Heliyon 7 (2021) e07366

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Correlation of non-clinical parameters with the hematological indices in type 2 diabetic Mellitus patients

Vamitha Paneerselvam Sampathkumar [a], Prathipa Krishnamurthy [a], Saravanan Balaraman [a], Dhivya Balaiya [a], Ravi Sivaraman [a], Reji Manjunathan [b,*]

[a] Department of Pathology, Government Chengalpattu Medical College, Chengalpattu, Tamilnadu, India
[b] Multi- Disciplinary Research Unit (MDRU), Government Chengalpattu Medical College, Chengalpattu, Tamilnadu, India

HIGHLIGHTS

- Correlation of the PLC value with the duration of diabetic predicts the severity of the condition in females with type 2 DM with complications.
- Correlation of the P-LCR value with the age predicts future complications in females with type 2 DM without complications.
- Corelation of the PCT value with the age predicts the future severity of complications in males with type 2 DM without complications.

ARTICLE INFO

Keywords:
Diabetic Mellitus
Hematological parameters
Vascular complications

ABSTRACT

Background: The study's main aim is to compare and correlate the levels of various hematological indices in type 2 DM patients with the gender, age, duration, and family history of diabetic conditions to predict diabetes-related complications.
Methods: The diabetic population is divided into 2, group 1- subjects with complications and group 2- subjects without complications. Hematological indices are measured using an automated analyzer.
Results: Females from group 1 show a significantly higher value for PLC ($3.72 \pm 4.79/<0.05$) and positively correlate with the diabetic duration. Females with >40 years of age from group 2 show a significantly higher value for platelet larger cell ratio (P-LCR/%) (40.17 ± 3.25 (>40)/<0.05) than those with <40 age and positively correlated with the age. Males with >40 years of age from group 1 show a significantly higher value for plateletcrit (PCT/%) (0.297 ± 0.067 (>40)/<0.05) than those from <40 age and positively correlated with the age. All the male subjects show significant higher values for hemoglobin concentration (HB/g/dl) (13.49 ± 2.22)/<0.05 for group 1) (13.61 ± 2.02)/<0.05 for group 2) and hematocrit (HCT/L/L) (37.30 ± 7.55/<0.05 for group 1) (38.64 ± 5.42/<0.05 for group 2).
Conclusion: Correlating the hematological indices with the gender, age, and duration of diabetic condition will help determine future complications and the severity of the diabetic condition in type 2 DM patients.

1. Introduction

Diabetes is a chronic metabolic disease linked with elevated blood glucose levels and causes critical damage to the heart, blood vessels, eyes, nerves, and kidneys [1]. Though diabetes is considered a global health issue, its prevalence is more in developed and middle-income countries. These nations report more than 80% of diabetic-related mortality every year. About 463 million people have diabetes with equal rates in women and men and are the 7th leading cause of death globally [2]. Diabetes is a potential epidemic in India with more than 65.1 million cases and is the second-highest number globally, with a projection of 109 million affected persons by 2025 [3]. According to the Indian Council of Medical Research (ICMR) reports, the patterns of diabetes in India are related to the geographical distribution and more prevalent in the urban population located towards India's southern states [4]. Tamilnadu is the worst affected state with a 10.4% weighted prevalence of diabetes than any other state in India [5]. The complications of diabetes can dramatically impair the quality of a person's life and can cause long-lasting disabilities such as microangiopathy, macro-vascular pathologies, and immune compromise. These disabilities are associated with non-modifiable

* Corresponding author.
E-mail address: rejimanjunath@gmail.com (R. Manjunathan).

https://doi.org/10.1016/j.heliyon.2021.e07366
Received 16 April 2021; Received in revised form 31 May 2021; Accepted 17 June 2021

demographic and gender factors and other health problems such as smoking, obesity, high blood pressure, lack of exercise, and elevated cholesterol level [6].

In recent years, there is renewed interest in red blood cells (RBC) and platelet-associated parameters to predict diabetic-related complications in type 2 diabetic Mellitus (DM) patients. Finding out the levels of hematological indices could identify the development of DM-related degenerative complications and the severity of disease in type 2 DM patients [7]. It has been observed that the hematological parameters play a crucial role in the development of macro and micro-vascular complications and are the reasons behind the increased morbidity and mortality in type 2 DM patients [8, 9, 10]. Furthermore, analysis of these parameters is relatively low in cost and can be obtained by routine haemograms using automated hematology analyzers [11]. Other potential risk factors related to type 2 DM include age, gender, duration of diabetes, lifestyle, and genetic risk factors [12].

In the present study, we primarily aimed to compare the levels of some of the clinically essential platelets and RBCs indices in type 2 DM patients noted with complications and without complications. Secondly, we try to correlate various factors such as age, gender, diabetic duration, and family history of the diabetic condition of these patients with the hematological parameters. Hence, for the first time, we try to explore the significance of considering both the non-clinical and the hematological parameters in type 2 DM patients while identifying DM-related complications other than finding the level most evaluated glycemic parameter, the HbA1C, the glycemic marker. Thus, we believe that we can have a subtle prediction and the proper management of the pathology of diabetic scenarios in type 2 DM patients.

