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Original Research

Complete blood count and cardiovascular risk markers in type 2 diabetes mellitus – findings from a cross-sectional study in south India

Ramya Samidurai[1], Sureka varaLakshmi Venkatesan[2], Chandan Bala Kataria[3], Ganesh Mano[4], Manikandan Sundaramalingham[5], Umamaheswari karmegam[6]

[1] Assistant Professor, Department of Physiology, VELS Medical College and Hospital, Vels Institute of Science, Tecnhnology and Advanced Studies (VISTAS), Thiruvallur, India
[2] Professor, Department of Physiology, ACS Medical College and Hospital, Dr MGR Educational University and Research Institute, Maduravoyal, Chennai, India
[3] Tutor, Faculty of Allied Health Sciences, Dr MGR Educational University and Research Institute, Maduravoyal, Chennai, India
[4] Professor and Head Department of Physiology, ACS Medical college and Hospital, Dr MGR Educational University and Research Institute, Maduravoyal, Chennai, India
[5] Professor, Department of Physiology, Tagore Medical College and Hospital, Chennai, India
[6] Assistant Professor, Department of Physiology, Karpaga Vinayaga Institute of Medical Sciences, Chengalpet, India

*Correspondence to: S.Ramya, Assistant Professor, Department of Physiology, VELS Medical College and Hospital, Vels Institute of Science and Advanced Studies.(VISTAS), Thiruvallur, India. E-mail: ramyabalaji2705@gmail.com

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Abstract

Background and Aim: Poorly controlled diabetes leads to various micro and macro vascular complications. Hematological indices can be an independent predictor of cardio vascular diseases risk ratios and associated with a high white blood cell count are comparable to other inflammatory markers. The main aim of the current work was to evaluate the correlation between cardiovascular risk markers with the complete blood count among type2 diabetes mellitus (T2DM). **Material and Methods:** Study population included 105 subjects with T2DM. Age group of the study participants was 40–60 years. Complete blood count and markers such as HsCRP, lipid profile, and Hepatic Enzymes were estimated. Data analysis was performed with SPSS 17. Differences among groups were calculated using t test and/or Mann-Whitney Test for parametric and nonparametric variables, respectively. Chi square test was used. The correlation analysis was performed by Pearson correlation/Kendall's tau method for parametric and nonparametric variables respectively. **Results and Conclusion:** On analysis, hematological parameter shows significance with various cardio vascular risk markers and can be used as biomarker to assess the severity of cardio vascular diseases.

Keywords: Hepatic enzymes, hematological parameters, high sensitive C-reactive protein, lipid profile.

Introduction

Diabetes is a major risk factor for the development of cardiovascular diseases (CVD). Poorly controlled diabetes leads to various micro and macro vascular complications such as coronary artery diseases, peripheral arterial disease, stroke, nephropathy, retinopathy, neuropathy, and oxidative damage to tissues and cells [1–5]. Globally CVD affects approximately 32.2% of all individuals with T2DM and is a major cause of mortality among people with T2DM. Coronary artery disease and

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stroke were the major contributors for mortality [6]. Many biomarkers have been used to predict the inflammation and risk of Cardio vascular diseases. Hematological indices are an independent predictor of cardio vascular diseases' risk ratios and along with a high white blood cell count are comparable to other inflammatory markers like Hs CRP [70].

Cellular elements in the blood are involved in the pathogenesis of atherosclerosis which is due to inflammation and leads to ischemia. The persistent increase in glycosylated hemoglobin as a result of poor glycemic management is associated with the structural and functional changes in hemoglobin (Hb) molecule, the osmotic disturbance, and the cytoplasm viscosity within each cell. All these changes have an imposing effect on any of the red blood cell indices including mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and the cell shape and deformability represented by red blood cell distribution (RDW). These indices are reported as cardiovascular risk markers in various populations [8, 9]. RDW, a measure of the variability in size of circulating RBC commonly used for the diagnosis of anemia, has recently drawn increased attention as a potential biomarker of CVD risk. Researchers have demonstrated that higher or even normal reference range of RDW was strongly associated with increased risk of cardiovascular disease (CVD) events in middle aged and older adults [10, 11]. WBC count is positively associated with increased cardiovascular mortality, mainly from coronary heart diseases [12–15]. Platelets, another element of the complete blood count (CBC), play a key role in the development of atherothrombosis, resulting in cardiovascular diseases in diabetes with respect to altered platelet morphology and function [16].

