Original Research Paper

Volume - 13 | Issue - 03 | March - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

General Medicine

STUDY OF BIOCHEMICAL PROFILE OF DIABETIC NEUROPATHY AND DIABETIC NEPHROPATHY WITH REFERENCE TO INFLAMMATORY MARKER

Dr. Vamsee Vuduta Post graduate student Department of General Medicine, Rajarajeswari medical college and Hospital, Bangalore, Karnataka, India.

Dr. Sai Rakesh Vadlamudi Post graduate student, Department of General Medicine, Rajarajeswari medical college and Hospital, Bangalore, Karnataka, India.

Dr. Harshitha* Assistant professor, Department of General Medicine, Rajarajeswari medical college and Hospital, Bangalore, Karnataka, India. *Corresponding Author

KEYWORDS :

INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome characterized by abnormal metabolism of carbohydrate, protein and fat resulting in hyperglycemia due to absolute or relative deficiency of insulin ending up in vascular complications leading to retinopathy, neuropathy and nephropathy[1]. Complications from diabetes can be classified as microvascular or macrovascular. Macrovascular complications include cardiovascular disease, stroke, and peripheral vascular disease. Peripheral vascular disease may lead to bruises or injuries that do not heal, gangrene, and, ultimately, amputation. Microvascular complications include peripheral nervous system damage (neuropathy), renal system damage (nephropathy) and eye damage (retinopathy)[2].

Recent studies have linked inflammation to β-cell dysfunction resulting from chronic exposure to hyperglycaemia[3]. CRP is an acute-phase reactant synthesized by hepatocytes, which is used for diagnosis in individuals with infection or inflammation[4]. Hs-CRP levels in serum can rise dramatically after myocardial infarction, stroke, stress, trauma, infection, inflammation, surgery or neoplastic proliferation[5]. Chronic systemic subclinical inflammation has also been identified as a driving force for insulin resistance, metabolic syndrome, and type 2 DM[6].

Serum ferritin is an acute phase reactant and is a marker of iron stores in the body. Elevated iron stores may induce diabetes through a variety of mechanisms, including oxidative damage to pancreatic beta cells, impairment of hepatic insulin extraction by the liver, and interference with insulin's ability to suppress hepatic glucose production[7]. Recent studies have found increased ferritin levels in association with such diabetic complications as retinopathy, nephropathy, and vascular dysfunction in patients with DM and with elevated FBG[8,9].

Since, inflammation appears to be a key component of many reactions associated with poor glycemic control and further pathogenesis of diabetes and its complications; this study was undertaken to evaluate dyslipidemia profile, Hs-CRP level and serum ferritin levels in Type 2 Diabetes Mellitus patients with complications.

MATERIALS & METHODS:

The study was cross sectional and was conducted in Rajarajeswari Medical College and Hospital, Bangalore from January 2021 to June 2022 for a period of 18 months. The study group included clinically diagnosed type 2 Diabetes mellitus patients with either/both complications of Diabetic neuropathy and Diabetic nephropathy attending the OPD/IPD of department of general medicine, RRMCH, Bangalore. Clearance from the institutional ethical committee was taken before starting the study. Study participants were included in the study by Purposive Sampling technique.

INCLUSION CRITERIA

1. Age Group: 30 – 70 years.
2. All Type 2 Diabetes mellitus patients with duration more than 5 years willing to give consent.
3. Patients with complications of Diabetic neuropathy and Diabetic nephropathy.

EXCLUSION CRITERIA

1. Type 1- Diabetes Mellitus cases.
2. Newly Diagnosed Type 2- Diabetes mellitus
3. Smoker
4. Alcohol
5. Collagen vascular disease.
6. Exposure to toxic chemicals.
7. Patients who received chemotherapy.
8. Hepatitis B infection.
9. Vitamin B12 deficiency
10. Amyloidosis
11. Myelopathy and other causes of neuropathy

ESTIMATION OF SAMPLE SIZE:

Based on statistics obtained from MRD, RRMCH, an average of 3 cases per month fitting the criteria of the study with study duration of 18 months, we can expect to have N=54. Based on this population size, using YAMANE equation, for a known population size, sample size (n) equal to

$n = N/1+Ne^2$

n=sample size

N=population size

e= margin of error (for 95% of confidence level, margin error =0.05)

$n=54/1+54*0.05*0.05 = 54/1.35 = 47.57$

Therefore, after approximating, the sample size of the study participants was fixed at 50.

