Original Research Article

# Comparison of fibrinogen levels in diabetic hypertensives vs diabetic normotensives

**Mudasir S[1], Anjali N Bhat[2], Sunil S[3*]**

*[1]Senior Resident, Department of Physiology, SKIMS Medical College, Srinagar, Jammu and Kashmir, India*
*[2]Professor, Principle, Govt. Medical College, Kathua, Jammu and Kashmir, India*
*[3]Professor & Head, Department of Physiology, Govt. Medical College, Jammu, Jammu and Kashmir, India*

**Received: 26-11-2021 / Revised: 28-12-2021 / Accepted: 10-01-2022**

## Abstract

**Background:** The metabolic dysregulation associated with DM causes secondary pathophysiological changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. **Aim:** To compare plasma fibrinogen levels in type-2 diabetics with hypertension and type-2 diabetics without hypertension. **Methods**: Prospective observational study was undertaken on 200 subjects aged 40-60 years from November 2019 to October 2020 with patients of Type-2 diabetes mellitus (both old and new cases) with hypertension without having any of the complications associated with diabetes and on age and sex matched diabetics without hypertension. **Results:** Mean value of fibrinogen of Group 1 was 484.91 ± 49.15 mg/dl and that of Group 2 was 436.53 ± 22.61 mg/dl, the difference between the two groups being statistically highly significant ($p<0.0001$). Mean systolic and diastolic blood pressure in Group 1 was 127.64 ± 13.41 and 86.20 ± 7.06 mmHg and that of Group 2 was 118 ± 10.80 and 77.52 ± 7.87 mmHg, the difference between the two groups being statistically highly significant ($p<0.0001$). Mean Fasting Blood sugar of Group 1 was 177.91 ± 62.52 mg/dl and that of Group 2 was 197.80 ± 74.75 mg/dl, the difference being highly statistically significant ($p= 0.043$). **Conclusion:** The mean fibrinogen levels in patients with both diabetes and hypertension were significantly higher than diabetes alone, indicating that elevated fibrinogen levels are a risk factor for development of macrovascular complications and thus a marker of morbidity and mortality.

**Keywords:** Type-2 diabetes mellitus, plasma fibrinogen, hypertension, pathophysiological changes.



## Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. With an increasing incidence worldwide, DM will be likely a leading cause of morbidity and mortality in the future**.**

Diabetes mellitus is accompanied by widespread biochemical, morphological and functional abnormalities, which may precipitate certain complications that may affect neural, cardiovascular and renal systems and also organs and tissues like skin, liver, collagen and elastic fibres, making diabetes a multisystem disorder affecting many organs of the body[1]**.** As per Indian Council of Medical Research studies, type-2 diabetes mellitus is directly responsible for 9% of acute myocardial infarction cases, 4% of stroke cases, 2% of neuropathies, and 32% of cataract cases[2,3]**.**

Type-2 diabetes is associated with long term damage, dysfunction and failure of various organs and its complications are mostly caused by macrovascular and microvascular damages. The microvascular complications appear within 15-20 years after the onset of diabetes. If diabetes mellitus is detected earlier and adequate steps are taken, it may be possible to significantly delay the occurrence of complications and thereafter their progression. Exercise is an important therapeutic strategy and has a positive impact on prevention of cardiovascular disease in patients with diabetes mellitus[4]**.**

## Methods

The present one year prospective observational study was undertaken in the postgraduate department of Physiology, Government Medical College and Hospital- Jammu, with effect from November 2019 to October 2020, on 200 subjects aged 40-60 years.

Subjects were selected from Government Medical College and Hospital, Jammu and associated hospitals. The study was conducted on patients of Type-2 diabetes mellitus (both old and new cases) with hypertension without having any of the complications associated with diabetes and on age and sex matched diabetics without hypertension. 200 subjects were selected by random sampling technique. After detailing the purpose and methodology of the study, all subjects found eligible were requested to participate in the study.

**1. Source of Data**

(a) Subjects were diagnosed patients of type-2 diabetes mellitus with hypertension (Both outpatient and inpatient).

(b) Controls comprised of the subjects diagnosed with type-2 diabetes mellitus without associated hypertension.

A detailed history was undertaken and clinical examination was conducted on subjects as per proforma. Height and weight was measured and body mass index (BMI) was calculated. Estimation of blood sugar and glycated hemoglobin (HbA1c), serum fibrinogen levels and lipid profile testing was performed on both the groups. Laboratory tests were performed in an automated analyzer by optimized methods.

