



ORIGINAL ARTICLE

The leucocyte profile in controlled and uncontrolled diabetes.

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ABSTRACT... Objective: To compare the white blood cell profile in controlled and uncontrolled diabetes. **Study Design:** Cross Sectional. **Setting:** Creek General Hospital, Karachi. **Period:** June to December 2021. **Material & Methods:** Conducted on 156 diabetic patients selected by convenient sampling technique. Inclusion Criteria was Type 2 diabetic adults. Exclusion Criteria is patients with other chronic diagnosed diseases, Type 1 Diabetes, age less than 30 years and recently diagnosed diabetes. Patients were divided in two groups according to glycemic control criteria: controlled diabetes was HbA1c less than 7.5% or RBS < 180mg/dl or FBS 70-100mg/dl in last two weeks and vice versa for uncontrolled diabetes. WBC parameters included total leukocyte count (TLC), Neutrophil, Lymphocyte, Eosinophil, Basophil and Monocyte differential. **Results:** Among the 156 patients, the leucocyte count was increased in 41(26%), normal in 109 (70%) and decreased in 6(3%). The neutrophils was raised in 62(39.7%), normal in 85(54.4%) and decreased in 9(5.7%). In controlled group the mean TLC value is 9047/L, mean neutrophil is 70.26%, mean lymphocyte is 26.96%, mean monocyte is 2.01%. In uncontrolled group the mean TLC value is 9270.5/L, neutrophil value is 69.7%, lymphocyte value is 26.4%, monocyte value is 1.82%. In both the controlled and uncontrolled groups: one fourth of the patients had increased TLC, more than one third of patients had raised neutrophils, and a significant percentage had decreased lymphocyte and monocytes. In uncontrolled group percentage of patients with raised TLC was equally high in both the genders and also higher in the elderly age group. In controlled group it was raised more in females and middle age group. In uncontrolled group the neutrophils was raised more in males and equally in both the genders in controlled group. In both the groups the neutrophils were higher in the elderly age bracket. In uncontrolled group the percentage of raised lymphocyte was higher in female while in the controlled group it was higher in males. In both the groups a significant percentage of elderly had decreased lymphocyte count. Monocyte count in the controlled group was decreased equally in both genders and in the middle age group. In uncontrolled group females, middle and elderly group had decreased monocyte count. **Conclusion:** There was a higher percentage of diabetics with elevated leucocyte and neutrophil count but a decreased lymphocyte and monocyte count in uncontrolled diabetes compared to controlled diabetes.

Key words: Diabetes, Leucocyte, Lymphocyte, Neutrophil.

INTRODUCTION

Leukocytosis has been linked to Diabetes Mellitus (DM) due to the subclinical inflammatory nature of the disease. Despite excluding any obvious source of infection research has associated increased white blood cell count (WBC) or certain component of its differentials example neutrophil count, etc with diabetes.¹ Chronic inflammation, depicted by the upsurge of cytokines and acute-phase reactants and the instigation of inflammatory signaling complexes are involved in the pathogenesis of type 2 diabetes.² This low

grade inflammation is the key constituent in Type 2 diabetes pathophysiology.³

White blood cells are also associated with insulin resistance and inversely related to insulin secretion.⁴ An elevated leukocyte count is linked with chronic diabetic complications and can be used to predict development of micro and macro vascular complications.⁵

Rationale for the study is that by studying the pattern of a white blood cell profile in a diabetic

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patient a clinician would be able to identify any occult signs of inflammation present and hence modify the management to prevent imminent complications. Local research and documented data investigating this topic is scarce and hence the initiative to do this study.

MATERIAL & METHODS

A cross sectional study was conducted on 156 diabetic patients presenting at Creek General Hospital, Karachi between June to December 2021, selected by convenient sampling technique. Ethical approval was taken by IRB committee (ref # UMDC/Ethics/2021/22/02/08/304).

Inclusion Criteria is Individuals more than 30 years old and diagnosed with Type 2 DM greater than 3 months. Exclusion Criteria is patients with other chronic diagnosed diseases including renal, cardiac, respiratory, hepatic, and autoimmune disease, with Type 1 DM or less than 30 years old and patients diagnosed with Type 2 DM less than 3 months ago.