2. Methodology

2.1. Study design and participants

The study is conducted in the Department of Pathology, Chengalpattu Government Medical College and Hospital, Chengalpattu, Tamilnadu, India. The research is conducted for three months. All the patients who met the inclusion criteria and provided the written consent are selected for the research analysis. Type 2 DM is diagnosed according to American Diabetic Association Criteria [13]. The study consists of 200 patients reported with type 2 DM with complications and without complications. Among the 200 patients, 165 patients are noted with various pathological conditions such as hypertension, heart problem, renal issues, neuropathy, and cataract. The remained 35 patients were identified with type 2 DM but without any complications. In addition, demographic information such as age, sex, diabetic duration, family history, the patients' clinical complications, smoking, dietary habits, and exercise are noted from the hospital records. Routine blood check-up is the only easily available and affordable methods for people who are visiting the government hospitals located at the rural region of India. Hence, within the restricted environment, we consider to correlate the easily available non-clinical indices with hematological parameters as a tool to predict complications in diabetic condition rather than analyzing highly expensive other pathological issues behind the scenario.

2.2. Calculation of sample size

The sample size is calculated based on the given formula $n = \frac{Z^2 \times p(1-p)}{e^2}$ in which n represents sample size, Z for Z score 1.96, P for population proportion 84.7%, and e for the margin of error 5% [14]. Based on this equation, the sample size is calculated for n = 200 for an infinite population. For samples with finite population, especially for Group 1 the formula applied is $n = \frac{\frac{Z^2 \times p(1-p)}{e^2}}{1+\frac{Z^2 \times p(1-p)}{e^2 N}}$ in which n represents the sample size, Z for Z score 1.96, P for population proportion 33%, e for margin of error 3%, and the N for the total population size 200. For group 2 the formula, the same formula is applied [15]. The n represents sample size, Z for Z score 1.96, P for population proportion 01%, e for margin of error 3%, and the N for the total population size 200.

2.3. Ethical approval

Human Ethical Clearance is obtained from the Institutional Ethical Committee (IEC) meeting held at the Medical Education Unit, Government Chengalpattu Medical College, Chengalpattu.

2.4. Measurement of RBC and platelet indices

2 mL of venous blood from each patient is collected in test tubes containing EDTA as an anti-coagulant. Samples were tested within one hour of collection to minimize variations. The blood samples are run on H360 Automated 3 part differential Hematologic Analyzer, Transasia Bio-Medicals. The platelet indices such as platelet count (PC in mcL), mean platelet volume (MPV in femtolitre), platelet distribution width (PDW in %), plateletcrit (PCT in %), platelet larger cell ratio (P-LCR in %), and the RBCs indices such as mean corpuscular volume (MCV in femtolitre), mean corpuscular hemoglobin (MCH in g/L) and mean corpuscular concentration (MCHC in femtolitre) are analyzed. White blood cell count (WBC in X 10^9/L), red blood cell count (RBC in a million/mm^3), hemoglobin concentration (HB in g/dl), hematocrit (HCT L/L), red cell distribution width (RDW in %), and Red blood cell distribution width standard deviation (RDW-SD in femtolitre) were also measured.

2.5. Inclusion and exclusion criteria

All non-insulin-dependent diabetic Mellitus (type 2) who attended the Chengalpattu Government Medical College during the specified period are included in the study. However, patients on antiplatelet drugs such as Aspirin and Clopidogrel or with certain conditions such as

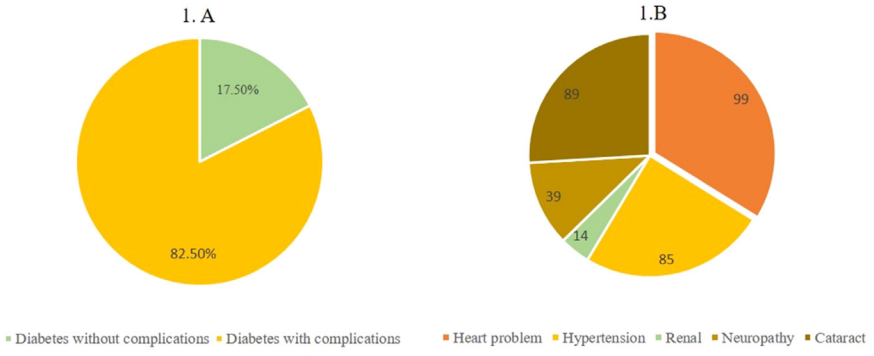

Figure 1. Distribution of study population.

nutritional anemia, thrombocytopenia, cardiovascular severe, hepatic, and renal diseases, and those diagnosed with any malignancy have excluded from the study.

2.6. Statistical analysis

The statistical software used for the study was SPSS Version 24. Qualitative variables are expressed as frequency, percentages, and quantitative variables as mean and standard deviation. Statistical tests used for handling the data were chi-square test for categorical variable, independent t-test for mean and comparison, and Pearson correlation coefficient to correlate various platelet and hematological indices with biochemical parameters. P-value of <0.05 was considered to be statistically significant.

