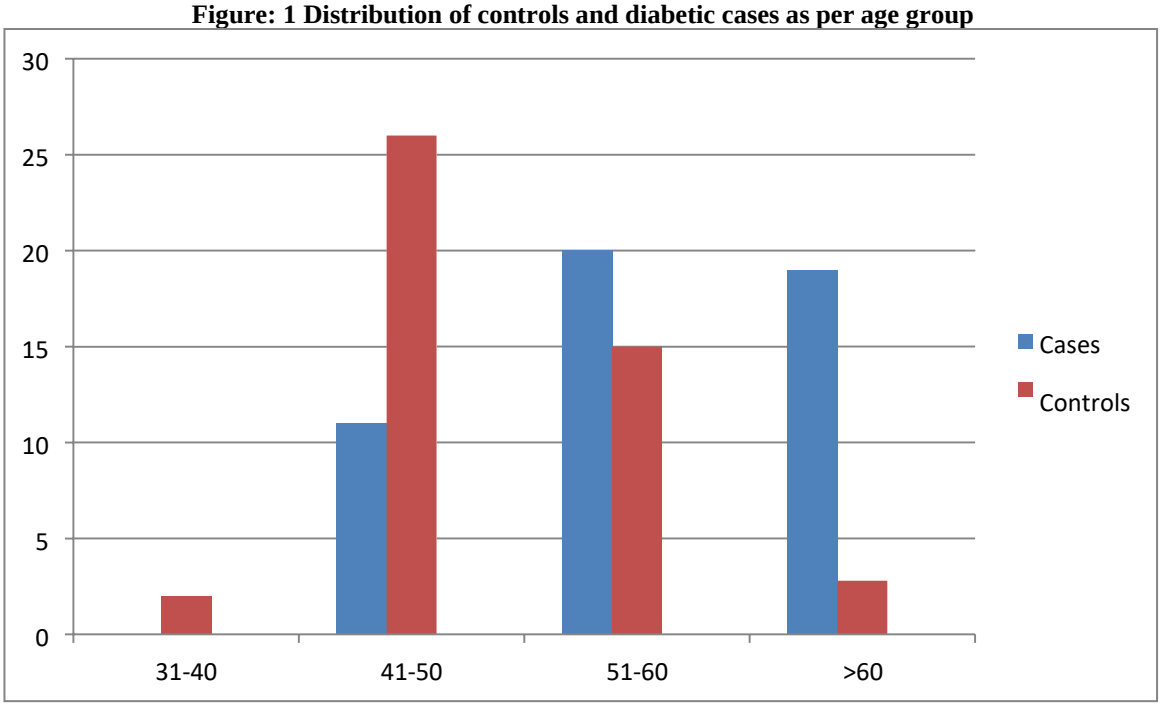

Table: 2 Gender wise Distribution

Gender	Case	Control
Male	34	38
Female	16	12
Total	50	50

Figure: 2 Gender wise Distribution

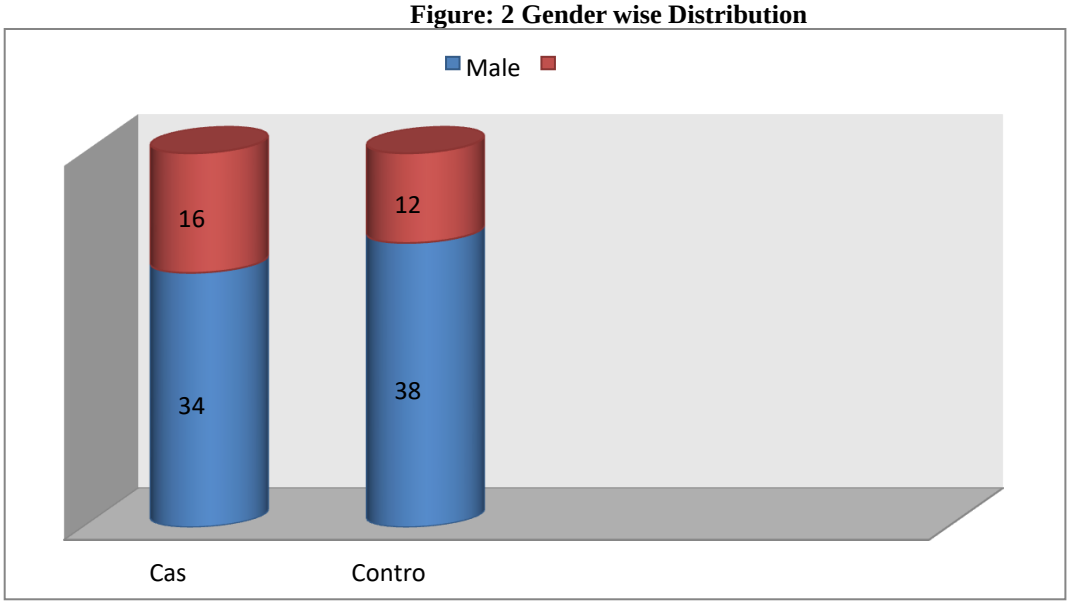

Table: 3 BMI (kg/m^2) distribution in controls and diabetic cases

BMI (kg/m^2)	Cases		Controls	
	No	%	No	%
18.6-22.9	4	08	28	56
23-25	11	22	12	24
26-30	21	42	10	20
> 30	14	28	0	0.0
Total	50	100.0	50	100.0
Mean ± SD	26.34±2.31		22.60±2.60	

