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How obesity affects the neutrophil/lymphocyte and platelet/lymphocyte ratio, systemic immune-inflammatory index and platelet indices: a retrospective study

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Abstract. – OBJECTIVE: Obesity is an important preventable cause of death and is a major risk factor for cardiovascular diseases as well as skeletal system diseases and malignancies. In many studies, complete blood count (CBC) and ratios derived from its results – such as the neutrophil/lymphocyte ratio, platelet/lymphocyte ratio and systemic immune inflammatory index have been associated with some diseases and their surveys. In these studies, the body mass index (BMI) and state of obesity of patients and the possible effects of these factors on CBC have not been defined. In this study, our aim was to evaluate the effect of BMI and smoking on CBC and ratios derived from CBC.

PATIENTS AND METHODS: In this cross-sectional, retrospective study; the data of male and female patients aged between 18-65 years who presented for a routine check-up or obesity was collected and subjects were grouped as normal weight, overweight, obese and morbidly obese accordingly BMI. Persons' smoking habits were calculated as pack/years. All complete blood count results were noted. Smoking status and BMI groups were compared to CBC findings and ratios derived from these findings.

RESULTS: After exclusion, 223 participants' data (104 female and 119 male) was included in the study. BMI was found to have a statistically significant positive linear correlation with lymphocyte number, PDW, SII and RDW ($p < 0.05$), and an extremely significant positive linear correlation ($p < 0.01$) was found between BMI and WBC, neutrophil count, PCT and platelet count. When BMI was not considered and 135 smokers were compared to 88 non-smokers, leukocytes and neutrophil counts were found to be higher in smokers ($p < 0.05$).

CONCLUSIONS: Our study has found that WBC, neutrophil count, lymphocyte count, platelet count, PCT, PDW and SII are significantly affected by BMI status. Future studies that use these parameters and indices must take the participants' BMI and smoking status into account.

Key Words:
Obesity, Neutrophil, Lymphocyte, Platelet.

Introduction

According to the World Health Organisation, obesity has increased two-fold since 1980 and as of 2014, 39% of adults are overweight and 13% are obese. There are also 42 million children aged < 5 years who are overweight or obese[1,2]. WHO defines being overweight as having a Body Mass Index (BMI) greater than or equal to 25, and obesity as a BMI ≥ 30. Having a high BMI is an important preventable cause of death and is a major risk factor for cardiovascular diseases such as heart failure and stroke as well as other skeletal system diseases and malignancies[2].

Complete blood count (CBC) is a cheap and easily available blood test. Neutrophil lympho-

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cyte ratio (NLR), platelet-lymphocyte ratio (PLR) and systemic immune inflammatory index (SII) are biomarkers calculated from CBC and have been reported to be useful in the diagnosis, follow-up and survey of many systemic inflammatory processes [3-10]. There are similar uses reported for platelet indices such as platelet count, mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW)[11-16].

Most studies of these biomarkers have either excluded obese patients or not evaluated/reported the BMI of participants. Some studies[17,18] have found that CBC parameters may be useful in the diagnosis, follow-up and survey of obesity-related diseases.

Although the use of CBC parameters or biomarkers calculated from the ratio of CBC parameters has been evaluated in many pathologies, we are unaware of any study that compares these parameters and biomarkers between normal weight, overweight and obese persons. The aim of our study was to evaluate the effect of weight and smoking status on these parameters and biomarkers.

Patients and Methods

This cross-sectional retrospective study was performed between August 2015 and December 2015. Medical files of patients aged between 18-65 years presenting to the obesity and check-up outpatient clinics of two institutes were included. This study was approved by the local Review Board (Medical Park Hospital Ethical Committee, Date: 29 Jan 2016, No: 0001). Patients with cardiovascular or endocrinological pathologies that have been previously reported to effect CBC parameters or ratios (such as diabetes mellitus, coronary artery disease, metabolic syndrome, hypo/hyperthyroidism, etc.), those with chronic medication use, those with any form of steroid use within the last three months and those with respiratory tract infection within the last 3 weeks were excluded from the study. Pregnant women, patients with insufficient medical history in their records, those who were found to have hyperlipidemia, hyperthyroidism, anemia, vitamin deficiency (Vitamins D and B12), or any haematological, biochemical or serological abnormality were also excluded.