Since there is paucity of data related to the association of different hematological parameters with risk markers for cardiovascular diseases in T2DM subjects, the main aim of the current work was to evaluate the correlation between cardiovascular risk markers with the complete blood count among T2DM. These tests are inexpensive, widely available, and easy to interpret.

Materials and Methods

We recruited 105 patients, with T2DM reported to Department of General Medicine, ACS medical college and hospital for routine checkup. This study included 48 males and 57 females. Subjects with cardio vascular diseases, recent surgeries, thyroid disorders, end stage renal disease, and any cancerous conditions were excluded from the study. All the participants were provided with the information sheet and informed written consent was obtained. The study was approved by institutional ethics committee.

Demographic parameters such as age, height, weight, and body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded for all the patients. After overnight fasting, venous blood samples were collected. Glycemic parameters such as fasting plasma glucose (FPG), HbA1c and complete blood count were estimated by fully automated bidirectional analyzer (sx part differential sysmex XN -1000). Red blood cell indices such as mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and red blood cell distribution width (RCDW), total WBC'S, differential leucocyte count, neutrophil lymphocyte ratio, platelet indices such as mean platelet volume (MPV) and platelet large cell ratio (PLCR) were estimated. Cardio vascular risk markers such as HsCRP, lipid profile which includes total cholesterol, low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), and triglycerides (TGL) were estimated. Hepatic enzymes such as asparate-aminotransferase (AST), alanine transaminase (ALT), gamma glutamyl transferase (GGT), and alkaline phosphatase (ALP) were also analyzed.

Data Analysis

Continuous data were presented as mean ± SD and comparison of continuous data between groups was done by independent t test and the association between the parameters was analyzed using Pearson correlation.

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Differences among groups were calculated using t test and/or Mann-Whitney Test for parametric and nonparametric variables, respectively. Chi square test was used. The correlation analysis was performed by Pearson correlation/Kendall's tau method for parametric and nonparametric variables respectively. Data analysis was performed with Statistical Package for Social Sciences version 17 for Windows (SPSS Inc., USA). $P < 0.05$ was considered as statistically significant.

Results

The participants recruited were in the age group of 40–60years (table 1). Mean age of the subjects was 49.96 ± 10.9. Subjects were divided in two groups- Group A (HbA1C < 7.0%) with 59 participants and Group B (HbA1C > 7.0%) with 46 and the mean value of HbA1c was 7.5 ± 2.3. Age and gender distribution of subjects are mentioned in table 1.

The mean values of total RBC, WBC, and platelets were higher in poorly controlled diabetic subjects (Group B) and there was a significant difference of MCV, MCH, and total WBC count (table 1). Association of hba1c with cardiovascular risk markers and hepatic enzymes shows that the mean values were higher in Group B except HDL and significant association was found with SBP, DBP, HsCRP, and GGT, ALP, TGL, LDL-C, and TC (table 2).

The Pearson correlation/Kendal tau method was used to find any significant relationship between hematological parameters and the cardiovascular risk markers and hepatic enzymes among the participants.

Table 1: Association of hematological parameters in with HbA1C.