The patients fitting the inclusion criteria were included in the study, till the sample size was reached. Written informed consent was taken from the study participants before collecting the data. A pre-tested, semi-structured questionnaire was used to collect information on socio-demographic variables and history of diabetes by interview method. Patients were examined, investigated, and evaluated for Diabetic Neuropathy, and Diabetic nephropathy. Nerve Conduction Studies were done. Inflammatory markers such as hs-CRP and serum ferritin levels were evaluated and the results were documented.

STATISTICALANALYSIS:

The data was collected and compiled in MS Excel. Descriptive statistics has been used to present the data. To analyse the data, SPSS (Version 26.0) was used. Significance level was fixed as 5% ($\alpha = 0.05$. Qualitative variables are expressed as frequency and percentages and Quantitative variables are expressed as Mean and Standard Deviation. To compare means between the variables, Anova test was used. To compare the proportion between 2 variables, chi-square test was used.

RESULTS:

The mean age of the samples selected for this study was 53.62+7.1. Among 50 subjects, nearly 21 persons (42%) belonged to 51-69 years of age, 16 persons (32%) belonged to 41-50 years age group, 11 persons (22%) belonged to 61-70 years age group, 2 persons (4.0%) belonged to 31-40 years age group. Among 50 subjects, 26(52%) were females and 24 (48%) were males.

The severity of diabetic neuropathy as per nerve conduction studies were mentioned in table 1. Among 50 subjects, 20 (40%) were normal

as per nerve conduction studies. Among the remaining 30 (60%) subjects, majority i.e., 14 (28%) subjects showed motor sensory neuropathy, (motor> sensory, symmetrical), 11 (22%) showed sensory motor neuropathy (sensory> motor, symmetrical), 3(6%) showed sensory motor neuropathy (sensory> motor, asymmetrical), 2 (4%) motor sensory neuropathy, (motor> sensory, asymmetrical). Among 50 subjects, 18 (36%) of them had Diabetic Nephropathy.

The association of Inflammatory markers with Severity of Diabetic Neuropathy was mentioned in table 2 and graph 1. When assessing the inflammatory markers, hs-CRP was maximum among subjects with motor sensory neuropathy(motor>sensory, symmetrical) and it was about 6.35786+1.833686. Mean value of serum ferritin was maximum among subjects with motor sensory neuropathy(motor>sensory, asymmetrical) and it was about 347.600+127.8449. hs-CRP was significantly associated with severity of Diabetic Neuropathy (P<0.05) whereas serum ferritin was not significantly associated with severity of Diabetic Neuropathy.

The association of Inflammatory markers with Severity of Diabetic Nephropathy was mentioned in table 3 and graph 2. hs-CRP and serum ferritin was more among subjects with Diabetic nephropathy than those without it and the values were 5.24772+2.927014 and 318.150+185.1982 respectively. Serum ferritin was significantly associated with Diabetic Nephropathy (P<0.05) whereas hs-CRP was not significantly associated with Diabetic Nephropathy.

The association of Inflammatory markers with Duration of Diabetes was mentioned in table 4 and graph 3. Mean values of the inflammatory markers were more among subjects with duration of diabetes of 7 years and the mean values were 8.90000+6.85412 and 634.400+253.038. Serum ferritin was significantly associated with duration of Diabetes (P<0.05) whereas hs-CRP was not significantly associated with duration of Diabetes.