Participants' medical records were reviewed and age, gender, height, weight, WBC, RDW, neutrophil number, lymphocyte number, platelet indices and other CBC parameters were collected. NLR, PLR and SII were calculated from this data. For participants with a history of smoking, smoking status was defined as Pack-years (number of cigarettes smoked per day x number of years smoked)/20.

Statistical Analysis

SPSS 16.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. Parameters were compared using independent samples test and intergroup comparison was performed using ANOVA test. Relations in between data were analyzed with Pearson Correlation analysis. The p value of < 0.05 was regarded as statistically significant.

Results

The medical records of 361 patients were retrospectively analysed. After exclusion, 223 participants' data (104 female and 119 male) was included in the study. Causes for exclusion were insufficient data in 41; systemic disease such as meolic syndrome, hypertension or diabetes mellitus in 62; chronic medication use in 12; active infection in four and laboratory test anomalies in 19 participants.

The average age of the participants was 39.10 ± 11.61 (range 15-81) and their average BMI was 29.98 ± 6.40 (range 20.6-50.0) There were 73 participants with BMI < 25, 53 participants with BMI 26-30, 74 participants with BMI 31-40 and 23 participants with BMI < 40. One hundred and thirty-five participants were smokers with an average pack-year of 13.15 ± 11.45 (range 1-50).

When participants were grouped by BMI, a statistically significant difference was found between SII and lymphocyte counts ($p < 0.05$), and an extremely significant difference was found between MCHC, plateletcrit (PCT), platelet count, neutrophil number and WBC ($p < 0.01$). Comparison of CBC parameters *versus* BMI groups are shown in Table I. WBC, neutrophil and lymphocyte count distribution according to obesity status are shown in Figure 1 and distribution of mean platelet volume (MPV), platelet distribution width (PDV), PCT and platelet count are shown in Figure 2.

When the correlation between CBC parameters and BMI were evaluated, BMI was found to have a statistically significant positive linear correlation with lymphocyte number, PDW, SII and

Table I. Comparison of BMI groups vs. CBC parameters.

BMI	< 25 (N:73) mean ± SD	26-30 (N: 53) mean ± SD	31-40 (N: 74) mean ± SD	> 40 (N: 23) mean ± SD	All Participants (N: 223) mean ± SD	*p*
Hb (g/dL)	14.6 ± 1.5	14.1 ±1.8	14.1 ± 1.6	14.6 ± 1.5	14.3 ± 1.6	0.214
Hct (%)	42.5 ± 3.7	41.6 ± 4.5	42.0 ± 4.2	43.6 ± 3.9	42.2 ± 4.1	0.256
WBC (10^3/mm^3)	6.83 ± 1.49	7.39 ± 1.68	8.24 ± 2.28	8.60 ± 2.50	7.61 ± 2.04	0.000**
NEUT (10^3/mm^3)	3.81 ± 1.00	4.29 ± 1.19	4.83 ± 1.90	5.07 ± 1.83	4.40 ± 1.55	0.000**
LYMPH (10^3/mm^3)	2.18 ± 0.6	2.23 ± 0.70	2.53 ± 0.74	2.42 ± 0.72	2.33 ± 0.71	0.012*
MCV (fL)	83.9 ± 5.1	85.5 ± 4.5	84.2 ± 4.7	84.8 ± 4.2	84.5 ± 4.7	0.287
MCH	28.8 ± 2.1	31.9 ± 2.4	28.3 ± 1.9	28.5 ± 1.3	29.8 ± 17.3	0.268
MCHC	34.4 ± 1.3	34.0 ± 1.2	33.6 ± 1.1	33.6± 1.2	33.9 ± 1.2	0.006**
RDW (%)	13.3 ± 1.1	14.1 ± 1.8	14.1 ± 1.6	14.6 ± 1.5	14.3 ± 1.6	0.186
PLT (10^3/mm^3)	228.5 ± 51.6	253.3 ± 68.7	271.5 ± 69.9	270.4 ± 54.3	253.0 ± 64.9	0.000**
MPV (fL)	9.21 ± 0.80	9.89 ± 1.30	11.3 ± 1.17	9.87 ± 1.55	10.14 ± 5.96	0.186
PDW (fL)	11.7 ± 2.6	13.3 ± 2.3	14.0 ± 2.8	13.6 ± 2.7	13.1± 6.6	0.196
PCT (%)	0.21 ± 0.04	0.25 ± 0.07	0.27 ± 0.07	0.26 ± 0.05	0.24 ± 0.07	0.000**
NLR	1.87 ± 0.72	2.14 ± 1.24	2.00 ± 0.94	2.15 ± 0.74	2.01 ± 0.94	0.395
PLR	112.1 ± 35.1	125.8 ± 58.7	114.8 ± 40.6	119.2 ± 39.3	117.0 ± 43.9	0.350
SII	425.4 ± 175.4	545.1 ± 327.2	569.2 ± 397.7	587.5 ± 268.7	518.3 ± 314.0	0.019*

