International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: SJIF: 5.995
Available Online at www.journalijcar.org
Volume 6; Issue 12; December 2017; Page No. 8475-8478
DOI: http://dx.doi.org/10.24327/ijcar.2017.8478.1369

Research Article

CORRELATION OF HAEMATOLOGICAL VARIABLES WITH DURATION OF TYPE 2 DIABETES MELLITUS: RESULTS FROM NORTH INDIAN POPULATION

Saurabh Agarwal[1]., Soumen Manna[2*] and Hanjabam Barun Sharma[3]

[1]Department of Medicine, Shri Guru Ram Rai Institute of Medical & Health Sciences, Dehradun, India
[2]Department of Physiology, VMMC & Safdarjung Hospital, New Delhi, India
[3]Department of Physiology, All India Institute of Medical Sciences, New Delhi, India

A R T I C L E I N F O

Article History:
Received 24th September, 2017
Received in revised form 15th October, 2017
Accepted 18th November, 2017
Published online 28th December, 2017

Key words:
Type 2 DM, haematological parameter, albumin-creatinine ratio, duration of diabetes, ferritin.

A B S T R A C T

Background & objectives: Altered haematological parameters are common and a risk factor for type 2 diabetes mellitus (T2DM). We tried to find out correlation of haematological parameter with duration of T2DM.
Methods: A hospital based cross sectional study was conducted in medical college of North India. 200 T2DM patients were included(male 135 and female 65). Complete haemogram, 24hour urinary protein (24UP), creatinine clearance (CrC) and urinary albumin to creatinine (A/C) ratio were estimated.
Results: There was significant positive correlation between duration of T2DM with ESR, ferritin level (except in females), 24 UP and A/C ratio. Duration of T2DM had significant negative correlations with Hb, MCV, MCH, MCHC, PCV (except in males) and CrC.
Interpretation & conclusions: The duration of diabetes mellitus had adverse effect on haematological parameter as well as renal function in type 2 DM patients.

INTRODUCTION

Diabetes mellitus (DM) is a disease of metabolism clinically presents with hyperglycemia and blood lipid and protein disorder. The number of diabetes population in the world has risen from 108 million in 1980 to 422 million in 2014 according to WHO epidemiological data and the percentage prevalence of among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014.[1, 2] It is estimated that in the year of 2030 there will be about 439 million diabetics.[3]

Currently in India have more than 62 million diagnosed diabetes populations, and it is predicted that by 2030 DM may afflict up to 79.4 million individuals in India. [4, 5]

Type 2 DM (T2DM) is a multifactorial disease with genetic and environmental risk factors. Among many risk factors, it had also been seen that routine haematological parameter such as white blood cell (WBC) count and hematocrit (HCT) level were altered in patients with insulin resistance.[6-9]

Persistent hyperglycaemia in DM causes an oxidative stress due to production of free radicals especially reactive oxygen species (ROS). Free radical mediated alterations of cell membrane fluidity affect the functions of blood cells as well as the coagulation system leading to abnormal haematological parameters in DM patient.[10-12]

Corresponding author:* **Soumen Manna
Department of Physiology, VMMC & Safdarjung Hospital, New Delhi, India

Duration of DM is also very important factor in the development of diabetic nephropathy as demonstrated in several studies.[13-15] Altered haematological parameter is also in diabetic nephropathy patients with anemia being the most common, consistent.[16]

Although there are many studied where haematological parameters had been studied in DM patient but the study of association between duration of T2DM and haematological parameter is lacking. Thus, in in this paper we aimed to study the correlation between haematological parameters and duration of T2DM in a population of North India.

MATERIALS AND METHODS

This study was conducted in the Department of Medicine at a medical college and hospital of North India, over a period of 12 month. The study was ethically approved by the Institute's Ethical Committee.

Patients suffering from type 2 DM, attending indoor and outdoor clinic of Department of Medicine were included in the study. All patients were subjected to detailed history taking including duration of T2DM and clinical examinations and investigation as per working proforma, after obtaining informed written consent.