3. Results

Two hundred patients diagnosed with type 2 DM were selected for the study and are grouped into 2. The first group consists of 165 subjects (82.50%) of 64 males, and 101 females reported type 2 DM with various complications. The second group consists of 35 subjects (17.50%) of 14 males and 21 females reported with type 2 DM without complications (Figure 1A). Within-group 1 (type 2 DM with complications), 99 subjects were reported with heart problems, 89 with cataracts, 85 with hypertension, 39 with neuropathy, and 14 subjects were with renal issues (Figure 1B). Among the 165 representatives from group 1, 95 patients identified with a family history of the diabetic condition. Fifty-five subjects reported more than 5 years of diabetic duration, and 115 were less than 5 years from the same group. All the male participants have the habit of consuming alcohol and smoking on daily basis and is noticed with diabetic with various complications. More than 36 males in the study population (46.16%) have the habit of daily intake of non-vegetarian foods in diet. Among the female candidates, 55 females (69.3%) have the habit of alcohol consumption at least thrice in a week and daily smoking habits and is noticed with diabetic with various complications. From the female group, 108 females (85%) from the study population have the habit of daily intake of non-vegetarian diet on daily basis. All the participants are representative of either from farmer or daily wage community worker and hence the role of physical exercise is negligible. Almost 142 representatives from group 1 were above the age of 40, and 23 were below 40. In group 2 (type 2 DM without complications), all of them reported no family history of a diabetic condition. Among them, 9 subjects were above the age of 40, and 26 were below the age of 40. From group 2, 21 subjects identified with more than 5 years of diabetic duration, and 14 were with less than 5 years. The frequency and the percentage of above- mentioned data are categorized based on gender and given in Table 1. We have not found any statistically significant difference for the mean value of age between the two groups, though the subjects from group 1 exhibit a higher mean age value than the group 2 members. While considering the duration of a diabetic condition, the female representatives from both the groups show a higher mean value and statistically significant between the female and the male subjects from the type 2 DM with complications group (<0.05) (Table 2).

We have not observed any statistically significant difference in the mean value of both the platelets and the RBCs parameters between the groups before considering the gender of the participants (Table 3). After considering the gender of the subjects, we observed that the female representatives from both groups show a higher mean value for platelet parameters, and the male subjects from both groups show a higher mean value for hematological parameters than the opposite gender. The female

Table 1. Frequency table.

DM with complications	Total	Males	Females
		(Number and Percentage)	
1) Subjects	165	64 (38.78%)	101 (61.22%)
2) Above 40 years	142	53 (37.32%)	89 (62.67%)
3) Below 40 years	23	11 (47.83%)	12 (52.17%)
4) Duration more than 5 years	50	14 (28%)	36 (72%)
5) Duration less than 5 years	115	50 (43.48%)	65 (56.52%)
6) With family history	95	35 (36.84%)	60 (63.16%)
7) With Hypertension	85	28 (32.94%)	57 (67.06%)
8) With Heart problem	99	34 (34.34%)	65 (65.66%)
9) With Renal problem	14	5 (35.71%)	9 (64.29%)
10) With Neuropathy	39	17 (43.59%)	22 (56.41%)
11) With Cataract	89	37 (41.57%)	52 (58.43%)
DM without complications			
1) Subjects	35	14 (40%)	21 (60%)
2) Above 40 years	9	2 (23.3%)	7 (77.7%)
3) Below 40 years	26	12 (46.15%)	14 (53.85%)
4) Duration more than 5 years	21	15 (71.43%)	36 (28.57%)
5) Duration less than 5 years	14	11 (78.57%)	3 (21.43%)
6) With family history	35	35 (36.84%)	60 (63.16%)

Table 2. The Mean age and Duration.

Variables	DM with complications			DM without complications		
	Mean ± SD			Mean ± SD		
	Male	Female	*p* value	Male	Female	*p* value
Age	53.28 ± 12	53.80 ± 10.11	0.765	50.86 ± 10.93	46.71 ± 9.67	0.247
Duration	4.07 ± 4.083	5.73 ± 4.90	**<0.05***	3.32 ± 3.19	4.88 ± 3.69	0.108

Independent T test for age and Mann Whitney U test for duration. $P < 0.05$ is considered as significant at 95% confidence interval and is marked in bold with *.

Table 3. Comparison of platelet and hematological parameters between DM with complications and without complications.

Variables	Platelets Parameters		
	Mean ± SD		
	DM with complications	DM without complications	*p* value
PLC	3.32 ± 3.80	2.84 ± 0.86	0.463
P-LCR	36.94 ± 7.01	36.22 ± 8.68	0.597
PCT	0.35 ± 0.51	0.31 ± 0.06	0.574
MPV	11.46 ± 1.84	11.77 ± 1.59	0.358
PDW	13.94 ± 2.39	13.98 ± 2.83	0.927
	Red Blood Cells Parameters		
HB	12.54 ± 2.08	12.33 ± 2.01	0.597
MCH	29.82 ± 11.14	29.46 ± 9.72	0.859
MCHC	34.25 ± 3.34	34.51 ± 3.43	0.678
HCT	35.77 ± 5.99	35.57 ± 5.41	0.859
MCV	78.29 ± 12.53	73.79 ± 20.42	0.090
RDW	13.77 ± 1.41	13.38 ± 1.45	0.090
RDW (SD)	40.57 ± 4.82	40.43 ± 2.21	0.866