p values; One-Way-ANOVA, Statistical significant (*$p < 0.05$, **$p < 0.01$). Hb, Hemoglobin; Hct, Hematocrit; WBC, White Blood Cells; NEUT, Neutrophils; LYMHO, Lymphocytes; MCV, Mean Corpuscular Volume; RDW, Red cell Distribution Width; PLT, Platelets; PDW, Platelet Distribution Width; MPV, Mean Platelet Volüme; PCT, Plateletcrit; NLR, Neutrophil lymphocyt Ratio; PLR, Platelet Lymphocyt Ratio, SII, Systemic immune-inflammatory index.

RDW ($p < 0.05$). An extremely significant positive linear correlation ($p < 0.01$) was found between BMI and WBC, neutrophil count, PCT and platelet count. There was an extremely significant negative correlation between BMI and MCHC ($p < 0.01$). The highest level of correlation was found between PCT and BMI, and its correlation graphic is shown in Figure 3.

When BMI groups were separated into two groups according to smoking status, in partici-

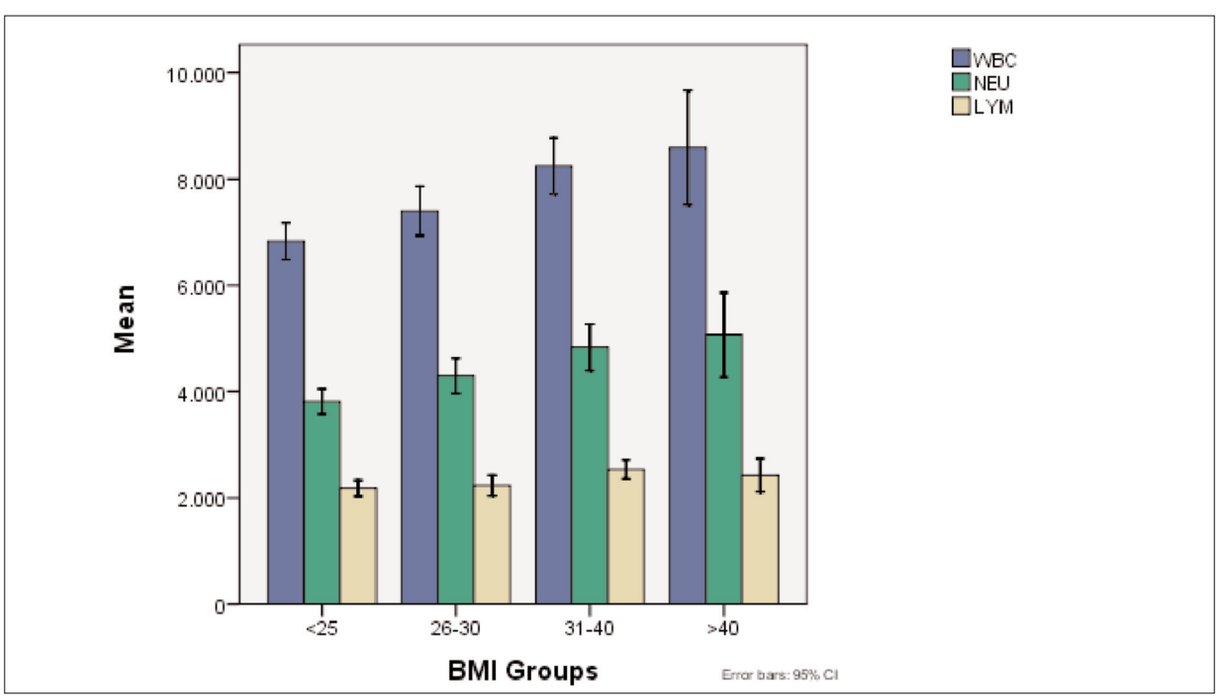

Figure 1. WBC, Neutrophil and lymphocyte count distribution according to BMI groups.

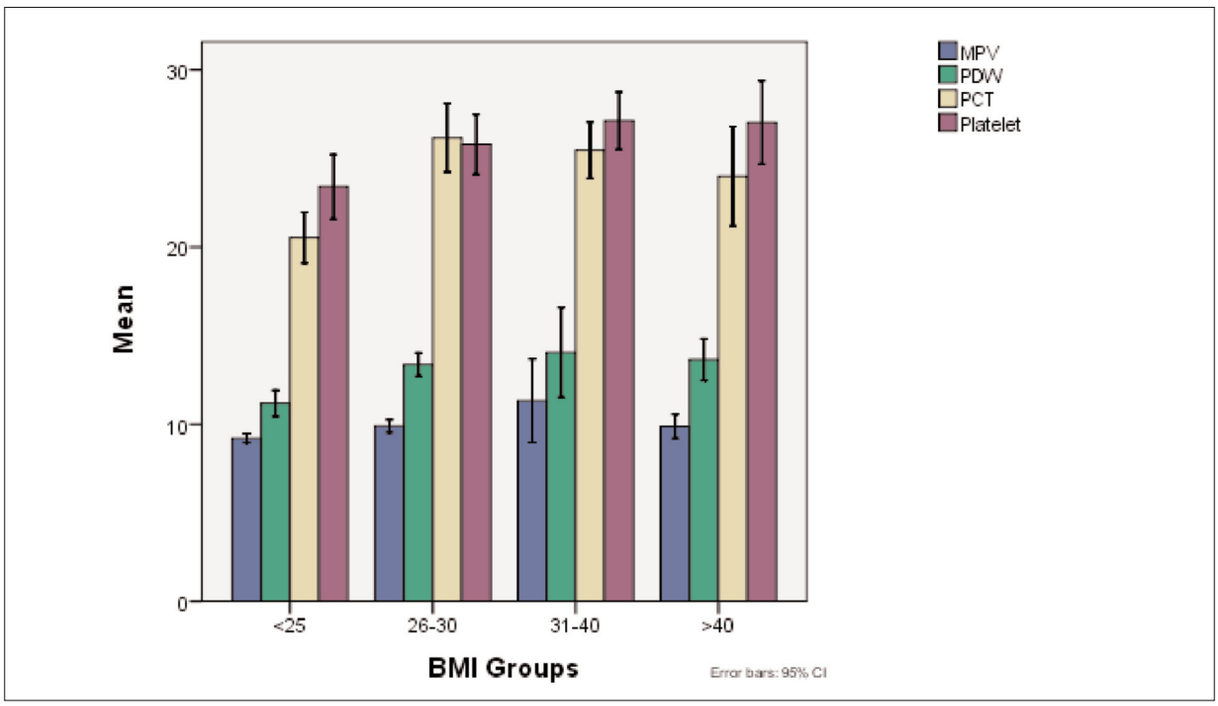

Figure 2. MPV, PCT (x 103), PDW and platelet count (/10) distribution according to BMI groups.

pants with a normal BMI, SII, MCV, neutrophil count ($p < 0.05$) and NLR ($p < 0.01$) were found to be higher in smokers when compared to non-smokers. While the average NLR was 1.618 ± 0.612 in non-smokers, it was 2.157 ± 0.737 in smokers (Table II).