Inclusion criteria for the study were: patients having T2DM according to ADA criteria.[17] Exclusion Criteria for the study was: pregnant female with DM, acutely ill patient of DM.

Anemia was diagnosed on the basis of WHO criteria,[18] which were: haemoglobin (Hb) less than 13 gm% in males and Hb less than 12 gm% in females.

After exclusion, 200 T2DM patients were included in the study (male 135 and female 65). All subjects underwent through following investigations: A complete hemogram including hemoglobin, total leukocyte count (TLC), differential leukocyte count (DLC), packed cell volume (PCV or, hematocrit), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), erythrocyte sedimentation rate (ESR), serum ferritin, were estimated by automated bio-analyzer (Roller 20 LC, Italy). Fasting and post prandial blood sugar levels were estimated according to ADA protocol.[19] In all patients, 24hour urinary protein (24UP) and urinary albumin to creatinine ratio (A/C) were also estimated and creatinine clearance (ml/min) was calculated using the Cockcroft-Gault equation.[20]

Statistical analysis

SPSS (Statistical Package for Social Science) version 19 was used for the data analysis. Visual method using histogram and Shapiro-Wilk test were used to check for normality. The data were presented in mean±standard deviation and median±quartile deviation. Comparison of the studied parameters was done using Mann-Whitney U test and Un-paired t test, whichever was appropriate. The association between duration of DM and selected variables was studied using Spearman's rho. Statistical significance was chosen at p-value (2-talied) of ≤0.05 for all the analyses.

RESULTS

The table 1 shows the descriptive statistics and also comparison of the studied parameters between the two genders. There was statistical significant difference only in the ferritin level between the two genders (Table 1).

Table 1 Descriptive statistics and comparison between the two genders

Parameters	Mean±S.D. (Median±Q.D.)			p-value
	Whole (n=200)	Male (n=135)	Female (n=65)	
Age (years)	56.93±10.12 (57.00±7)	57.06±10.29 (57.50±6.5)	56.65±9.83 (55.00±5.88)	.788#
Duration of DM (years)	13.00±8.03 (11.50±5.5)	13.64±8.04 (13.50±5.5)	11.66±7.88 (9.00±5.88)	.094
Hb (g/dl)	10.71±2.62 (10.85±2.22)	10.79±2.70 (10.85±2.38)	10.54±2.46 (10.85±1.88)	.548
ESR (mm/hr)	32.80±23.45 (26.50±16.63)	33.17±22.79 (27.50±16.5)	32.03±24.91 (24.00±17)	.528
24UP (mg)	1232.97±1386.96 (285.00±1065)	1364.54±1465.24 (292.50±1156.25)	957.48±1170.02 (265.00±606.88)	.073
Ferritin (ng/ml)	126.15±83.06 (120.00±42.45)	145.63±88.39 (146.00±42.5)	83.99±48.74 (80.00±30.13)	<.001**
MCV (fL)	77.76±14.92 (83.05±12.21)	77.66±14.59 (82.50±12.08)	77.96±15.72 (85.40±12.43)	.512
MCH (pg)	22.72±6.97 (22.35±6.11)	22.59±6.96 (21.90±6.07)	22.97±7.04 (22.95±6.33)	.962
MCHC (%)	26.62±6.21 (25.40±5.55)	26.55±6.10 (25.50±5.61)	26.78±6.49 (25.40±5.49)	.986
PCV (%)	35.13±10.41 (41.45±10.85)	35.28±10.46 (41.15±10.85)	34.82±10.39 (41.70±10.88)	.598
CrC (ml/min)	74.72±24.16 (76.93±15.55)	73.47±23.26 (76.27±15.62)	77.30±25.94 (81.55±15.75)	.288
A/C ratio (mg/mmol)	105.74±117.07 (12.70±113.99)	116.46±119.76 (13.05±118.9)	83.48±108.82 (11.75±70.93)	.065

**p–value≤0.01: highly significant. Mann-Whitney U test; #Un-paired t test.
S.D.=standard deviation, Q.D.=quartile deviation.

The correlations of duration of DM with various selected variables are given in table 2 & 3. There was significant positive correlation between duration of DM with ESR, ferritin level (except in females), 24 UP and A/C ratio (Table 2 & 3).