Analyzed the hematological parameters without gender and age classification. Independent T test for P-LCR, MPV, PDW, HB, MCH, MCHC, HCT, MCV, RDW, RDW (SD) and Mann Whitney U test for PLC and PCT. $P < 0.05$ is considered as significant at 95% confidence interval. DM = diabetic mellitus, SD = standard deviation, PC = platelet count (mcL), MPV = mean platelet volume (L), PDW = platelet distribution width (%), PCT = plateletcrit (%), P-LCR = platelet larger cell ratio (%), MCV = mean corpuscular volume (FI), MCH = mean corpuscular hemoglobin (g/L), MCHC = mean corpuscular concentration (fL), HB = hemoglobin concentration (g/dl), HCT = hematocrit (L/L), RDW = red cell distribution width (%) and RDW-SD = Red blood cell distribution width standard deviation (fL).

subjects from the type 2 DM with complications group showed statistically significant higher mean value for PLC (<0.05) (Figure 2A). While considering the type 2 DM without complications group, we have not found any statistically significant difference in the mean value of platelet parameters between the gender. The male subjects from the type 2 DM with complications group show statistically significant higher mean value for HB, MCHC, and HCT (<0.05) (Figure 2C), and the same gender from the type 2 DM without complications group shows statistically

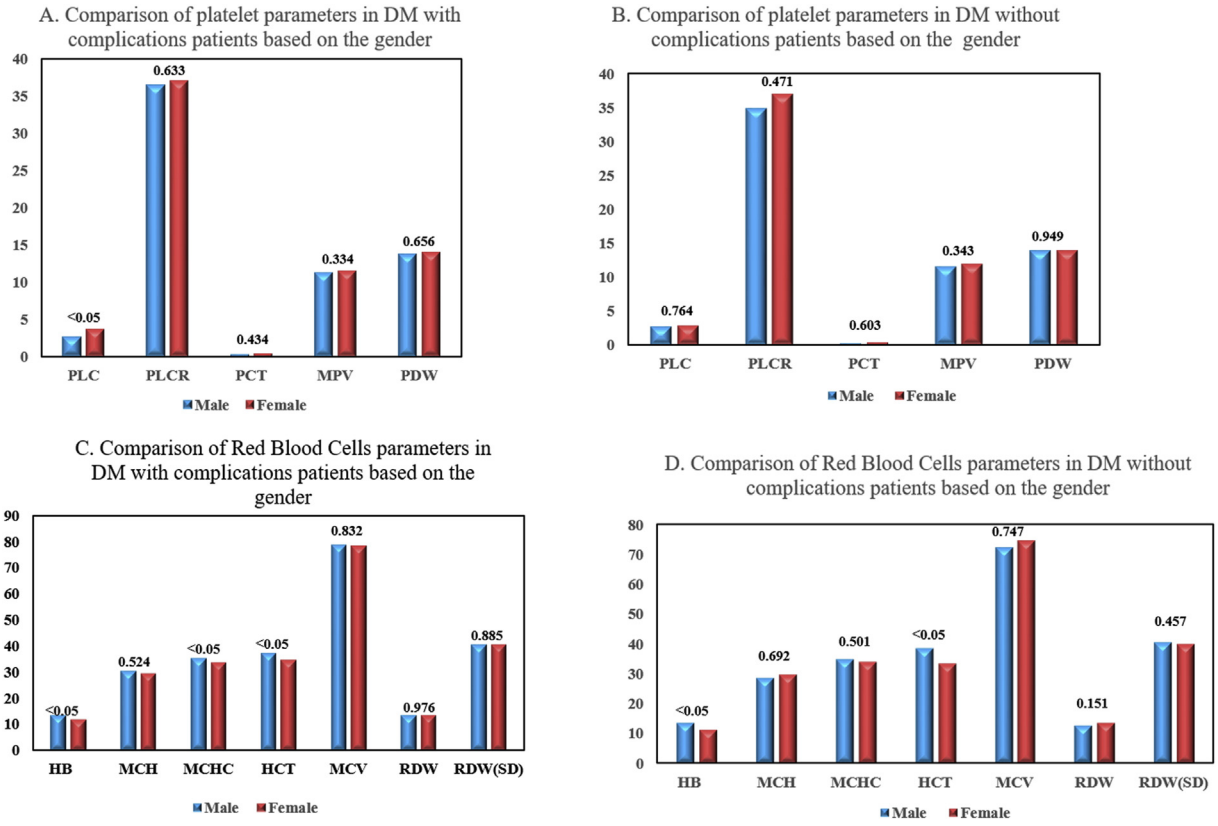

Figure 2. Comparison of haematological parameters between DM with complications and without complications groups based on the gender. Bar chart depicting comparison of platelet and RBC indices between the DM with complications and without complications patients based on the gender. A- the female subjects from the type 2 DM with complications group showed statistically significant higher mean value for PLC (<0.05). B- no statistically significance for the parameters in type 2 DM without complications based on gender. C- the male subjects from the type 2 DM with complications group show statistically significant higher mean value for HB, MCHC, and HCT (<0.05) than the female subjects. D- the male subjects from the type 2 DM without complications group shows statistically significant higher mean value for HB and HCT than the female subjects. $P < 0.05$ is considered as significant at 95% confidence interval.