Parameters	HbA1C (%)		
	Group A ≤ 7	Group B > 7	P value
Total RBC ($\times 10^6$ µl)	4.56 ± 0.55	4.67 ± 0.42	0.284
Hb (g/dL)	12.95 ± 1.94	12.80 ± 1.91	0.69
PCV (%)	41.02 ± 4.69	40.89 ± 4.81	0.889
MCV (fL)	91.20 ± 8.73	87.52 ± 6.00	0.016*
MCH (pq)	28.48 ± 3.46	27.27 ± 2.71	0.054*
MC HC (g/dL)	31.16 ± 1.76	31.09 ± 1.68	0.829
RDW-SD (fL)	48.41 ± 6.75	46.25 ± 4.20	0.06
WBC ($\times 10^3$ µl)	7.34 ± 1.65	8.26 ± 2.01	0.012*
Neutro (%)	57.69 ± 10.38	58.87 ± 8.15	0.527
Lympho (%)	32.51 ± 7.56	32.20 ± 7.60	0.834
NL ratio (%)	1.97 ± 0.97	2.02 ± 0.91	0.795
Monocytes (%)	3.98 ± 1.12	3.64 ± 0.76	0.08
Eosinophils (%)	4.67 ± 4.64	4.81 ± 4.78	0.959
Basophils (%)	0.19 ± 0.75	0.18 ± 0.09	0.634
Platelet count ($\times 10^3$ µl)	272.34 ± 65.29	295.52 ± 78.24	0.101
PLCR(%)	28.05 ± 7.82	29.32 ± 6.55	0.379
PCT (%)	0.28 ± 0.05	0.30 ± 0.07	0.112
PDW (fL)	11.96 ± 2.02	12.49 ± 2.44	0.23
MPV (fL)	10.42 ± 0.96	10.68 ± 1.08	0.23

(*p < 0.05)

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Table 2: Association of cardiovascular risk markers with HbA1C.

Parameters	HbA1C (%)		
	≤7	>7	p value
SBP (mmHg)	121.02 ± 10.1	130.52 ± 17.05	0.001**
DBP (mmHg)	81.63 ± 5.311	85.52 ± 7.133	0.002*
BMI (Kg/m²)	25.9 ± 4.26	26.6 ± 4.68	0.432
HsCRP (mg/dL)	4.21 ± 4.59	7.45 ± 2.95	0.000**
GGT (U/l)	26.90 ± 9.60	35.23 ± 11.47	0.000**
SGOT (U/l)	24.70 ± 7.57	24.86 ± 8.46	0.917
SGPT (U/l)	22.34 ± 8.47	23.98 ± 11.33	0.396
ALP (U/l)	100.12 ± 23.05	114.41 ± 28.02	0.005*
HDL-C (mg/dL)	43.54 ± 9.75	42.96 ± 8.65	0.749
TGL (mg/dL)	135.59 ± 83.20	199.70 ± 171.65	0.033*
LDL-C (mg/dL)	114.27 ± 32.47	126.91 ± 33.35	0.053*
CHO (mg/dL)	179.46 ± 38.93	199.67 ± 42.08	0.012*

*p < 0.05 ** p <0.001

Table 3: Association between hematological parameters and cardiovascular risk markers among the entire study population (n = 105).

	HbA1C(%)		BMI(Kg/m²)		SBP(mmHg)		DBP(mmHg)	
	R	p value	R	p value	R	p value	r	p value
Total RBC (×10⁶ µl)	0.171	0.081	0.292**	0.003*	0.120	0.223	0.171	0.082
Hb (g/dL)	0.026	0.792	0.233*	0.017*	0.182	0.063	0.203**	0.037*
PCV (%)	0.51	0.603	0.224*	0.021*	0.105	0.289	0.118	0.229
MCV (fL)	–0.206*	0.035*	–0.044	0.658	–0.014	0.884	–0.057	0.56
MCH (pq)	–0.149	0.128	0.005	0.963	0.134	0.171	0.108	0.271
MC HC (g/dL)	0.022	0.826	0.097	0.323	0.317**	0.001*	0.333**	0.001*
RDW-SD (fL)	–0.226*	0.02*	–0.135	0.168	–0.203*	0.038*	–0.243*	0.012*
WBC (×10³ µl)	0.231	0.018	0.148	0.132	0.034	0.733	0.031	0.755
Neutro (%)	0.007	0.946	–0.029	0.772	0.066	0.507	0.013	0.895
Lympho (%)	–0.023	0.817	0.149	0.13	–0.104	0.289	–0.081	0.41
NL ratio (%)	–0.013	0.846	–0.108	0.103	0.057	0.437	0.042	0.581
Monocytes (%)	–0.128	0.194	–0.087	0.376	0.009	0.923	–0.065	0.51
Eosinophils (%)	0.008	0.907	–0.046	0.487	0.033	0.658	0.105	0.17
Basophils (%)	–0.054	0.586	–0.089	0.365	–0.047	0.633	–0.067	0.496
Platelet count (×10³ µl)	0.033	0.737	–0.026	0.792	–0.07	0.478	–0.029	0.769
PDW(fL)	0.177	0.071	0.083	0.400	0.063	0.526	0.027	0.788
MPV(fL)	0.199*	0.042*	0.065	0.511	0.034	0.733	–0.019	0.848
PLCR(%)	0.160	0.103	0.038	0.698	0.036	0.712	–0.008	0.934
PCT (%)	0.35	0.726	–0.030	0.758	–0.128	0.194	–0.089	0.368