Table 2 Correlation between duration of DM with age and haematological variables

Variables	Duration of DM (years)		
	All (n=200)	Male (n=135)	Female (n=65)
Age	.097	.097	.102
Hb	-.541**	-.575**	-.502**
ESR	.740**	.762**	.710**
Ferritin	.219**	.240**	-.012
MCV	-.365**	-.353**	-.380**
MCH	-.469**	-.466**	-.471**
MCHC	-.402**	-.378**	-.446**
PCV	-.198**	-.146	-.326**

**p–value≤0.01: highly significant. Spearman's rho.

Table 3 Correlation between duration of DM with 24 hour urinary protein, creatinine clearance and urinary albumin to creatinine ratio

Variables	Duration of DM (years)		
	All (n=200)	Male (n=135)	Female (n=65)
24UP	.839**	.837**	.825**
CrC	-.736**	-.709**	-.745**
A/C ratio	.811**	.818**	.779**

**p–value≤0.01: highly significant. Spearman's rho.

Duration of DM had significant negative correlations with Hb, MCV, MCH, MCHC, PCV (except in males) and CrC (Table 2 & 3).

DISCUSSIONS

Evidence suggests that high plasma glucose in DM changes the morphology of RBC as well as haematological indices. We found a positive correlation betweenduration of DM with ESR, 24 hr urinary proteins and albumin creatinine ratio, in both the gender, but serum ferritin positively correlated only in male patients. Negative correlation between duration of T2DM with Hb, PCV, MCV, MCH, MCHC and creatinine clearance were found in both male and female patients.

Previous studies showed a positive association between insulin resistant and high RBC count or, high haematocrit level[21-23] contrary to our. The possible reasons argued for high PCV or, Hb level in these studies were that, high insulin (due to insulin resistance in T2DM) has synergistic effect with erythropoietin on erythroid precursor stimulation[24], stimulatory effects of insulin on erythropoietin production[25] and stimulation of progenitor cell by insulin independently of erythropoietin.[26] It is therefore possible that a vicious cycle will develops in chronic insulin resistance state like DM, where haematological parameter and insulin resistance will mutually enhances one another. However, two of these studies were done on non-diabetics and none of these studies had correlated the haematological parameters with duration of T2DM.

In our study, there was negative correlation between duration of T2DM with various haematological variables like PCV, Hb, RBC indices. Although we didn't do comparative study of these with those of non-diabetics control individuals. The possible mechanism for the negative correlation is high oxidative stress induced damaged of RBC membrane.[10-12] Hyperglycemia generates reactive oxygen species (ROS).[27-29] Oxidative stress develops in DM due to imbalance between

antioxidants and antioxidant in favor of the later as low level of antioxiadant are seen in DM.[30, 31]

Positive correlation of 24 hour urine protein with diabetic duration indicates decline in renal function as evidenced by multiples studies.[32-34] Although clinical renal involvement occurs after occurs after 15 to 20 years after the onset of DM, some T2DM patient had kidney damaged at the time of diagnosis[35, 36] and about one third of DM patient suffers from microalbuminuria after 15 years of onset of the disease.[37] The mean duration of DM in our study was approximately 13 (13.64 for males and 11.66 for females) years from the time of diagnosis.

Urine albumin to creatinine ratio, which is an early and sensitive indicator of renal involvement was positively correlated with duration of T2DM in our study. Also there was negative correlation between duration of T2DM with creatinine clearance. The result was consistence with other studies on different populations.[38-40]

CONCLUSION

We conclude that duration of DM has adverse effect on haematological parameter as well as renal function in type 2 DM patients. Hence, early diagnosis of T2DM should be emphasised and prioritized.

