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Obesity correlates with neutrophilia

Abstract

Background: Obesity is a global health problem imposing risk for many serious diseases. Lately, obesity has been described as a state of low-grade inflammation with leukocytes playing a major role. Mild leukocytosis was noticed in obese patients with no co morbidities. This study aimed at defining the association between obesity and leukocytosis.

Methods: In this retrospective study, we reviewed files and medical history of 281 patients. Body Mass Index (BMI) was calculated and differential leukocyte was recorded. Individuals with obesity related conditions like hypertension, diabetes, hyperlipidemia or malignancies were excluded. Data analysis was performed to assess the relationship between variables.

Results: Among the 281 participants included in the study the BMI was used as a determinant of obesity with a cut-off point of 30 (127 were non-obese and 154 were obese). There was a statistically significant difference in the white blood cells (WBC) count among the two groups (p-value <0.001). In addition, 88.9% of those with leukocytosis were obese, while 11.1% non-obese. There is a positive correlation between the WBC count and the BMI (r=0.391, p-value <0.001). Neutrophilia is the rationale behind leukocytosis with the mean of 8.3 X 109±3.

Conclusion: The positive correlation between obesity and leukocytosis proves the relationship but does not establish causation. Although most obese patients in this study had a normal WBC count, their counts were higher than the non-obese group due to prominent neutrophilia. The association highlighted will have an impact on patients during the pre-operative work up for bariatric surgery, as neutrophilia is a risk factor for metabolic and cardiovascular complications requiring detection and treatment to minimize this risk. The incidental detection of neutrophilia in obese patients is not yet rationalized and requires further research

Keywords: obesity, neutrophilia, leukocytosis, bariatric surgery

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Abbreviations: BMI, body mass index; WBC, white blood cells; CRP, C-reactive protein; DM, diabetes mellitus; HTN, hypertension

Introduction

Obesity is a global issue that threatens millions of people around the world in both developing and developed countries. Prevalence of obesity has duplicated two fold since 1980 and it is predicted that by 2030 it will affect more than one billion people.[1,2] Obesity is a major risk factor for type 2 diabetes, coronary heart disease, hypertension, atherosclerosis, arterial thrombosis, heart failure and sudden cardiac death.[3] According to the WHO, obesity is defined as body mass index (BMI) of 30, while a value greater than 40 is considered extreme or morbid obesity. Recently, obesity has been described as a state of low-grade inflammation,[4–6] with leukocytes playing an important role in this state. Leukocytosis is an increase in the total number of White blood cell (WBC) count with a value greater than 11,000/mm^3 (11×10^9/L) due to any cause such as infection, inflammation, allergic reaction, malignancy, hereditary disorders, or other miscellaneous causes.[7]

A Study conducted in Turkey reported that WBC, neutrophils and lymphocyte counts are significantly affected by BMI status.[8] In China, it was found that levels of WBCs and C-reactive protein (CRP) in morbidly obese patients who underwent surgical weight loss significantly decreased after the surgery.[9] Furthermore, a relation between leukocytosis and obesity-related co morbidities has been established. A study conducted by Ryder et al, showed that a high WBC count in obese patients is associated with insulin resistance.[10] Another cross-sectional study also concluded that an elevated WBC count is linked to the prevalence and future development of metabolic syndrome in the young population.[11] However, to what extent a high WBC count in obese patients can be considered alarming is still unknown. Most of the studies in this area focused on leukocytosis in obese patients with obesity-related comorbidities; little work has been done regarding leukocytosis in asymptomatic obese individuals. We therefore aim in this paper, to study the level of correlation between leukocytosis and obesity in a cohort of healthy and obese subjects.

Material and methods

This retrospective study was conducted during the month of June 2016 in King Abdulaziz University Hospital, Jeddah, Saudi Arabia. It was approved by the Research Ethics committee of KAU. Medical records of 326 adult patients were reviewed; 131 of whom were obese subjects going for bariatric surgery whiles 195 were volunteer donors. The sample size was calculated using the following equation, with confidence interval of 95% and margin of error=6%.

$$Sample\ Size = \frac{\frac{z^2 \times p(1-p)}{e^2}}{1+(\frac{z^2 \times p(1-p)}{e^2 N}}$$