p<0.001

Figure: 3 BMI (kg/m^2) distribution in controls and diabetic cases

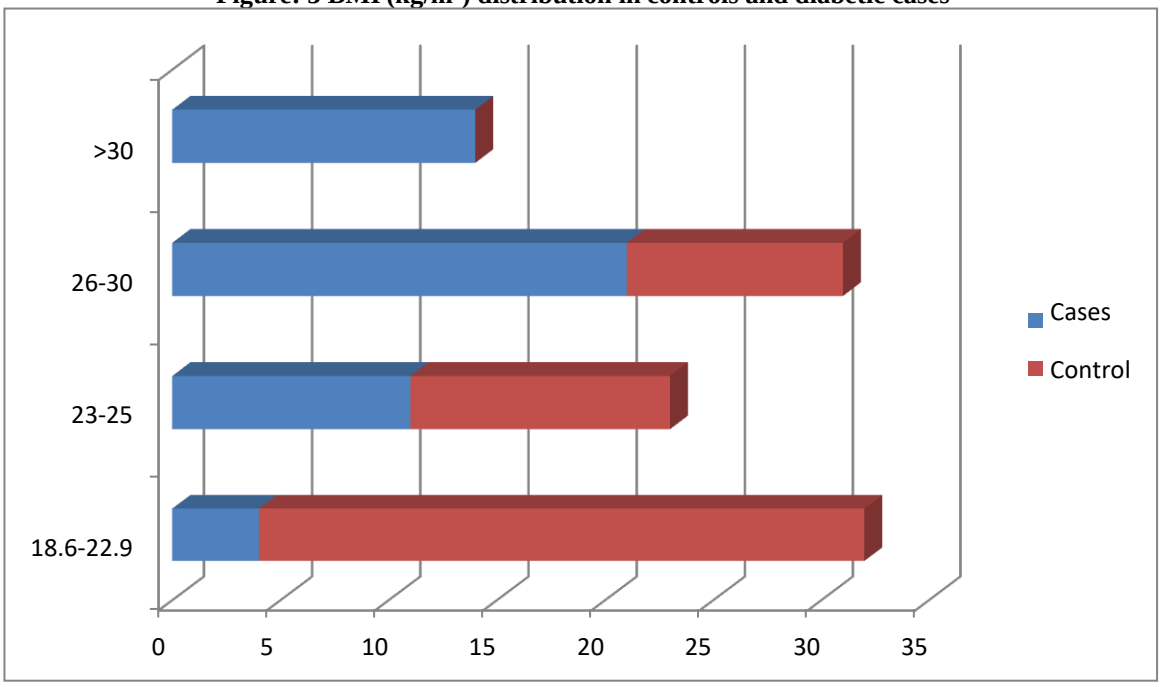

Table: 4 Fasting blood sugar level (mg/dl) in diabetics and controls (mean ± S.D)

FBS (mg/dl)	Cases		Controls	
	No	%	No	%
<100	0	0.0	50	100.0
100-120	04	08	0	0.0
>120	46	92	**0**	**0.0**
Total	50	100.0	50	100.0
Mean ± SD	188.20 ± 58.89		90.93 ± 6.27	