Plasma fibrinogen was be measured by **Clauss method.** The available methods of determining fibrinogen can be classified into two groups 'functional' and direct. The first category involves tests based on the determination of coagulation time, which in turn is proportional to the fibrinogen concentration. The most widely used method for functional fibrinogen assay is the Clauss method, which records the time taken to reach the coagulation end point. The second group of tests quantifies fibrinogen molecules directly either immunologically, gravimetrically or by precipitation.

## Statistical Analysis

The data was analyzed using computer software Microsoft Excel and SPSS version 20.0 for windows. Data reported was as mean ±

*Correspondence
**Dr. Sunil S**
Professor & Head, Department of Physiology, Govt. Medical College, Jammu, Jammu and Kashmir, India
**E-mail:** sunilsachdev1221@gmail.com

standard deviation and proportions deemed as appropriate for quantitative and qualitative variable respectively. The statistical difference in mean value was tested using unpaired't' test. ANOVA of variance was also performed to evaluate statistical significance in more than two groups. A p-value of < 0.05 was considered statistically significant. All p-values reported were two-tailed.

**Results**

After detailing the purpose and methodology of the study, all subjects found eligible were requested to participate in the study. The present research work was aimed to compare levels of fibrinogen profile in type-2 diabetics with hypertension and type-2 diabetics without hypertension, so as to compare the derangement in these parameters in both groups.

The demographic profile of the study population in given in (table).

**Table 1: Patient demographic characteristics**

| Parameters | Group 1 | Group 2 | P value |
|---|---|---|---|
| Age (years) | 53.65±6.14 | 49.49±6.86 | <0.0001* |
| Height (mts) | 1.61±0.10 | 1.63±0.09 | 1.102 |
| Weight (kgs) | 72.58±12.12 | 68.38±9.78 | 0.008 |
| Sex M/F | 39/61 | 52/48 | 0.064 |

Values in the table are mean ± SD or absolute numbers (percentage). SD = Standard deviation, * staticall significance

Mean systolic and diastolic blood pressure of Group 1 was 127.64 ± 13.41 and 86.20 ± 7.06 mmHg and that of Group 2 was 118 ± 10.80 and 77.52 ± 7.87 mmHg , the difference between the two groups being statistically highly significant (p<0.0001) (table 2).

**Table 2: Group comparison for blood pressure**

| Blood pressure (mmHg) | Mean ± Standard deviation | | p-value |
|---|---|---|---|
| | Group 1 | Group 2 | |
| Systolic blood pressure | 127.64 ± 13.41 | 118.19 ± 10.80 | <0.0001 |
| Diastolic blood pressure | 86.20 ± 7.06 | 77.52 ± 7.87 | <0.0001 |

The mean duration of type-2 diabetes mellitus ± standard deviation in group 1 was 5.90 ± 4.48 years in comparison to a mean duration of 4.85 ± 3.63 years in group 2 subjects, the difference being statistically not significant (p=0.070) (fig 1).