Patients were divided in two groups according to glycemic control criteria: good glycemic control (controlled diabetes) is HbA1c less than 7.5% while HbA1c > 7.5% indicated poor glycemic control (uncontrolled T2DM). If HbA1c was not available, controlled T2DM was RBS < 180mg/dl or FBS 70-100mg/dl in last two weeks and vice versa for poor control. Duration of diabetes, medications (only those on Metformin, Sulphonylurea or conventional insulin were included), presence of other comorbid (like hypertension, coronary artery disease, cerebrovascular disease, chronic liver disease, and chronic kidney disease), smoking status and glycemic control status was recorded. WBC parameters included TLC (total leukocyte count), Neutrophil, Lymphocyte, Eosinophil, Basophil and Monocyte differential. Four milligram of blood samples for CBC were collected in specialized tubes containing ethylene di-amino tetra acetic acid (EDTA) and calculated by an automatic counting machine at the Laboratory and Diagnostics Centre of Creek General Hospital. The data was analyzed using Statistical Package for Social Sciences IBM version 22. The reference range are as follows⁶;

Total leukocytes: 4000-11000/L

WBC differential ranges:

- Neutrophils - 55-70%
- Lymphocytes - 20-40%
- Monocytes - 2-8%
- Eosinophil - 1-4%
- Basophils - 0.5-1%

RESULTS

There were 64(41%) males and 92(59%) females in the study. 15(9.6%) were in the young (18-39 years) age group, 93(59.6%) were in the middle (40 – 59 years) age group and 48(30.7%) were above 60 years, elderly age group. The TLC was increased in 41(26%), normal in 109(70%) and decreased in 6(3%) of the total diabetics. Among the 156 patients, the neutrophils was raised in 62(39.7%), normal in 85(54.4%) and decreased in 9(5.7%). In control group the mean TLC value is $9047 \pm 3081/L$, neutrophil value $70.26 \pm 11.2\%$, lymphocyte value $26.96 \pm 10.01\%$, monocyte value $2.01 \pm 0.89\%$, eosinophil value $2 \pm 0.80\%$, and basophil value $0.01 \pm 0.11\%$. In uncontrolled group the mean TLC value is $9270.51 \pm 2826/L$, neutrophil value $69.78 \pm 9.03\%$, lymphocyte value $26.49 \pm 8.2\%$, monocyte value $1.82 \pm 0.86\%$, eosinophil value $2.19 \pm 1.08\%$, and basophil value $0.01 \pm 0.11\%$. Mean Neutrophil to lymphocyte ratio (NLR), which is got by simply division of mean neutrophil count by lymphocyte count was 2.6 in both controlled and uncontrolled groups.

In the uncontrolled group, the TLC was raised in 6(20%) of the males and 13(22%) of the females. It was normal in 23(76.7%) males and 34(71%) of females [$p=.749$]. In controlled group, the TLC was raised in 8(23%) of the males and 14(32%) of the females. It was normal in 25(73.5%) males and 27(61%) of females [$p=.483$]. In uncontrolled group the TLC was raised equally in both genders. In controlled group it was raised more in females. In the uncontrolled group among the 3 patients in the young age group, 1(33%) had raised TLC count and the other 2(66%) had normal count. In the middle group [53 patients], 9(17%) had increased and 43(81%) had normal leucocyte. 9(41%) and 12(54.5%) had increased and normal TLC in the 22 elderly patients, respectively.

[p=.216] In the controlled group among the 12 in young age group, 3(25%) had raised TLC count and the rest 9(75%) had normal count. In the middle group 14(35%) had increased and 23(52%) had normal leucocyte number among the 40 patients. 5(19%) and 20(77%) had raised and normal TLC range respectively among the 26 elderly patients [p=.460]. In uncontrolled group the TLC was raised more in the elderly. In controlled group it was raised more in the middle group. In the controlled group, 61 patients were on oral hypoglycemic among which 16(27%) had raised TLC. Among the 8 patients who were exclusively on insulin, 3(37%) had raised TLC. [p=.850]. In the uncontrolled group, 52 patients were on oral hypoglycemic among which 12(23%) had raised TLC. Among the 15 patients who were on insulin, 4(26%) had elevated TLC. [p=.893]. Inference is that uncontrolled group had nearly equal number of subjects with raised TLC count. In controlled group it was higher in those on insulin management. Duration of diabetes was not associated with the TLC count in any of the control groups.

In the uncontrolled group, the neutrophils was raised in 15(50%) of the 30 males and 14(29%) of the 48 females. It was normal in 14(46.7%) males and 33(69%) of females. It was decreased in 1(3%) of the males and 1(2%) of females. [p=0.152]. In controlled group, the neutrophils was raised in 15(44%) of the 34 males and 18 (41%) of the 44 females. It was normal in 14(41%) males and 24(54.5%) of females. It was decreased in 5(14%) of the males and 2(4.5%) of females. [p=0.228]. Thus, in the uncontrolled group the neutrophils

were raised more in males while in the controlled group it was raised equally in both the genders.