References

1. Schwarz PE, Gallein G, Ebermann D, Muller A, Lindner A, Rothe U, *et al*. Global Diabetes Survey--an annual report on quality of diabetes care. *Diabetes Res Clin Pract* 2013;100:11-8.
2. WHO. Global report on diabetes. Geneva. 2016.
3. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract 2010*;87:4-14.
4. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract* 2011;94:311-21.
5. Anjana RM, Ali MK, Pradeepa R, Deepa M, Datta M, Unnikrishnan R, *et al*. The need for obtaining accurate nationwide estimates of diabetes prevalence in India - rationale for a national study on diabetes. *Indian J Med Res* 2011;133:369-80.
6. Wannamethee SG, Perry IJ, Shaper AG. Hematocrit and risk of NIDDM. *Diabetes* 1996;45:576-9.
7. Tamariz LJ, Young JH, Pankow JS, Yeh HC, Schmidt MI, Astor B, *et al*. Blood viscosity and hematocrit as risk factors for type 2 diabetes mellitus: the atherosclerosis risk in communities (ARIC) study. *Am J Epidemiol* 2008;168:1153-60.
8. Gokulakrishnan K, Deepa R, Sampathkumar R, Balasubramanyam M, Mohan V. Association of leukocyte count with varying degrees of glucose intolerance in Asian Indians: the Chennai Urban Rural Epidemiology Study (CURES-26). *Metab Syndr Relat Disord* 2009;7:205-10.
9. Gkrania-Klotsas E, Ye Z, Cooper AJ, Sharp SJ, Luben R, Biggs ML, *et al*. Differential white blood cell count and type 2 diabetes: systematic review and meta-analysis of cross-sectional and prospective studies. PLoS One 2010;5:e13405.
10. Ishikawa K, Takenaga K, Akimoto M, Koshikawa N, Yamaguchi A, Imanishi H, *et al*. ROS-generating mitochondrial DNA mutations can regulate tumor cell metastasis. *Science* 2008;320:661-4.
11. Halliwell B. Free radicals and antioxidants - quo vadis? *Trends Pharmacol Sci* 2011;32:125-30.
12. Kumar R. Biochemical changes in erythrocyte membrane in type 2 diabetes mellitus. *Indian J Med Sci* 2012;66(5-6):131-5.
13. Rudberg S, Osterby R, Dahlquist G, Nyberg G, Persson B. Predictors of renal morphological changes in the early stage of microalbuminuria in adolescents with IDDM. *Diabetes Care* 1997;20:265-71.
14. Hou X, Wang J, Feng P. Relations of glycemic control to diabetic nephropathy in patients with non-insulin-dependent diabetes mellitus (NIDDM)--a pair-matched case-control study. *Chinese J Epidemio* 2000;21:264-6.
15. Gruden G, Cavallo-Perin P, Olivetti C, Repetti E, Sivieri R, Bruno A, *et al*. Albumin excretion rate levels in non-diabetic offspring of NIDDM patients with and without nephropathy. *Diabetologia* 1995;38:1218-22.
16. Rathod SG AA, Shekokar PP. A Study of Haematological Changes in Chronic Renal Failure. *Sch J App Med Sci* 2014;2:1232-4.
17. American Diabetes A. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010;33 Suppl 1:S62-9.
18. World Health Organization. Nutritional anaemias: report of a WHO scientific group. 1968 [13-17 March].
19. American Diabetes A. Standards of medical care in diabetes--2014. *Diabetes Care* 2014;37 Suppl 1:S14-80.
20. Botev R, Mallie JP, Couchoud C, Schuck O, Fauvel JP, Wetzels JF, *et al*. Estimating glomerular filtration rate: Cockcroft-Gault and Modification of Diet in Renal Disease formulas compared to renal inulin clearance. *Clin J Am Soc Nephrol* 2009;4:899-906.
21. Barbieri M, Ragno E, Benvenuti E, Zito GA, Corsi A, Ferrucci L, *et al*. New aspects of the insulin resistance syndrome: impact on haematological parameters. *Diabetologia* 2001;44:1232-7.
22. Catalano C, Muscelli E, Natali A, Mazzoni A, Masoni A, Bernardini B, *et al*. Reciprocal association between insulin sensitivity and the haematocrit in man. *Eur J Clin Invest* 1997;27:634-7.
23. Hanley AJ, Retnakaran R, Qi Y, Gerstein HC, Perkins B, Raboud J, *et al*. Association of hematological parameters with insulin resistance and beta-cell dysfunction in nondiabetic subjects. *J Clin Endocrinol Metab* 2009;94:3824-32.
24. Bersch N, Groopman JE, Golde DW. Natural and biosynthetic insulin stimulates the growth of human erythroid progenitors in vitro. *J Clin Endocrinol Metab* 1982;55:1209-11.
25. Masuda S, Chikuma M, Sasaki R. Insulin-like growth factors and insulin stimulate erythropoietin production in primary cultured astrocytes. *Brain Res* 1997;746:63-70.
26. Kurtz A, Jelkmann W, Bauer C. Insulin stimulates erythroid colony formation independently of erythropoietin. *Br J Haematol* 1983;53:311-6.
27. Casoinic F, Sampelean D, Buzoianu AD, Hancu N, Baston D. Serum Levels of Oxidative Stress Markers in Patients with Type 2 Diabetes Mellitus and Non-