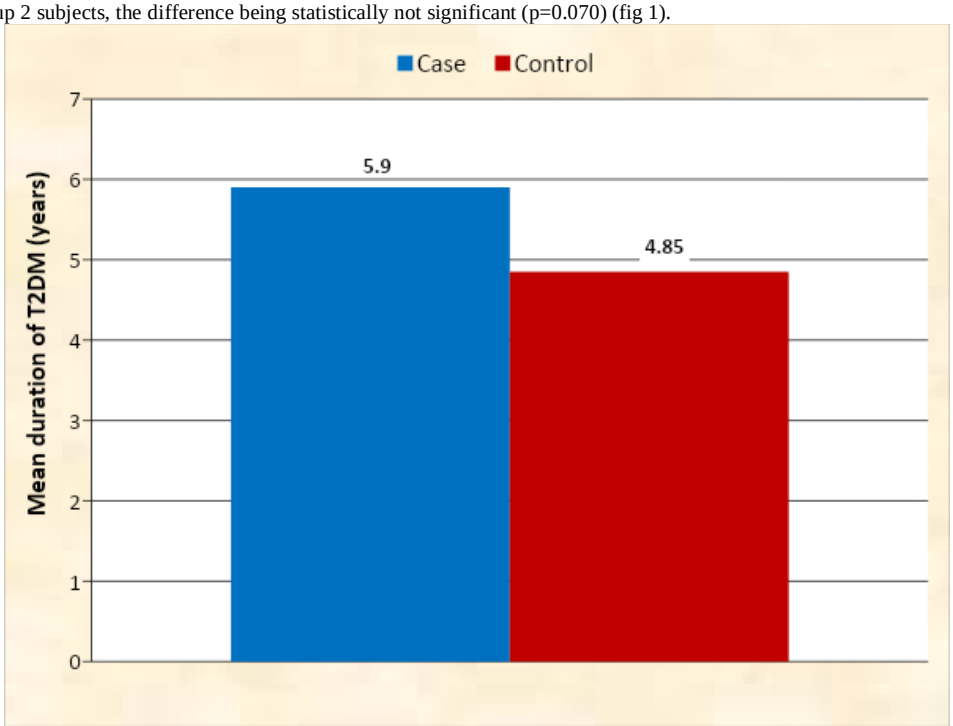


**Fig 1**

Mean Fasting Blood sugar of Group 1 was 177.91 ± 62.52 mg/dl and that of Group 2 was 197.80 ± 74.75 mg/dl, the difference being highly statistically significant (p= 0.043). Mean HbA1c of Group 1 was 9.15 ± 2.18 % and that of Group 2 was 9.15 ± 2.18 %, the difference being statistically not significant (p= 0.179) (table 3).

**Table 3: Group comparison for blood sugar and HbA1C**

| Variables | Mean ± Standard deviation | | p-value |
|---|---|---|---|
| | Group 1 | Group 2 | |
| Fasting blood sugar (mg/dl) | 177.91 ± 62.52 | 197.80 ± 74.75 | 0.043 |
| HbA1c (%) | 9.15 ± 2.18 | 8.72 ± 2.33 | 0.179 |

Mean value of fibrinogen of Group 1 was 484.91 ± 49.15 mg/dl and that of Group 2 was 436.53 ± 22.61 mg/dl, the difference between the two groups being statistically highly significant (p<0.0001) (fig 2).

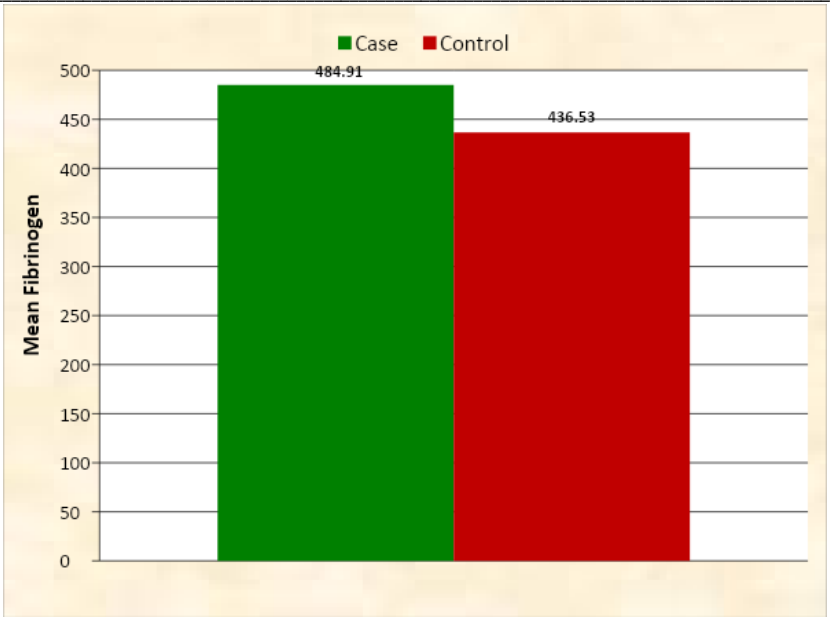


**Fig 2**

**Discussion**

Diabetes mellitus is a chronic condition that occurs when the body cannot produce enough or effectively use of insulin. Compared with individuals without diabetes, patients with type 2 diabetes mellitus have a considerably higher risk of cardiovascular morbidity and mortality, and are disproportionately affected by cardiovascular disease. Most of this excess risk is associated with an augmented prevalence of well-known risk factors such as hypertension, dyslipidemia and obesity in these patients. However the cardiovascular disease in type-2 diabetes mellitus patients cannot be attributed solely to the higher prevalence of traditional risk factors. Therefore other non-traditional risk factors may be important in people with type 2 diabetes mellitus. Cardiovascular disease is increased in type 2 diabetes mellitus subjects due to a complex combination of various traditional and non-traditional risk factors that have an important role to play in the beginning and the evolution of atherosclerosis over its long natural history from endothelial function to clinical events (Martín-Timón I et al., 2014)[5].

Hypertension is present in more than 50% of patients with diabetes mellitus and contributes significantly to both microvascular and macrovascular disease in type-2 diabetes mellitus. Indeed the risk for cardiovascular disease is four fold higher in patients with both diabetes mellitus and hypertension as compared to normotensive non diabetic controls (Stamler J et al., 1993)[6].