The distribution of Inflammatory markers according to age group was mentioned in table 5. Mean value of hs-CRP was maximum in 30-40 years age group (6.1+3.8) and minimum in 51-60 years age group (4.3+2.9). Mean value of Serum ferritin was maximum in 61-70 years age group (243.7+116.5) and was minimum in 30-40 years age group (202.8+99.8).

Table 1: The severity of diabetic neuropathy as per nerve conduction studies

Severity of Diabetic Neuropathy		Frequency	Percent
NORMAL		20	40.0
MOTOR SENSORY NEUROPATHY, MOTOR > SENSORY	SYMMETRICAL	14	28.0
MOTOR SENSORY NEUROPATHY, MOTOR > SENSORY	ASYMMETRICAL	2	4.0
SENSORY MOTOR NEUROPATHY SENSORY > MOTOR	SYMMETRICAL	11	22.0
SENSORY MOTOR NEUROPATHY SENSORY > MOTOR	ASYMMETRICAL	3	6.0

Table 2: Association of Inflammatory markers with Severity of Diabetic Neuropathy

Severity of Diabetic Neuropathy		hs-CRP	Sr Ferritin
MOTOR SENSORY NEUROPATHY, MOTOR > SENSORY, SYMMETRICAL	Mean	6.35786	295.279
	Std. Deviation	1.833686	207.2711
MOTOR SENSORY NEUROPATHY, MOTOR > SENSORY, ASYMMETRICAL	Mean	6.00000	347.600
	Std. Deviation	.989949	127.8449
NORMAL	Mean	3.72321	207.680
	Std. Deviation	2.874163	69.6662
SENSORY MOTOR NEUROPATHY SENSORY > MOTOR, ASYMMETRICAL	Mean	6.16667	302.600
	Std. Deviation	2.608320	175.7051
SENSORY MOTOR NEUROPATHY SENSORY > MOTOR, SYMMETRICAL	Mean	4.18091	228.691
	Std. Deviation	2.892829	99.7846
P Value		0.049*	0.280	

Table 3: Association of Inflammatory markers with Diabetic Nephropathy

Diabetic nephropathy		hs-CRP	Sr Ferritin
Absent	Mean	4.57361	208.731
	Std. Deviation	2.636541	81.1344
Present	Mean	5.24772	318.150
	Std. Deviation	2.927014	185.1982
P Value		0.411	0.006*	

*-SIGNIFICANT

Table 4: Association of Inflammatory markers with Duration of Diabetes

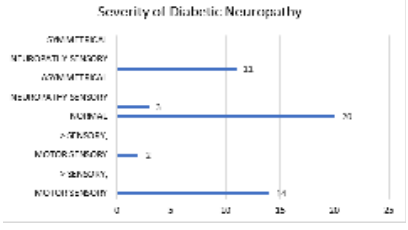
Duration of diabetes in years		hs-CRP	Sr Ferritin
2	Mean	3.83400	139.050
	Std. Deviation	4.830954	6.0104
3	Mean	5.70742	233.550
	Std. Deviation	2.772206	192.4801
4	Mean	4.77664	260.287
	Std. Deviation	2.538237	100.9996
5	Mean	4.49990	276.630
	Std. Deviation	2.592344	113.4168
6	Mean	3.93120	202.040
	Std. Deviation	2.794015	75.8458
7	Mean	8.90000	634.400
	Std. Deviation	6.85412	253.038
P Value	0.437	0.042*	

*-SIGNIFICANT

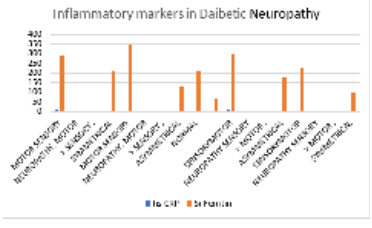
Table 5: Distribution of Inflammatory markers according to Age group