Table 4. Comparison of hematological parameters between DM with complications and without complications based on the gender.

Variables	Platelet Parameters					
	DM with complications			DM without complications		
	Mean ± SD			Mean ± SD		
	Male	Female	*p* value	Male	Female	*p* value
PLC	2.67 ± 0.72	3.72 ± 4.79	**<0.05***	2.79 ± 1.06	2.88 ± 0.71	0.76
P-LCR	36.61 ± 6.76	37.15 ± 7.19	0.633	34.90 ± 9.52	37.10 ± 8.19	0.471
PCT	0.28 ± 0.07	0.40 ± 0.65	0.434	0.30 ± 0.07	0.31 ± 0.06	0.603
MPV	11.28 ± 1.94	11.57 ± 1.78	0.334	11.45 ± 1.40	11.98 ± 1.71	0.343
PDW	13.83 ± 2.23	14.01 ± 2.50	0.656	14.02 ± 2.14	13.96 ± 3.26	0.949
	Red Blood Cells Parameters					
HB	13.49 ± 2.22	11.93 ± 1.75	**<0.05***	13.61 ± 2.02	11.48 ± 1.52	**<0.05***
MCH	30.52 ± 10.91	29.38 ± 11.32	0.52	28.64 ± 3.86	30.00 ± 12.25	0.692
MCHC	35.27 ± 3.83	33.61 ± 2.82	**<0.05***	35.00 ± 4.02	34.19 ± 3.03	0.501
HCT	37.30 ± 7.55	34.79 ± 4.52	**<0.05***	38.64 ± 5.42	33.52 ± 4.45	**<0.05***
MCV	78.56 ± 13.89	78.13 ± 11.66	0.832	72.39 ± 24.34	74.71 ± 17.94	0.747
RDW	13.76 ± 1.43	13.77 ± 1.40	0.976	12.95 ± 0.90	13.67 ± 1.67	0.151
RDW(SD)	40.64 ± 6.38	40.53 ± 3.54	0.885	40.78 ± 2.33	40.20 ± 2.16	0.457

Analyzed the hematological parameters based on gender classification. Independent T test for P-LCR, MPV, PDW, HB, MCH, MCHC, HCT, MCV, RDW, RDW (SD) and Mann Whitney U test for PLC and PCT. $P < 0.05$ is considered as significant at 95% confidence interval and is marked in bold with *. DM = diabetic mellitus, SD = standard deviation, PC = platelet count (mcL), MPV = mean platelet volume (L), PDW = platelet distribution width (%), PCT = plateletcrit (%), P-LCR = platelet larger cell ratio (%), MCV = mean corpuscular volume (FI), MCH = mean corpuscular hemoglobin (g/L), MCHC = mean corpuscular concentration (fL), HB = hemoglobin concentration (g/dl), HCT = hematocrit (L/L), RDW = red cell distribution width (%) and RDW-SD = Red blood cell distribution width standard deviation (fL).

Table 5. Comparison of hematological parameters between DM with complications and without complications based on the age and gender.

Variables	DM with complications					DM without complications			
Platelet parameters	Age	Male	*P* value	Female	*P* value	Male	*P* value	Female	*P* value
		Mean ± SD		Mean ± SD		Mean ± SD		Mean ± SD	
PLC	<40	2.327 ± 0.549	0.082	2.633 ± 0.782	0.403	3.75 ± 0.77	0.176	2.64 ± 0.79	0.299
	>40	2.742 ± 0.733		3.872 ± 5.079		2.63 ± 1.04		2.99 ± 0.67	
P-LCR	<40	34.400 ± 7.700	0.236	33.800 ± 8.648	0.087	31.20 ± 6.08	0.574	30.95 ± 11.61	**<0.05***
	>40	37.07 ± 6.531		37.60 ± 6.911		35.52 ± 10.05		40.17 ± 3.25	
PCT	<40	0.227 ± 0.454	**<0.05***	0.293 ± 0.07	0.537	0.34 ± 0.16	0.410	0.30 ± 0.06	0.499
	>40	0.297 ± 0.067		0.417 ± 0.692		0.29 ± 0.05		0.31 ± 0.06	
MPV	<40	10.636 ± 1.338	0.227	10.716 ± 1.54	0.077	11.20 ± 1.27	0.798	11.69 ± 1.94	0.590
	>40	11.418 ± 2.028		11.68 ± 1.78		11.49 ± 1.47		12.13 ± 1.65	
PDW	<40	12.92 ± 1.743	0.138	13.22 ± 3.145	0.215	12.35 ± 0.07	0.247	12.47 ± 4.16	0.144
	>40	14.02 ± 2.285		14.11 ± 2.40		14.29 ± 2.19		14.70 ± 2.56	
Red Blood Cells Parameters									
HB	<40	14.40 ± 1.540	0.135	12.141 ± 1.435	0.653	12.90 ± 2.97	0.164	10.99 ± 1.90	0.304
	>40	13.30 ± 2.30		11.89 ± 1.189		13.72 ± 1.98		11.72 ± 1.31	
MCH	<40	29.73 ± 2.760	0.795	28.50 ± 5.584	0.777	27.00 ± 1.41	0.537	27.29 ± 5.82	0.487
	>40	30.68 ± 11.943		29.49 ± 11.898		28.92 ± 4.10		31.66 ± 14.46	
MCHC	<40	35.45 ± 1.036	0.859	34.83 ± 4.609	0.111	34.00 ± 2.83	0.720	34.71 ± 4.99	0.588
	>40	35.23 ± 4.191		33.45 ± 2.477		35.17 ± 4.26		33.93 ± 1.54	
HCT	<40	37.67 ± 12.14		34.92 ± 5.583		37.50 ± 6.36	0.761	77.57 ± 4.64	0.619
	>40	37.22 ± 6.374		34.78 ± 4.400		38.83 ± 5.54		73.28 ± 21.8	
MCV	<40	75.955 ± 23.15	0.499	81.50 ± 6.067	0.288	80.00 ± 1.41	0.652	32.14 ± 6.38	0.327
	>40	79.094 ± 11.35		77.67 ± 12.17		71.13 ± 26.22		34.21 ± 3.16	
RDW	<40	13.427 ± 0.966	0.398	13.67 ± 1.271	0.806	12.20 ± 0.14	0.216	14.11 ± 1.27	0.406
	>40	13.832 ± 1.508		13.78 ± 1.42		13.08 ± 0.92		13.45 ± 1.84	
RDW (SD)	<40	40.581 ± 3.033	0.974	41.866 ± 2.203	0.164	41.80 ± 2.83	0.524	40.32 ± 1.98	0.853
	>40	40.652 ± 6.869		40.34 ± 3.64		40.61 ± 2.33		40.13 ± 2.31	