In our study the mean value of fibrinogen levels in Group 1 subjects was 484.91 ± 49.15 mg% and that in Group 2 subjects was 436.53 ± 22.61 mg%. The levels of fibrinogen were increased in both groups whereas in subjects with both type-2 diabetes and hypertension the mean value of fibrinogen was higher than the subjects having type-2 diabetes only. In group 1 subjects, the mean levels of fibrinogen were highest in age group 46-50 years (508.50 ± 43.77 mg %), followed by age group 40-45 years (504.57 ± 71.11 mg %), followed by age group 51-55 years (477.58 ± 50.76 mg %) and the mean levels of fibrinogen recorded in age group 56-60 years were ( 471.98 ± 37.65 mg %). . In group 2 subjects, the mean levels of fibrinogen were highest in age group 56-60 years (439.86 ± 25.53 mg %), followed by age group 51-55 years (436.31 ± 22.10 mg %), followed by age group 46-50 years (436.16 ± 24.89 mg %) and the mean levels of fibrinogen recorded in age group 40-45 years were ( 434.89 ± 19.99 mg %). The difference in mean fibrinogen levels between the two groups was statistically highly significant ($p<0.0001$).

Our observations are in agreement with Lee AJ et al., (1993)[7] who reported that persons with a family history of heart disease or a personal history of high blood pressure, diabetes, stroke or presence of intermittent claudication, all had higher plasma fibrinogen concentrations than those without these comorbidities.

Similar results were shown by Bruno G et al., (1996)[8] who studied plasma fibrinogen levels in 1574 patients with type-2 diabetes mellitus Fibrinogen levels were available for 1525 of the 1574 patients who were examined (669 men and 856 women). The mean age (±SD) was 67.3 ± 10.3 years for men and 70.7 ± 10.7 years for women. The mean plasma fibrinogen level (±SD) was 360 ± 90 mg/L; levels slightly differed between men and women. In 50.3% of patients, plasma fibrinogen level exceeded 350 mg/L. In men, fibrinogen level increased with age ($P < 0.001$). Patients with non–insulin-dependent diabetes mellitus had a high prevalence of hyperfibrinogenemia. Fibrinogen level was independently associated with HbA1c value and albumin excretion rate, which suggests that fibrinogen may be involved in the increased cardiovascular risk of patients with diabetes mellitus.

The results of our study also matched the results of Barazzoni R et al., (2000)[9] who conducted a study on fibrinogen production in type-2 diabetic individuals. Their study demonstrated a substantial increase in fibrinogen production in type 2 diabetic patients compared to matched control subjects, and this alteration is likely to represent a major determinant of the hyperfibrinogenemia often observed in the disease.

The results of our study also matched the results obtained by Asakawa H et al., (2000)[10] who reported that plasma fibrinogen and Thrombin-antithrombin complex (TAT) levels were significantly higher in patients with type-2 diabetes mellitus and hypertension.

Findings of Khan TM et al., (2005)[11] are also in agreement with our results who reported body weight, body mass index, fibrinogen concentration and relative plasma viscosity were all significantly more in hypertensive diabetics than normotensive diabetics and healthy control subjects.

Similar results were shown by the study of Taj Muhammad Khan et al., (2005)[12] who reported fibrinogen concentration and plasma viscosity was significantly elevated in diabetics with complications.

Our observation was also in agreement with Le DS et al., (2008)[13] who reported that plasma fibrinogen concentration was associated with diabetic microvascular disease, in particular nephropathy.

Kafle DR and Shrestha P (2010)[14] reported that fibrinogen levels were significantly higher in diabetic patients with coronary artery disease than those who had only diabetes or coronary artery disease, this being in agreement with our study.

Our study is also in agreement with Bembde AS (2012)[15] who carried out a study on Plasma Fibrinogen Level in Type-2 Diabetes Mellitus. She concluded that diabetic subjects had a higher fibrinogen level when compared to controls and it was statistically highly significant.

Gupta P et al., (2016)[16] studied plasma fibrinogen level and its relation to glycemic control in type-2 diabetes mellitus patients and reported that type-2 diabetic patients had significantly higher levels of fibrinogen, which is in correspondence to our study.

Similar results were shown in their study by Pankaj Kumar Saini et al., (2016)[17], who reported that patients with type-2 diabetes mellitus had higher levels of fibrinogen.

Our results are also in agreement with Abdul Razak MK and Sultan AA (2019)[18], who in their study reported that type-2 diabetics have raised plasma fibrinogen levels and it is important to measure levels of plasma fibrinogen in type-2 diabetic patients.

Elhasadde A et al., (2020)[19] reported fibrinogen levels were significantly higher in type-2 diabetics, which again is in agreement with the results of our study.