Figure: 4 Fasting blood sugar level (mg/dl) in diabetics and controls

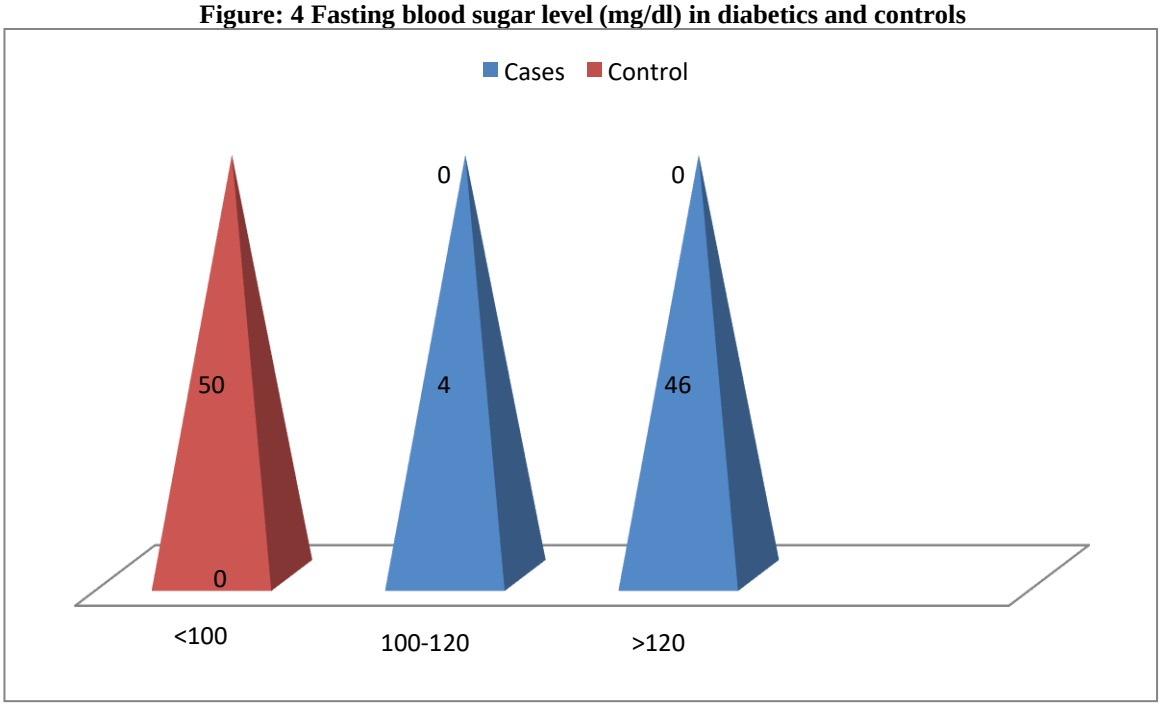

Table: 5 Hypertension Among control and case group

Hypertension	Case	Control
Presence	10	-
Absence	40	50
Total	50	50

Figure: 5 Hypertension Among control and case group

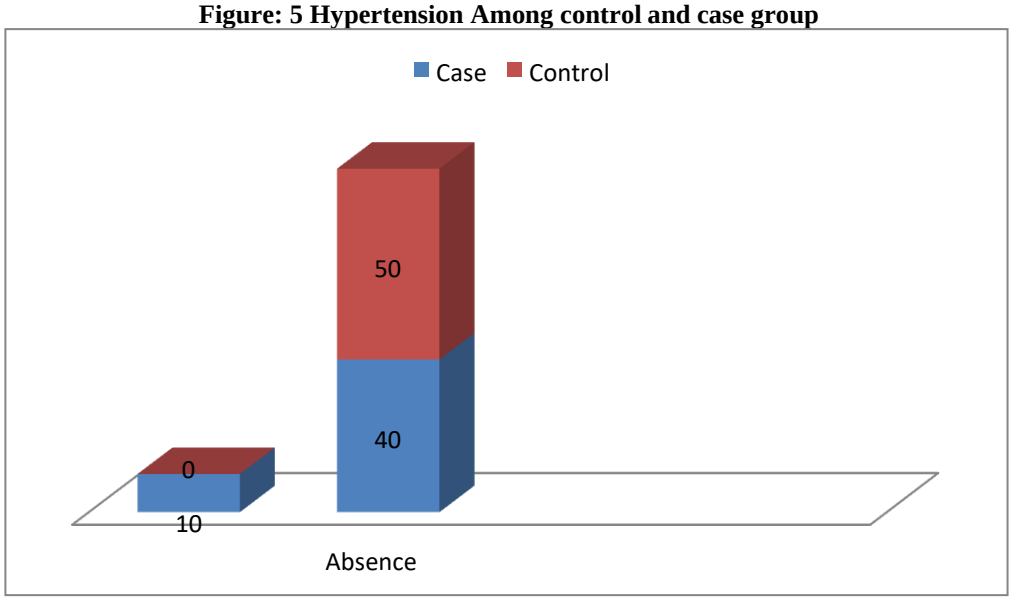

Table: 6 HbA1c wise Distribution

		HbA1c (%)
Controls	Mean ± SD	5.42 ± 0.47
Cases	Mean ± SD	8.59 ± 1.83
Cases v/s Controls	p-value Significance	< 0.001 HS

Table: 7 Shows Comparisons of Fasting Serum Glucose and Ferritin Levels InControls and type 2 Diabetic Subjects

		Fasting serum glucose (mg/dL)	**Ferritin (ng/mL)**
Controls	Mean ± SD	90.93 ± 6.27	101.55 ± 78.76
Cases	Mean ± SD	188.20 ± 58.89	263.34 ± 82.65
Cases v/sControls	p-value Significance	< 0.001 HS	< 0.001 HS

Table: 8 Shows Comparisons of HbA1c and BMI vs. Ferritin Levels In Controls andType 2 Diabetic Subjects

		HbA1c(%)	**BMI (kg/m^2)**	**Ferritin (ng/mL)**
Controls	Mean ± SD	5.42 ± 0.47	22.60±2.60	101.55 ± 78.76
Cases	Mean ± SD	8.59 ± 1.83	24.34±2.31	263.34 ± 82.65
Cases v/s Controls	p-value Significance	< 0.001 HS	< 0.001 HS	< 0.001 HS