Age group		hs-CRP	Sr Ferritin
30-40	Mean	6.10000	202.800
	Std. Deviation	3.82160	99.8435
40-50	Mean	5.36450	261.344
	Std. Deviation	2.705219	141.1375
51-60	Mean	4.33238	244.662
	Std. Deviation	2.930649	153.8141
61-70	Mean	4.84809	243.736
	Std. Deviation	2.577406	116.5128
Total	Mean	4.82124	248.122
	Std. Deviation	2.736182	137.4002

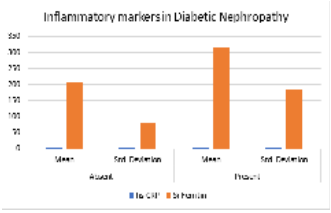
Graph 1: Graph showing distribution of study subjects as according to Severity of Diabetic Neuropathy



Graph 2: Graph showing mean of Inflammatory markers among subjects with Diabetic Neuropathy



Graph 3: Graph showing mean of Inflammatory markers in Diabetic Nephropathy



DISCUSSION

Total 50 subjects participated in the study. Mean age in this study was 53.62+7.1 which was similar to a study by Mottaghi et al10 and Son et al11 in which it was 58.76+9.53 and 59.96±11.26 respectively. In this study, among 50 subjects, majority i.e., 21 (42%) belonged to 51-69 years of age following which 16 (32%) belonged to 41-50 years age group, 11 (22%) belonged to 61-70 years age group and only 2(4.0%) belonged to 31-40 years age group. In this study there was equal distribution of males and females i.e., 26/50(52%) were females and 24/50 (48%) were males. This was similar to a study by Mottaghi et al10 in which 50.5% were males.

In this study, among 50 subjects, 20 (40%) were normal as per nerve conduction studies. Among the remaining 30 (60%) subjects, majority i.e., 14 (28%) subjects showed motor sensory neuropathy, (motor> sensory, symmetrical), 11 (22%) showed sensory motor neuropathy (sensory> motor, symmetrical), 3(6%) showed sensory motor neuropathy (sensory> motor, asymmetrical), 2 (4%) motor sensory neuropathy, (motor> sensory, asymmetrical). Among 50 subjects, 18 (36%) of them had Diabetic Nephropathy.

In this study, mean value of Inflammatory markers such as hs-CRP was maximum among subjects with motor sensory neuropathy(motor>sensory, symmetrical) and it was about 6.35786+1.833686. Mean value of serum ferritin was maximum among subjects with motor sensory neuropathy(motor>sensory, asymmetrical) and it was about 347.600+127.8449. In this study hs-CRP was significantly associated with severity of Diabetic Neuropathy (P<0.05) which was similar to a study by Canpolat et al12 and Kassem et al13 whereas in this study serum ferritin was not significantly associated with severity of Diabetic Neuropathy.

In this study, mean value of Inflammatory markers such as hs-CRP and serum ferritin was more among subjects with Diabetic nephropathy than those without it and the values were 5.24772+2.927014 and 318.150+185.1982 respectively. Serum ferritin was significantly associated with Diabetic Nephropathy (P<0.05). hs-CRP was not significantly associated with Diabetic Nephropathy in this study which was contrary to a study by Zbaar et al14 in which CRP was significantly associated with Diabetic nephropathy (P<0.001). In a study by Ain et al15, CRP levels were more in subjects with nephropathy which was contrary to this study In this study, mean values of the inflammatory markers were more among subjects with duration of diabetes of 7 years and the mean values were 8.90000+6.85412 and 634.400+253.038 respectively. In this study, Serum ferritin was significantly associated with duration of Diabetes (P<0.05) which was similar to a study by Amin et al16 whereas hs-CRP in this study was not significantly associated with duration of Diabetes.

CONCLUSION

This study was done to correlate inflammatory markers with severity of Diabetic Neuropathy and Diabetic Nephropathy. Inflammatory marker hs-CRP was significantly associated with severity of Diabetic Neuropathy (P<0.05) whereas serum ferritin was not significantly associated with severity of Diabetic Neuropathy. Contrary to this Serum ferritin was significantly associated with Diabetic Nephropathy (P<0.05) whereas hs-CRP was not significantly associated with Diabetic Nephropathy. Serum ferritin was significantly associated with duration of Diabetes (P<0.05) whereas hs-CRP was not significantly associated with duration of Diabetes. We conclude that raised inflammatory markers are the predictors for Diabetes and its complications.