**References**


1. Alvin C Powers. Diabetes mellitus. In: Harrison's Principles of Internal Medicine, 15th edition. New York: McGraw-Hill 2001; p. 2112.
2. Larsen PR, Kronenberg HM, Melmed S, Polonsky KS. Complications of diabetes Mellitus. William's textbook of endocrinology, 10th edition. Elsevier India Publisher 2003; 1428-31.
3. Gupta OP, Pathak S. Pandemic trends in prevalence of Diabetes Mellitus and associated coronary heart disease in India. Int J Diab Dev Countries 2003; 23(4): 937.
4. Francisco CO, Catai AM, Moura-Tonello SCG, Lopes SLB, Benze BG, Leal AMO et al. Cardio respiratory fitness in non-smoking individuals with diabetes. Braz J Med Biol Res 2014; 47(5):426-31.
5. Martín-Timón I, Sevillano-Collantes C, Segura-Galindo A, Del Cañizo-Gómez FJ. Type 2 diabetes mellitus and cardiovascular disease. World J Diabetes 2014; 5(4): 444-470.
6. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the multiple risk factor intervention trial. Diabetes care. 1993; 16(2): 434-44.
7. Lee AJ, Lowe GD, Woodward M, Tunstall-Pedoe H. Fibrinogen in relation to personal history of prevalent hypertension, diabetes, stroke, intermittent claudication, coronary heart disease, and family history: the Scottish Heart Health Study. Br Heart J. 1993; 69(4):338-42.
8. Bruno G, CP Paolo, Bargero G, Borra M, D'Errico N. Association of Fibrinogen with Glycemic Control and Albumin Excretion Rate in Patients with Non-Insulin-Dependent Diabetes Mellitus: Ann Intern Med. 1996; 125:653-65.
9. Barazzoni R, Zanetti M, Davanzo G, Kiwanuka E, Carraro P, Tiengo A et al. Increased Fibrinogen Production in Type 2 Diabetic Patients without Detectable Vascular Complications: Correlation with Plasma Glucagon Concentrations. The Journal of clinical endocrinology and metabolism, vol 85, No 9: 2000.
10. Asakawa H, Tokunaga K, Kawakami F. Elevation of fibrinogen and Thrombin-antithrombin III complex levels of type 2 diabetes mellitus patients with retinopathy and nephropathy. J Diabetes Complications 2000; 14:121-6.
11. Khan TM, Marwat MA, Rehman H. Comparison of plasma viscosity and fibrinogen concentration in hypertensive and normotensive diabetics. J Ayub Med Coll Abbottabad. 2005 Oct-Dec; 17(4):45-47.
12. Taj Muhammad Khan, Mumtaz Ali Marwat, Purdil Khan, Farman-ullah Wazir, Amir Rehman. Plasma Fibrinogen Levels in diabetics with complication- A prospective study. Gomal Journal of Medical Sciences 2005; 3:2.
13. Le DS, Miles R, Savage PJ, Cornell E, Tracy RP, Knowler WC, Krakoff J. The association of plasma fibrinogen concentration with diabetic microvascular complications in young adults with early-onset of type 2 diabetes. Diabetes Res Clin Pract. 2008; 82(3):317-23.
14. Kafle DR, Shrestha P. Study of fibrinogen in patients with diabetes mellitus. Nepal Med Coll J. 2010; 12(1): 34-7.
15. Bembde AS. A Study of Plasma Fibrinogen Level in Type-2 Diabetes Mellitus and its Relation to Glycemic Control. Indian J Hematol Blood Transfus 2012; 28(2):105–08.
16. Gupta P, Bhambani P, Narang S. Study of plasma fibrinogen level and its relation to glycemic control in type-2 diabetes mellitus patients. Int J Res Med Sci. 2016 Sep;4(9):3748-54.
17. Pankaj Kumar Saini, Manoj Saluja, S.R. Meena, Shyam Bihari Meena, Study of plasma fibrinogen level in type 2 diabetes mellitus and its association with microalbuminuria and glycemic control, Current Medicine Research and Practice. 2016; 6(3): 113-6.
18. Abdul Razak MK, Sultan AA. The importance of measurement of plasma fibrinogen level among patients with type- 2 diabetes mellitus. Diabetes Metab Syndr. 2019; 13(2): 1151-58.
19. Elhassade A, Saad A, Falleh A, Alamin K, Eltira E. Fibrinogen Level in Non-Insulin Dependent Diabetes Mellitus (NIDDM). Int J Rec Innov Med Clin Res. 2020; 2(3): 101-105.


**Conflict of Interest: Nil Source of support: Nil**