Analyzed the hematological parameters based on gender and age classifications. Independent T test for P-LCR, MPV, PDW, HB, MCH, MCHC, HCT, MCV, RDW, RDW (SD) and Mann Whitney U test for PLC and PCT. $P < 0.05$ is considered as significant at 95% confidence interval and is marked in bold with *. DM = diabetic mellitus, SD = standard deviation, PC = platelet count (mcL), MPV = mean platelet volume (L), PDW = platelet distribution width (%), PCT = plateletcrit (%), P-LCR = platelet larger cell ratio (%), MCV = mean corpuscular volume (FI), MCH = mean corpuscular hemoglobin (g/L), MCHC = mean corpuscular concentration (fL), HB = hemoglobin concentration (g/dl), HCT = hematocrit (L/L), RDW = red cell distribution width (%) and RDW-SD = Red blood cell distribution width standard deviation (fL).

Table 6. Correlation of hematological parameters with demographic data (based on gender).

Variables (Platelet)		DM with complications				DM without complications			
		Male		Female		Male		Female	
		Pearson correlation	*P* value	Pearson correlation	*P* value	Pearson correlation	*P* value	Pearson correlation	*P* value
Age	PLC	0.153	0.226	0.136	0.175	-0.328	0.252	0.155	0.503
	P-LCR	0.166	0.190	0.138	0.169	0.138	0.637	0.520	**<0.05***
	PCT	0.316	**<0.05***	0.075	0.458	-0.126	0.669	-0.025	0.913
	MPV	0.154	0.223	0.050	0.619	-0.056	0.850	0.074	0.751
	PDW	0.226	0.073	0.054	0.589	0.255	0.378	0.168	0.467
Duration	PLC	0.044	0.732	0.252	**<0.05***	- 0.039	0.895	0.184	0.424
	P-LCR	0.285	**<0.05***	0.166	0.098	0.473	0.088	0.433	0.050
	PCT	0.171	0.171	0.156	0.119	0.181	0.536	0.072	0.757
	MPV	0.112	0.378	0.079	0.430	0.305	0.290	0.285	0.211
	PDW	0.278	**<0.05***	0.059	0.559	0.211	0.469	0.290	0.203
Variables (Red Blood cells)									
Age	HB	-0.326	**<0.05***	0.027	0.792	- 0.303	0.293	-0.11	0.961
	MCH	0.124	0.328	-0.005	0.964	- 0.115	0.669	-0.134	0.562
	MCHC	-0.132	0.297	-0.170	0.089	-0.284	0.325	0.246	0.282
	HCT	-0.138	0.277	0.086	0.392	-0.121	0.681	0.051	0.825
	MCV	-0.009	0.946	0.044	0.665	-0.396	0.161	-0.144	0.535
	RDW	0.226	0.073	0.054	0.589	0.618	0.018	-0.154	0.506
	RDW (SD)	0.015	0.906	0.080	0.428	0.445	0.111	-0.238	0.298
Duration	HB	-0.197	0.120	-0.063	0.533	- 0.030	0.920	-0.170	0.461
	MCH	0.041	0.745	0.037	0.712	0.355	0.213	0.047	0.840
	MCHC	-0.026	0.836	0.007	0.946	0.000	1.000	-0.168	0.466
	HCT	-0.215	0.089	-0.085	0.397	-0.027	0.926	-0.116	0.616
	MCV	-0.010	0.938	-0.011	0.911	0.062	0.834	-0.016	0.945
	RDW	-0.109	0.390	0.143	0.155	0.316	0.270	-0.212	0.356
	RDW (SD)	-0.069	0.589	-0.059	0.556	0.024	0.935	-0.072	0.755