In the uncontrolled group, the lymphocyte was raised in 7(9%) of the 34 males and 14(29%) of the 48 females. It was normal in 14(46.7%) males and 33(69%) of females. It was decreased in 1(3%) of the males and 1(2%) of females. [p=0.152]. In controlled group, the lymphocyte was raised in 6(18%) of the 34 males and 1 (2%) of the 44 females. It was normal in 18(52%) males and 27(61%) of females. It was decreased in 10(29%) of the males and 16(36%) of females. [p=0.062]. Thus, in the uncontrolled group the percentage of raised lymphocyte was higher in female while in the controlled group frequency of raised lymphocyte was higher in males.

In the controlled group among the 34 males, normal monocyte count was found in 24(70%) and a decreased monocyte value was present in 10(29%). Among the 44 females, 32(72%) had normal monocyte count and 12(27%) had decreased count [p=.516] In the uncontrolled group, there were 30 males among which the normal monocyte count was found in 21(70%) males and decreased monocyte percentage was found in 9(30%). Among the 48 females, 24(50%) was present in each category of normal and decreased monocyte count. Hence, in the controlled group, monocyte value was decreased equally in both the genders while in the uncontrolled group, females had a high percentage of decreased monocyte count compared to males.

WBC Parameter	Controlled Group				Uncontrolled Group			
	Increased	Normal	Decreased	Total	Increased	Normal	Decreased	Total
TLC	22(28.2%)	52(56.7%)	4(5%)	78(100%)	19(24%)	57(73%)	2(2.6%)	78(100%)
Neutrophil	33(42.3%)	38(48.7%)	7(9%)	78(100%)	29(37.2%)	47(60.3%)	2(2.6%)	78(100%)
Lymphocyte	7(9%)	45(57.7%)	26(33.3%)	78(100%)	3(3.8%)	60(76.9%)	15(19.2%)	78(100%)
Monocyte	0	56(71.8%)	22(28.2%)	78(100%)	0	45(57.7%)	33(42.3%)	78(100%)
Basophil	0	78(100%)	0	78(100%)	0	78(100%)	0	78(100%)
Eosinophil	1(1.3%)	77(98.7%)	0	78(100%)	4(5%)	73(93.6%)	1(1.3%)	78(100%)

Table-I. The frequency profile of TLC and its differential count in controlled and uncontrolled group (n=156)

Age Group	Neutrophil Count							
	Controlled Group p=.025				Uncontrolled Group p=.034			
	Increased	Normal	Decreased	Total	Increased	Normal	Decreased	Total
Young (18-39years)	2(16.7%)	8(66.7%)	2(16.7%)	12(100%)	1(33%)	2(66%)	0	3(100%)
Middle(40-59 years)	16(40%)	23(57.5%)	1(2.5%)	40(100%)	14(26.4%)	38(71.7%)	1(2%)	53(100%)
Elderly(>60 years)	15(57.7%)	7(27%)	4(15.4%)	26(100%)	14(63.6%)	7(31.8%)	1(4.5%)	22(100%)
total	33(42%)	38(48.7%)	7(9%)	78(100%)	29(37%)	47(60.3%)	2(2.6%)	(100%)

Table-II. A comparison of the neutrophil count in age groups of controlled and uncontrolled group. Percentages are according to the count in that age group.

Age Group	Lymphocyte Count							
	Controlled Group(n=78) p=.551				Uncontrolled Group(n=78) p=.012			
	Increased	Normal	Decreased	Total	Increased	Normal	Decreased	Total
Young (18-39 years)	2(16.7%)	8(66.7%)	2(16.7%)	12(100%)	0(0%)	3(100%)	0	3(100%)
Middle(40-59 years)	3(7%)	24(60%)	13(32%)	40(100%)	1(2%)	46(87%)	6(11%)	53(100%)
Elderly(>60 years)	2(7%)	13(50%)	11(42%)	26(100%)	2(9%)	11(50%)	9(40%)	22(100%)
total	7(9%)	45(57.7%)	28(33%)	78(100%)	3(100%)	60(100%)	15(100%)	78(100%)

Table-III. The association of lymphocyte count with respect to age group in controlled and uncontrolled group. Percentages are according to the count in that age group.

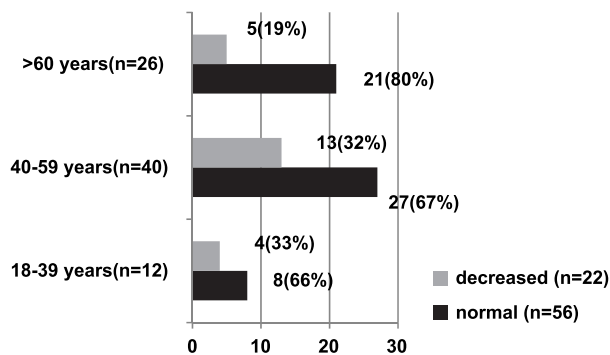


Figure-1. Association of monocyte count with age group in controlled group (n=78, p=0.460). Percentages are according to the count in that age group.