Information obtained from the medical records included age, gender, height, weight and differential leukocyte count. Body mass index was calculated by dividing (weight in kg) over (height in m^2); patients with BMI≥30 were considered obese while those with BMI≤30 were non-obese according to WHO's classification of body mass index (BMI). Leukocytosis was determined the total WBC count ≥11.5mmol/L as stated by the KAUH hematological laboratory. Patients of both sexes ages 18 and above, were included in the study. Exclusion criteria included the following: Diabetes Mellitus (DM), hypertension (HTN), hyperlipidemia, metabolic syndrome, cardiovascular diseases, malignancies and recent infection (body temperature >38°C). In addition to diseases or drugs known to influence the immune system and secondary obesity (hypothyroidism, Cushing syndrome), SPSS version 21 was used for statistical analysis. The relation between the two variables was studied using chi-square and the one-way ANOVA test. A p-value <0.05 was considered as significant.

Results

The records of 326 patients from KAUH were reviewed and analyzed. 45patients were excluded because they had associated co morbidities including hypertension, diabetes, hyperlipidemia, thyroid disease and malignancies. Of the 281 patients included in the study, 127 were non-obese with BMI<30 and 154 were obese with BMI>30. The characteristics of the participants studied are shown in Table 1. As shown in Figure 1, there is a positive correlation between BMI and Total WBC count-Pearson's correlation coefficient=0.391, p-value <0.001. Leukocytosis was found in 18 of the participants studied; 88.9 % of whom were obese and only 11.1% were non obese. To assess the effect of severity of obesity with leukocytosis, we further grouped the participants according to their BMI as shown in Table 2. When comparing the means of WBC count between the groups using the one-way ANOVA test, a significant difference was found as shown in Figure 3. We also found that BMI of 35 or higher is significantly associated with leukocytosis (p-value=0.01). While measuring odds ratio between leukocyte count and obesity; it was found to be 7.2%. Among the various WBC types, neutrophilia is the rationale behind leukocytosis with the mean of 8.3X109±3 (4.5-11-11.5x10^9/l.). Furthermore, we deduced that there was no gender difference when relating obesity with leukocytosis using chi-square test, p-value=0.373.

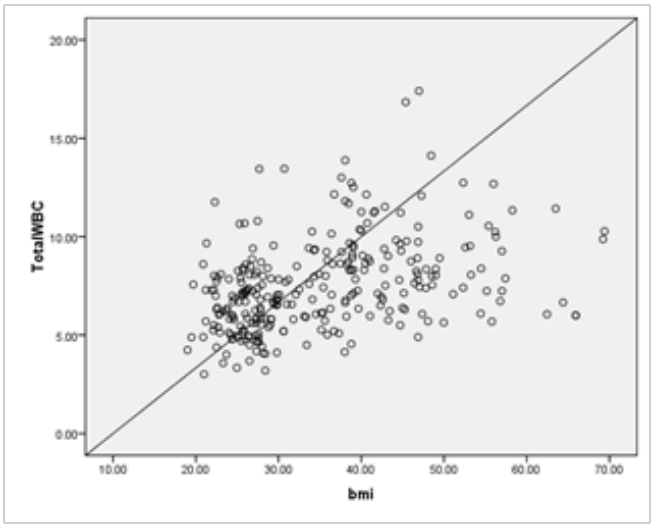

Figure 1 Correlation between WBC count and BMI.

Table 1 The characteristics of the participants studied

	Non-obese group(n=127)	Obese group(n=154)
Male/Female	101/26	65/89
Age, Years	30.9(range= 19-54years)	33.1(range=18-60 years)
BMI(kg/m^2)	25.7(±2.5)	42.9(±8.6)
Mean WBC count	6.4(±1.7)	8.4(±2.3)

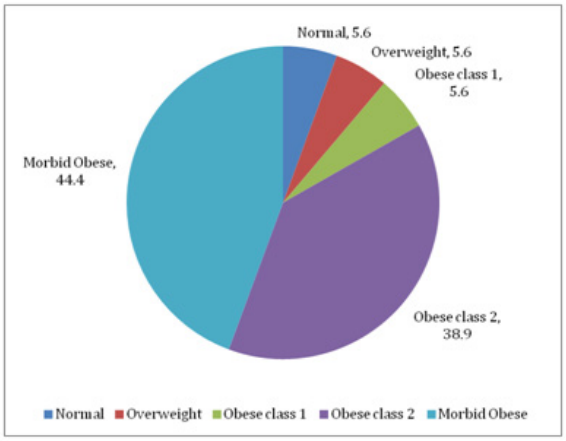

Figure 2 Distribution of leukocytosis among BMI classes.