Hemoglobin and hematocrit levels were higher in smokers for BMI 31-40 and BMI > 40 groups ($p < 0.01$). No other correlation was found in these groups. When BMI was not considered and 135 smokers were compared to 88 non-smokers, leukocyte and neutrophil counts were found to be higher in smokers ($p < 0.05$) (Table II).

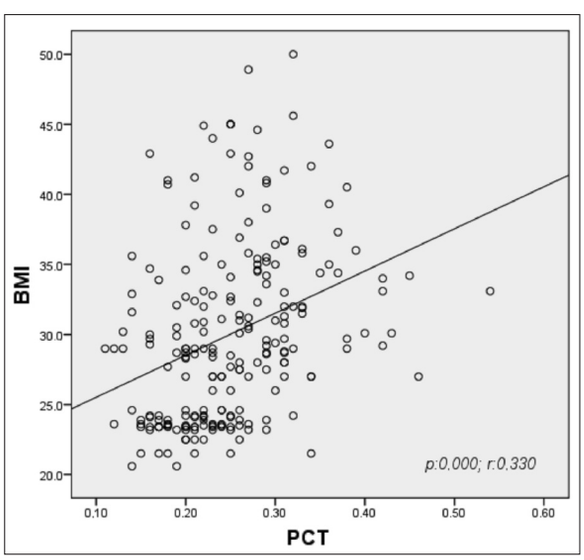

Figure 3. Correlation between BMI and plateletcrit.

Discussion

This study evaluated the effect obesity has on CBC parameters as well as NLR, PLR and SII that are obtained from CBC measurements. Our study demonstrated that BMI is positively correlated with neutrophil, lymphocyte, WBC counts, SII and all platelet indices other than MPV. While there was no difference between smokers and non-smokers when groups of BMI were compared for most parameters, when participants were compared according to smoking status independent of BMI, WBC and neutrophil counts were found to be higher in smokers. It was striking that in participants with normal BMI, smokers had a higher NLR.

In a study by Yılmaz et al[18] where the diagnostic value of NLR for diabetes mellitus in morbidly obese patients and patients with normal weight were evaluated, NLR was found to be signifi-

Table II. Comparison of smoking and weight status vs. CBC parameters.

	Normal weight			All participants		
	Smoker (N: 35) mean ± SD	Non-smoker (N: 33) mean ± SD	*p*	Smoker (N: 135) mean ± SD	Non-smoker (N: 88) mean ± SD	*p*
Hb (g/dL)	14.4 ± 1.7	14.7±1.2	0.455	14.4 ± 1.6	14.1 ± 1.61	0.159
Hct (%)	42.41 ± 4.25	42.59 ± 3.30	0.840	42.66 ± 4.26	41.61 ± 3.93	0.086
WBC (10^3/mm^3)	6.974 ± 1.484	6.700 ± 1.511	0.437	7.846 ± 2.096	7.266 ± 1.913	0.038*
NEUT (10^3/mm^3)	4.096 ± 1.051	3.547 ± 0.901	0.019*	4.560 ± 1.593	4.139 ± 1.462	0.048*
LYMPH (10^3/mm^3)	2.017 ± 0.585	2.331 ± 0.653	0.035	2.363 ± 0.763	2.294 ± 0.631	0.483
MCV (fL)	85.40 ± 3.71	82.66 ± 5.69	0.020*	85.56 ± 4.33	82.97 ± 4.90	0.196
MCH	29.08 ± 1.72	28.64 ± 2.40	0.365	29.04 ± 1.71	28.19 ± 1.13	0.001**
MCHC	34.06 ± 1.24	34.62 ± 1.37	0.074	33.95 ± 1.19	33.98 ± 1.41	0.892
RDW (%)	13.23 ± 1.17	13.42 ± 1.13	0.467	13.47 ± 1.33	13.50 ± 1.40	0.879
PLT (10^3/mm^3)	221.4 ± 45.1	234.6 ± 56.4	0.299	249.5 ± 63.6	257.9 ± 66.9	0.362
MPV (fL)	9.16 ± 0.77	9.18 ± 0.74	0.916	9.74 ± 1.28	10.76 ± 9.36	0.214
PDW (fL)	12.36 ± 2.73	11.21 ± 2.31	0.057	13.03 ± 2.56	13.20 ± 10.17	0.855
PCT (%)	0.20 ± 0.04	0.21 ± 0.04	0.244	0.24 ± 0.07	0.25 ± 0.07	0.377
NLR	2.157 ± 0.732	1.618 ± 0.612	0.001**	2.090 ± 1.054	1.891 ± 0.742	0.126
PLR	117.22 ± 34.93	107.41 ± 34.89	0.234	116.01 ± 47.68	118.59 ± 37.66	0.669
SII	475.82 ± 176.19	379.13 ± 163.56	0.018*	533.62 ± 351.47	494.90 ± 246.05	0.370