*p < 0.05, ** p < 0.001

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Discussion

In our study HbA1C shows significance and negative correlation with MCV and RDW (table 3) as shown in the study done by B.N.Alamri et al., [17]. Inflammation which influences erythropoiesis could be a causative factor. Sadeer G. Al-Kindi et al., explained the association of RDW in the diabetes population with diabetes-related complications such as MI, stroke, and CKD [18]. In this study it was also observed that Hba1c shows significant and positive correlation with MPV. Manoj Saluja et al., observed that the development of vascular complication resulted in higher MPV which shows the activity of platelets in subjects with poor glycemic status. Based on this they concluded that MPV can be used as simple measures to find the vascular events in diabetes [16].

BMI shows a weak positive correlation with hematological parameters like RBC count, hemoglobin, RDW and neutrophil. Abdominal fat accumulation and insulin resistance mediates the general association between BMI and hematological parameters [19]. In our study total RBC count, Hb, and PCV show significance and positive correlation with BMI (table 3). Subjects recruited in our study were non- obese, as they were in the study done by Belete Biadgo et al. High RBC, hemoglobin, and hematocrit in diabetes could contribute to identify insulin resistance in non-obese individuals [20].

A study done on RDW in cardio vascular diseases shows a strong positive correlation of RDW with blood pressure [21]. Similarly, in our study RBC indices such as MHC and RDW show significant and positive correlation with SBP and DBP. Hb was found to be significant and positively

Table 4: Association between hematological parameters and lipid profile among the entire study population (n = 105).

	HDL-C(mg/dL)		TGL(mg/dL)		LDL-C(mg/dL)		CHO(mg/dL)	
	r	p value	r	p value	r	p value	r	p value
Total RBC ($\times 10^6$ µl)	–0.206*	0.035*	0.019	0.78	0.226*	0.02*	0.19*	0.052*
Hb (g/dL)	–0.210*	0.032*	0.132*	0.048*	0.139	0.156	0.161	0.1
PCV (%)	–0.217*	0.026*	0.157*	0.018*	0.179	0.068	0.199*	0.042*
MCV (fL)	–0.100	0.308	–0.077	0.247	–0.076	0.44	–0.014	0.891
MCH (pq)	–0.058	0.559	0.031	0.646	–0.066	0.504	0.007	0.945
MC HC(g/dL)	–0.038	0.700	–0.033	0.626	–0.009	0.929	0.051	0.605
RDW-SD(fL)	–0.093	0.347	–0.118	0.076	–0.177	0.07	–0.122	0.214
WBC($\times 10^3$ µl)	0.102	0.300	0.026	0.696	0.075	0.449	0.092	0.35
Neutro (%)	–0.099	0.316	–0.061	0.359	–0.188*	0.055*	–0.174	0.075
Lympho (%)	0.081	0.411	0.072	0.280	0.216*	0.027*	0.231*	0.018*
NL ratio (%)	–0.056	0.406	–0.060	0.364	–0.19**	0.004*	–0.193**	0.004*
Monocytes (%)	–0.100	0.308	0.042	0.536	–0.103	0.296	–0.098	0.321
Eosinophils (%)	0.055	0.416	–0.026	0.698	–0.006	0.927	0.000	0.996
Basophils (%)	–0.169	0.085	–0.006	0.942	0.076	0.443	0.093	0.343
Platelet count ($\times 10^3$ µl)	0.131	0.185	0.084	0.208	0.15	0.126	0.234*	0.016*
PDW(fL)	–0.054	0.586	–0.009	0.890	0.003	0.977	–0.040	0.684
MPV(fL)	–0.090	0.362	–0.030	0.651	0.012	0.901	–0.056	0.572
PLCR(%)	0.121	0.217	–0.018	0.790	0.020	0.838	–0.044	0.657
PCT (%)	0.113	0.252	0.083	0.219	0.197*	0.044*	0.026**	0.007*