Pearson correlation was done between the age and duration with hematological indices. $P < 0.05$ is considered as significant at 95% confidence interval and is marked in bold with *. DM – diabetic mellitus, SD = standard deviation, PC = platelet count (mcL), MPV = mean platelet volume (L), PDW = platelet distribution width (%), PCT = plateletcrit (%), P-LCR = platelet larger cell ratio (%), MCV = mean corpuscular volume (FI), MCH = mean corpuscular hemoglobin (g/L), MCHC = mean corpuscular concentration (fL), HB = hemoglobin concentration (g/dl), HCT = hematocrit (L/L), RDW = red cell distribution width (%) and RDW-SD = Red blood cell distribution width standard deviation (fL).

significant higher mean value for HB and HCT than the female subjects from the corresponding groups (Table 4 and Figure 2D).

We also try to find if any statistically significant connection exists between the studied parameters with the subjects' age. The subjects were categorized into 2, based on the age as above and below 40 years. The data emphasized that both the gender grouped above the age of 40 years from both the groups show higher mean value for platelet parameters than the below the 40 years of age. In PLC and PCT values, the male candidates grouped under the age below 40 years from group 1 show a higher mean value than those from group 2. In the type 2 DM with complications group, those male subjects above the age of 40 years show a statistically significant mean value for PCT than those males below the age below 40 years (<0.05). The female subjects above the age of 40 from the group type 2 DM without complications show a statistically significant mean value for P-LCR than those below 40. At the same time, we have not found any statistically significant connection between the mean values of RBCs parameters with the subjects' age (Table 5).

In this study, we try to correlate the platelets and RBCs parameters with the demographic data such as age and duration of the diabetic condition. The result pointed out that, while considering the platelet parameters from type 2 DM with complications group, the age of the male candidates is positively correlated with the PCT value significantly (<0.05) and the age of the female candidates from type 2 DM without complications is positively correlated with the P-LCR value significantly (<0.05). Considering duration, the female candidates from the type 2 DM with complications group show a significant positive correlation with PLC value (<0.05). The males from the same group show a significant positive correlation with P-LCR and PDW values. There was no correlation between the diabetic duration and the subjects' platelet parameters from the type 2 DM without complications group. Moving to the RBCs parameters, we found a statistically significant negative correlation between the age and the HB value of male candidates. Apart from this observation, we cannot find any significant correlation of RBCs parameters with the age and the duration of both the genders from the studied two groups (Table 6). We could also hinge no statistically significant connection between the family history of diabetic (Yes/No) condition with the platelet and the RBCs parameters of the representatives from both the groups (Table 7).

4. Discussion

In developing countries, the prevalence of type 2 DM is on the rise and is a growing health problem associated with an increased risk of micro and macrovascular complications [16]. It is a big challenge for the healthcare system and public health and retards its socio-economic development [11]. In patients with type 2 DM, persistent hyperglycemia exposes RBCs to elevated glucose concentrations, resulting in the clotting mechanism's glycation [17]. Platelet function plays a significant role in the progression of macro and micro vascular-related health issues in type 2 DM. It has been documented as an unavoidable reason for increased morbidity and mortality [9]. Therefore, many efforts put forward to identify and prove the utility of some of the clinically essential RBCs and platelet parameters to act as biomarkers for the early detection of diabetic complications [7, 11, 18].

Table 7. Comparison of hematological parameters with family history in DM with complications subjects.

Variables	Family History	Mean ± SD	*P* value
Platelet parameters			
PLC	Yes	3.43 ± 3.74	0.455
	No	3.15 ± 3.91	
P-LCR	Yes	37.63 ± 6.5	1.491
	No	35.99 ± 7.59	
PCT	Yes	0.40 ± 0.67	1.314
	No	0.29 ± 0.06	
MPV	Yes	11.62 ± 2.03	1.306
	No	11.24 ± 1.534	
PDW	Yes	13.95 ± 2.42	0.088
	No	13.92 ± 2.37	
Red Blood Cell parameters			
HB	Yes	12.5 ± 2.01	0.910
	No	12.51 ± 2.18	
MCH	Yes	29.43 ± 10.56	0.605
	No	30.34 ± 11.93	
MCHC	Yes	34.18 ± 2.92	0.736
	No	34.36 ± 3.84	
HCT	Yes	36.35 ± 5.37	0.140
	No	34.96 ± 6.69	
MCV	Yes	78.94 ± 10.53	0.437
	No	77.40 ± 14.85	
RDW	Yes	13.79 ± 1.48	0.801
	No	13.79 ± 1.31	
RDW(SD)	Yes	40.55 ± 5.18	0.960
	No	40.59 ± 4.31	

Independent T test for P-LCR, MPV, PDW, HB, MCH, MCHC, HCT, MCV, RDW, RDW (SD) and Mann Whitney U test for PLC and PCT. $P < 0.05$ is considered as significant at 95% confidence interval. DM = diabetic mellitus, SD = standard deviation, PC = platelet count (mcL), MPV = mean platelet volume (L), PDW = platelet distribution width (%), PCT = plateletcrit (%), P-LCR = platelet larger cell ratio (%), MCV = mean corpuscular volume (FI), MCH = mean corpuscular hemoglobin (g/L), MCHC = mean corpuscular concentration (fL), HB = hemoglobin concentration (g/dl), HCT = hematocrit (L/L), RDW = red cell distribution width (%) and RDW-SD = Red blood cell distribution width standard deviation (fL).