REFERENCES

1. Thakur T, Chauhan V, Negi R. Role of HbA 1C in diabetes mellitus. Journal, Indian Academy of Clinical Medicine 2009 Jan;10(1):52–4
2. Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. Physical Therapy 2008 Nov 1 [cited 2022 Nov 18];88(11):1254–64.
3. Joshi SR. Metabolic syndrome--emerging clusters of the Indian phenotype. J Assoc Physicians India. 2003 May; 51:445–6.
4. Ford ES. The metabolic syndrome and C-reactive protein, fibrinogen, and leukocyte count: findings from the Third National Health and Nutrition Examination Survey. Atherosclerosis. 2003 Jun;168(2):351–8.
5. Pradhan AD. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA 2001 Jul 18 [cited 2022 Nov 18];286(3):327.
6. Rifai N, Ridker PM. High-sensitivity C-reactive protein: a novel and promising marker of coronary heart disease. Clin Chem. 2001 Mar;47(3):403–11.
7. International expert committee report on the role of the a1c assay in the diagnosis of diabetes. Diabetes Care 2009 Jul [cited 2022 Nov 18];32(7):1327–34.
8. Rajpathak S, Ma J, Manson J, Willett WC, Hu FB. Iron intake and the risk of type 2 diabetes in women: a prospective cohort study. Diabetes Care. 2006 Jun;29(6):1370–6.
9. Jiang R, Ma J, Ascherio A, Stampfer MJ, Willett WC, Hu FB. Dietary iron intake and blood donations in relation to risk of type 2 diabetes in men: a prospective cohort study. Am J Clin Nutr. 2004 Jan;79(1):70–5.
10. Mottaghi T, Khorvash F, Khorvash F, Maracy M, Kheirrollahi M, Askari G. Association between BMI, and inflammation among diabetic polyneuropathy patients. Int J Prev Med 2019 [cited 2022 Nov 18];10(1):212.
11. Son NE. Influence of ferritin levels and inflammatory markers on HbA1c in the Type 2 Diabetes mellitus patients: Inflammatory markers on HbA1c in the Type 2 Diabetics. Pak J Med Sci 2019 Jul 9 [cited 2022 Nov 18];35(4).
12. Wadham C, Albanese N, Roberts J, Wang L, Bagley CJ, Gamble JR, et al. High-density lipoproteins neutralize C-reactive protein proinflammatory activity. Circulation. 2004 May 4;109(17):2116–22.
13. Kassem A, Fathy S, Abo-Elenin M. Study of the plasma levels of tgf- β1, il-6, hba1c, and crp in egyptian type ii diabetic patients with peripheral neuropathy. AL-AZHAR ASSIUT MEDICAL JOURNAL 2015 Oct [cited 2022 Nov 18];13(4):156–64.
14. Zbaar SA, Sarhat ER, Khalaf SJ. Association of c-reactive protein with risk of complications of diabetic nephropathy. Egyptian Journal of Chemistry 2022 Aug 1 [cited 2022 Nov 18];65(8):483–7.
15. Ain QU, Butt RZ, Bari S, Sarwar U, Khan WU, Naseem ST, et al. Association between cystatin c, crp in patients of diabetic nephropathy with type 2 diabetes mellitus. Pakistan Journal of Medical & Health Sciences 2022 Mar 27 [cited 2022 Nov 18];16(03):63–63.
16. Amin RF, El Bendary AS, Ezzat SE, Mohamed WS. Serum Ferritin level, microalbuminuria, and non-alcoholic fatty liver disease in type 2 diabetic patients. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2019 May [cited 2022 Nov 18];13(3):2226–9.