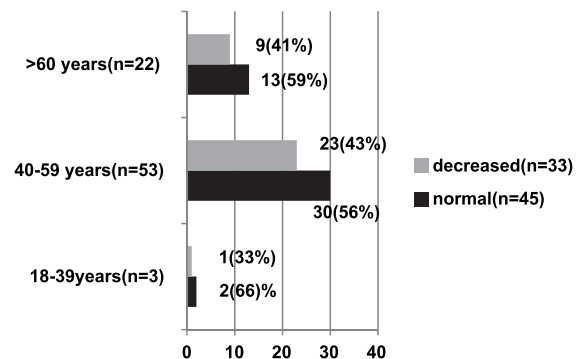


Figure-2. Association of monocyte with age group in uncontrolled group (n=78, p=0.931) Percentages are according to the count in that age group

DISCUSSION

The study compared the data of a leucocyte differential in a controlled and uncontrolled group. In both the control groups, mean value is on the upper limit of range for TLC and neutrophils but comparatively, it was moderately higher in uncontrolled group compared to controlled group. Biadgo indicated that the leucocyte count, neutrophil and lymphocyte count was invariably higher in diabetic patients.⁷ Milosevic compared the leucocyte parameter in controlled and uncontrolled diabetes but did not find any correlation between both groups.⁸ This is in agreement to our results where both controlled and uncontrolled group had raised TLC and neutrophils. Lorenzo⁹ and Arkew¹⁰ found elevated

leucocyte, neutrophil and lymphocyte count in diabetics while our study showed higher number of diabetics with decreased lymphocyte and monocyte percentage. Lorenzo⁹ emphasized that irrespective of gender and ethnicity lymphocyte count had the strongest association with incidence of diabetes. In his study on diabetics, Naredi¹¹ quoted 56% of subjects having increased leucocyte count which is a higher number than in our study.

Neutrophils have been involved in the initiation and continuation of autoimmune diabetes along with the pathogenesis of β cell autoimmunity as well as diabetic complications. Previous studies showed that type 1 diabetes patients

had higher neutrophil figures than the controls, and augmented neutrophil count correlate with a added risk of vascular disease.¹² Yu reported the link between neutrophils and chronic kidney disease in type 2 diabetes.¹³ Dowey emphasized that hyperglycemia as in uncontrolled sugars was the key force in the alteration of neutrophil function with dysregulation found in patients even on anti-hyperglycemic management.¹⁴ This study showed a higher percentage of neutrophils in diabetics regardless of glycemic control. In a comprehensive review, Rachel¹⁵ discussed the concept of NETosis, neutrophil-related cell death and by products of neutrophil extracellular traps (NETs) which were increased in diabetics and were a major regulator of diabetes and diabetes-associated complications.

Lymphocytes are also being credited to play a role in the pathogenesis of diabetes. A 2017 study, implicated T cells in the development of insulin resistance and henceforth the inflammatory phenomenon of diabetes.¹⁶ However a 2016 review said that B cells regulate inflammation in diabetics by cytokine production and promote pro-inflammatory T cell functions and that in obese diabetics B cell adaptive response is compromised contributing to higher inflammation in diabetics with raised BMI.¹⁷

A higher NLR is linked with directly with diabetic complications by Wan.¹⁸ In the current study, the neutrophil to lymphocyte ratio was the same in controlled and uncontrolled groups but in Duman's research the diabetics with increased HBA_{1c} had a higher NLR.¹⁹

Monocyte count was decreased below range in nearly half of diabetics with uncontrolled diabetes in our data which is in contrast to Naredi's¹¹ and Davidson's study²⁰ which showed elevated monocytes. Local studies in this geographical area need to be done with respect to monocyte pattern to confirm this finding.

The study highlighted the role of leucocyte and its differentials in the course of diabetes. The attending physician would be aware of the derangement that can occur in the leucocyte

profile hence prompting further recommended management which in turn will control end complications. Limitations to study were the short sample size and the monocentric nature of study. However, it is a gateway to further multicentric local research to establish the association between the leucocyte count and diabetes.

CONCLUSION

There is a higher percentage of diabetics with elevated leucocyte and neutrophil count but a decreased lymphocyte and monocyte count in uncontrolled diabetes compared to controlled diabetes.



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3	Ayesha Nageen	Data analysis, Manuscript writing.	