It is well documented that both the gender are equally affected with type 2 DM related complications [2]. This study found a female preponderance in the whole population with more female candidates under type 2 DM with complications group, expressly noted with cardiac issues. Most of the type 2 DM subjects with complications group are above 40 with less than 5 years of diabetic condition and a family history of diabetes. Our inference is almost in accordance with the earlier report done by Klein and co-workers. In this report they suggested that the diabetic patients are more vulnerable to develop complications after the age of thirty [19]. Our finding emphasizes that if the patient is above the age of 40 with a diabetic condition, then the chance of developing complications especially cardiac related issues occurs in an earlier period and is found to be accelerated if there is a family history of diabetes. This observation is well suited with the female gender grouped under type 2 DM with complications because they show statistically significant value for the duration of diabetic condition than the opposite gender.

Type 2 DM is a complex disease and has been considered a 'prothrombotic state' due to enhanced platelet activity [20]. MPV and PDW are more relevant among the platelet indices and are considered clinical predictive biomarkers of diabetic-related microvascular complications [7, 11, 21]. In our study, we found that, in general, the values of hematological indices from both groups are observed to more or less equal without any statistically significant changes. On the other hand, after categorizing the subjects based on gender, we can find statistically significant changes for some of the analyzed parameters. For example, the females from the type 2 DM with complications group showed a statistically significant high mean value for PLC and are positively correlated significantly with the duration of the diabetic condition and is in accordance with previous reports [22, 23]. Thus, this observation indicates that considering the PLC value and the duration of the diabetic condition in females (in type 2 DM with complications) will mark the severity of the diabetic condition. Those females who are above the age of 40 from the type 2 DM without complications group showed statistically significant higher mean value for P-LCR and is positively correlated significantly with the age of the subjects. Considering the P-LCR value and the age will help predict type 2 DM-related complications in those female subjects who already identified with type 2 DM without complications. While considering the male subjects, the men with age above 40 from type 2 DM with complications group showed statistically significant higher mean value for PCT and is positively correlated significantly with the age of the subjects. Prediction of the severity of type 2 DM-related complications is highly possible if we consider the PCT value and the age of the male subjects diagnosed with type 2 DM without complications. Though the male subjects from the type 2 DM with complications group show a significant positive correlation between the PDW and the duration of the diabetic condition, it failed to gain a statistically significant relationship with the indices.

Jamen et al., stated that among the RBC indices, MCHC and RDW could act as a foremost prognosticator and may be applied as the auxiliary indicators to deteriorate the inflammatory state of glucoregualtion in type 2 DM patients. This observation also helped determine the pathology of coronary artery disease in type 2 DM without complications patients, which is considered the main reason for increased mortality in diabetic patients globally [3, 24]. All the male subjects in the study showed statistically significantly higher value for HB and HCT irrespective of the groups. Among these indices, the HB value was found to negatively correlate with the age of the male subject's representative of the type 2 DM with complications group. Even though the male from the type 2 DM with complications group showed significantly higher value

for the HCT than the female subjects, we could not find any significant correlation with the age and duration of the diabetic condition. The whole study family history of diabetic condition does not show any significant correlation with the analyzed indices.

5. Conclusion

The study majorly accentuates the importance of considering the gender, age, and duration of diabetic subjects and the canonical clinical, hematological indices for predicting and managing type 2 DM-related complications. In diabetic female subjects, to find out the severity of microvascular complications, it is highly advisable to consider both the PLC value and the duration of the diabetic condition to improve the pathology of the situation. For the same gender, considering the age and the P-LCR value in parallel will predict diabetic complications such as cardiac issues and hypertension in the future. On the other hand, considering the age and the PCT value in male diabetic subjects with complications will be more accurate to find the severity of diabetic-related pathology than considering the PDW value alone. One can also easily interpret the severity of type 2 DM-related complications in those diabetic male subjects with complications after considering the HB value and age. Thus, considering the clinical and hematological indices along with the gender, age, and duration of diabetic condition will help determine the future complications and the severity of the diabetic situation of the candidates towards the amelioration of the scenario. The data also underscore that the female gender is more vulnerable to type 2 DM and develops major cardiovascular issues. However, further study with a larger sample is needed to investigate the relationship between the findings with the definite micro and macrovascular complications and the mode of progression.

Declarations

Author contribution statement

Reji Manjunathan: Conceived and designed the experiments; Wrote the paper.

Vamitha Paneerselvam Sampathkumar: Performed the experiments.

Saravanan Balaraman: Analyzed and interpreted the data.

Dhivya Balaiya and Ravi Sivaraman: Contributed reagents, materials, analysis tools or data.

Funding statement

This work was supported by Chengalpattu Government Medical College MultiDisciplinary Research Unit (MDRU).

Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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