p-values; independent samples test, statistical significant (*$p < 0.05$, **$p < 0.01$).

cantly higher in the morbidly obese patients. Also, a high NLR was found to be a strong predictor for the diagnosis of diabetes. It is logical that our results did not correlate with these findings because we excluded patients with diabetes. In a separate study, 19 obese and 9 normal weight patients were evaluated and a positive correlation was found between BMI and leukocyte plus BMI and lymphocyte count in obese patients. However, there was no correlation between NLR and BMI[19]. Authors stated that obesity should be considered as a chronic inflammatory process. In our study, we demonstrated that an increase of BMI led to increased WBC, lymphocyte and neutrophil counts. While there was no correlation between NLR and BMI, this could be explained by the increase of neutrophil and lymphocyte counts together.

Vuong et al[20] used waist circumference to classify patients as obese or not, and then considered whether the normal ranges of CBC parameters should be reviewed in obese patients. In the evaluation of 6700 patients, a positive correlation was found between waist circumference and WBC, neutrophil count, lymphocyte count, platelet counts and MPV. Our results are very similar to these previously reported findings.

Increased WBC is a direct risk factor for the development of metabolic syndrome[21,22]. Similar to NLR and PLR, platelet indices are also an immune response marker that increases with chronic inflammation[8,11].

In our study, we also evaluated the effect of smoking status and density. We are unaware of any other studies that evaluated the effect of obesity and smoking status on CBC parameters. Our study found that NLR is high in normal BMI smokers, which demonstrates the systemic inflammatory response that smoking causes secondary to chronic hypoxia. However, we did not find the same correlation as BMI increased. This is most likely due to the exclusion of patients with metabolic syndrome. We are unaware of any previous study that compares NLR and PLR between smokers and non-smokers. Further studies are required to evaluate the effect of smoking on CBC parameters.

Platelet indices such as platelet count, MPV, PCT and PDW have evaluated for use in the diagnosis, treatment and survey of several diseases or conditions[11,15,23-29]. However, almost no studies grouped patients according to their BMI. Our data has shown that PDW, PCT and platelet count increase as BMI increases. Therefore, any study of platelet indices must also take obesity as a confounding factor.

There are very few studies[8,30,31] that evaluate the effect of obesity on SII – a newly defined index. Our data has shown that NLR and SII are higher in smokers with a normal BMI. Also,

BMI was found to positively correlate with SII. Once again, studies involving SII must take into account the patient's BMI.

Although we have thoroughly defined our inclusion and exclusion criteria according to reports in literature, our retrospective design required the exclusion of patients without full medical history. This could have led to a bias of our results. Again, the retrospective design meant that we were unable to randomise participants according to demographical properties. Further randomised, prospective studies need.

Conclusions

Many studies have reported the use of CBC parameters and ratios derived from them for the diagnosis, treatment and survey of many pathologies. However, most of these studies have not investigated the effect of increased BMI. Our study has found that WBC, neutrophil count, lymphocyte count, platelet count, PCT, PDW and SII are significantly affected by BMI status. Future studies that use these parameters and indices must take the participants' BMI and smoking status into account.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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