alcoholic Steatohepatitis. *Rom J Intern Med* 2016;54:228-36.
28. Tiwari BK, Pandey KB, Abidi AB, Rizvi SI. Markers of Oxidative Stress during Diabetes Mellitus. *J Biomark* 2013;2013:378790.
29. Maritim AC, Sanders RA, Watkins JB, 3rd. Diabetes, oxidative stress, and antioxidants: a review. *J Biochem Mol Toxicol.* 2003;17:24-38.
30. Palanduz S, Ademoglu E, Gokkusu C, Tamer S. Plasma antioxidants and type 2 diabetes mellitus. *Res Commun Mol Pathol Pharmacol* 2001;109:309-18.
31. Bajaj S, Khan A. Antioxidants and diabetes. *Indian J Endocrinol Metab* 2012;16(Suppl 2):S267-71.
32. Goderis G, Van Pottelbergh G, Truyers C, Van Casteren V, De Clercq E, Van Den Broeke C, *et al*. Long-term evolution of renal function in patients with type 2 diabetes mellitus: a registry-based retrospective cohort study. *BMJ Open*. 2013;3:e004029.
33. Biradar SB, Kallaganad GS, Rangappa M, Kashinakunti SV, Retnakaran R. Correlation of spot urine protein-creatinine ratio with 24-hour urinary protein in type 2 diabetes mellitus patients: A cross sectional study. *J* Res *Med Sci.* 2011;16:634-9.
34. Dabla PK. Renal function in diabetic nephropathy. *World J Diabetes* 2010;1:48-56.
35. Shahbazian H, Rezaii I. Diabetic kidney disease; review of the current knowledge. *J Renal Inj Prev*. 2013;2:73-80.
36. Gall MA, Rossing P, Skott P, Damsbo P, Vaag A, Bech K, *et al*. Prevalence of micro- and macroalbuminuria, arterial hypertension, retinopathy and large vessel disease in European type 2 (non-insulin-dependent) diabetic patients. *Diabetologia* 1991; 34:655-61.
37. Mogensen CE. Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. *N Engl J Med* 1984; 310:356-60.
38. Blessing O OF, Olarewaju M. Plasma glucose, creatinine and urea levels in type 2 diabetic patients attending a Nigerian teaching hospital. *Research Journal of Medical Science* 2011;5:1-3.
39. Singh PK, Salman; Mittal, Rabindra Kumar. Glycemic status and renal function among type 2 diabetics. *Bangladesh Journal of Medical Science* 2014; 13:406-10.
40. Karar T, Alniwaider RA, Fattah MA, Al Tamimi W, Alanazi A, Qureshi S. Assessment of microalbuminuria and albumin creatinine ratio in patients with type 2 diabetes mellitus. *J Nat Sci Biol Med* 2015;6(Suppl 1):S89-92.

How to cite this article:

Saurabh Agarwal *et al* (2017) 'Correlation of Haematological Variables with Duration of Type 2 Diabetes Mellitus: Results From North Indian Population', *International Journal of Current Advanced Research,* 06(12), pp. 8475-8478.
DOI: http://dx.doi.org/10.24327/ijcar.2017.8478.1369

****