*$p < 0.05$, ** $p < 0.001$

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correlated with DBP (table 3). B O Gobel et al., explained a possible mechanism for increase in blood pressure due to increased Hb levels which could lead to increase in blood viscosity which, in turn, can worsen cardiovascular function [22].

Numerous studies have shown that a high level of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) and lower levels of high-density lipoprotein cholesterol (HDL-C) are associated with increased risk of CVD [23–26]. In this study we observed that HDL –C is significant and negatively correlated with RBC Count, HB and PCV. Previous studies have shown that a high erythrocyte count can potentially plays protective role in patients with coronary atherosclerosis [27].Whereas TGL shows significant and positive correlation with Hb and PCV, LDL-C and total CHO are significant and negatively correlated with neutrophil and NL ratio and positively correlated with RBC's and lymphocytes. Total CHO was found to be significant and positively correlated with lymphocytes, platelets, and PCT (table 4). Similar study showed that lymphocyte count was significantly associated with high LDL-C, high TG, and low HDL-C. A study conducted on Chinese population provided evidence that both, the neutrophil count and the global registry of acute coronary events risk score, are independent and joint predictors for major adverse cardiovascular events [29]. Total CHO and TG levels were also consistently and positively associated with total leukocyte, neutrophil, and lymphocyte counts [29]. Modulation of platelet activity in platelets biogenesis takes place in hypercholestremia [30]. In our study we also found that WBC, RBC, platelets, and its indices showed significance with different lipid parameters.

In our study HsCRP, a prime systemic inflammatory marker, shows strong significance and positive correlation with total WBC, neutrophil, and platelet indices such as MPV, PLCR and PCT, whereas it shows significance and negative correlation with RDW, lymphocytes, NL ratio, and monocytes (table 5). Similarly, several studies have reported a relationship between various markers of inflammation and blood cell indices. A correlation between serum levels of CRP and RDW has been described in patients with hypertension, coronary artery disease, Alzheimer's disease and in overweight adolescents [31–35]. Studies have shown that hsCRP, as well as WBC count, high neutrophils levels and low lymphocytes levels, can independently predict vascular risk in apparently both healthy men and women and also in patients with signs of CVD [36–39].

In our finding we found positive correlation of HsCRP with PCT, MPV, and PLCR. Mean platelet volume (MPV) is a major determinant of platelet functionality and higher MPV is related with a risk of cardiovascular disease like stroke, myocardial infarction, and transient ischemic attacks [40]. Similar to our study, Farah Jabeen et al., show a positive association of platelet indices with HsCRP in T2DM and also concluded that platelet indices are vital markers in early detection of diabetic complications [41].

Of all hepatic enzymes, GGT has emerged as a biomarker of cardiovascular diseases [9] Christian Obirikorang et al showed that GGT has accuracy in predicting the risk of cardiovascular diseases among diabetes mellitus individuals [43]. Previous studies demonstrated the relation between GGT and cardio vascular diseases such as hypertension, arterial stiffness, coronary artery diseases, heart failure, and pulmonary embolism [44–48]. In our study GGT are significant and positively correlated with RBC's and its indices. AST, ALT and ALP also show significance and correlation with different blood parameters. Vipin Goyal et al., explained that RBC count, HGB, and WBC count and concentration, were all higher in FLD group with increased GGT, ALP and AST. Possible mechanism could be that the oxidative stress might enhance compensatory erythropoiesis in chronic inflammatory diseases, such as atherosclerosis, coronary artery disease, metabolic syndrome, and FLD. The main physiological roles of RBCs are not only transporting oxygen and carbon dioxide but also scavenging reactive oxygen and nitrogen species. As FLD is frequently accompanied with inflammation and oxidative damage, RBC indices have been suggested to be associated with inflammatory markers, generation of RBCs may be increased. Also the capacity of spleen and liver for scavenging RBCs might be damaged

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Table 5: Association between the hematological parameters with inflammatory. Marker and hepatic enzymes among the entire study population (n = 105).

	HsCRP(%)		GGT(U/l)		AST(U/l)		ALT(U/l)		ALP(U/l)	
	R	p value	R	p value	R	p value	r	p value	r	p value
Total RBC (×10⁶ µl)	0.182	0.064	0.281**	0.004*	0.058	0.557	0.295**	0.002*	0.105	0.288
Hb (g/dL)	–0.111	0.259	0.387**	0.000	0.286**	0.003*	0.459**	0.000	–0.017	0.861
PCV (%)	–0.069	0.484	0.388**	0.000*	0.218*	0.025*	0.414**	0.000	0.006	0.951
MCV (fL)	–0.391*	0.000*	0.172	0.08*	0.23*	0.018*	0.202*	0.039*	–0.154	0.117
MCH (pq)	–0.329**	0.001	0.238*	0.015*	0.338**	0.000*	0.322**	0.001*	–0.110	0.265
MC HC (g/dL)	–0.084	0.395	0.248*	0.011*	0.346**	0.000*	0.369**	0.000*	0.023	0.814
RDW-SD (fL)	–0.196*	0.045*	–0.065	0.507	0.108	0.272	–0.074	0.455	–0.189	0.053
WBC (×10³ ML)	0.365**	0.000*	0.15	0.126	–0.106	0.283	–0.046	0.643	0.28**	0.004*
Neutro (%)	0.294**	0.002*	–0.083	0.398	–0.053	0.591	–0.115	0.244	0.074	0.451
Lympho (%)	–0.259**	0.008*	0.139	0.157	0.107	0.279	0.199*	0.042*	–0.086	0.384
NL ratio (%)	–0.189**	0.005*	–0.103	0.119	–0.180**	0.007*	–0.166*	0.012	0.023	0.723
Monocytes (%)	–0.206*	0.035*	–0.028	0.779	0.129	0.19	0.111	0.262	–0.103	0.297
Eosinophils (%)	–0.019	0.775	–0.055	0.406	–0.035	0.597	–0.093	0.162	0.082	0.216
Basophils (%)	–0.157	0.11	0.043	0.666	0.094	0.342	0.008	0.932	–0.078	0.431
Platelet count (×10³ µl)	0.168	0.088	–0.010	0.917	–0.189	0.053	–0.192*	0.050*	–0.144	0.142
PDW(fL)	0.11	0.910	0.037	0.706	–0.120	0.223	–0.077	0.435	–0.043	0.660
MPV(fL)	–0.005	0.957	0.049	0.618	–0.079	0.423	–0.044	0.656	–0.039	0.693
PLCR (%)	0.067	0.500	0.048	0.628	–0.078	0.426	–0.045	0.646	–0.059	0.552
PCT (%)	0.154	0.116	0.026	0.769	–0.211*	0.031*	–0.187	0.057	0.105	0.285

*p < 0.05, ** p < 0.001

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in FLD condition, leading to further increase of RBC count [49, 50].

Conclusion

Even though HsCRP and hepatic enzymes are known to be effective biomarkers for evaluating risk of cardio vascular diseases in T2DM patients, from our study it is concluded that hematological parameters such as Total RBC, WBC, platelet count along with its indices can also be used for assessing risk factors of cardio vascular diseases. Periodic estimation of HbA1C with Complete Blood Count profile in T2DM patients will help in the early detection of inflammatory changes and prognosis of Cardio vascular diseases.

Conflict of Interest

The authors declare no conflict of interest.

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