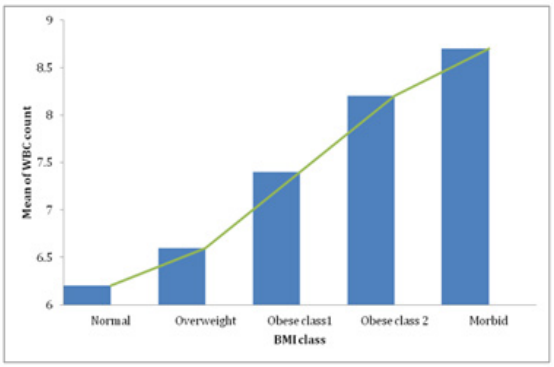

Figure 3 One-way ANOVA test to compare the mean of each group.

Table 2 The association between leukocyte count and BMI class

	BMI class	Number of subjects	
		Normal	Leukocytosis
BMI	Normal(18.5-24.9)	43(16.3%)	1(5.6%)
	Overweight(25-29.9)	82(31.2%)	1(5.6%)
	obese class1(30-34.9)	24(9.1%)	1(5.6%)
	obese class2(35-39.9)	38(14.4%)	7(38.9%)
	morbid obese >40	76(28.9%)	8(44.4%)
	Total	263(100%)	18(100%)

*Frequencies were found using chi-squared

Discussion

Our study aims to determine whether there is an association between obesity and leukocytosis. We found that the more obese

an individual is more likely he or she is to have a high WBC count. An explanation for this is that obesity is known to be a chronic inflammatory condition with white blood cells infiltrating into adipose tissue and pro-inflammatory cytokines (tumor necrosis factor-a and interleukin-6) are produced by adipocytes and WBCs.[12–14] It has been postulated that one of the major determinants of the significant association of obesity and a high leukocyte count is the associated presence of metabolic syndrome.[15] However, our study shows that even in the absence of metabolic syndrome, obese individuals are found to have leukocytosis. We found that there is a correlation between BMI and total leukocyte count ($r=0.360$, $P<0.001$). The mean WBC count of the obese group is 8.5±2.5 compared to 6.67±1.8 for the non-obese group. Nonetheless, the absolute leukocyte number of obese individuals is still within the normal range (4-11.5mmol/L).[16] This supports findings of previous studies which demonstrated a positive association between WBC count and BMI.[8,9,17] Furthermore, while looking at the differential leukocyte counts, Neutrophils were found to be elevated in morbidly obese patients mean 8.3X109±3. (Normal range: 2-7.5K/mmol). This may be because chemokines are produced by adipose tissue which play a role in bone marrow granulopoiesis and also demarginate intravascular neutrophils.[18–20]

The odds ratio for leukocytosis in obese patients with BMI >30 is 7.2, which implies that obese individuals who have BMI >30 are 7.2 times more likely to develop leukocytosis than those who are non-obese. Similarly, a cross-sectional study conducted in the Israel found that for every one kg/m^2 increase in BMI, the risk of having leukocytosis was increased by 11%.[21] The study also showed no significant difference between leukocytosis in obese females when compared to age-matched obese males, supporting our findings of no difference between genders. This supports the hypothesis that high body weight affects inflammatory markers, regardless of variation in body fat distribution peculiar to each gender. Children aged 6-12years, has a significant neutrophilia and higher CRP concentration correlating with obesity. Thus it may be used as an obesity-related inflammatory marker in young obese patients.[22] Given our retrospective study design, the limitations we encountered included omitting the assessment for the smoking status, CRP level and the waist circumference.

Moreover, within clinical settings leukocytosis should not to be ignored, as an elevated leukocyte count even if within the normal range has been shown to be a risk factor for metabolic syndrome and cardiovascular disease.[11,23–25] A retrospective 5-year cohort study found that patients who developed Coronary Artery Disease initially had a high baseline leukocyte count when compared to normal patients.[26] However, the patho-physiology of leukocytosis and in turn, cardiovascular disease, caused by an increase in BMI is not clearly understood. It could be explained by the co-existence of metabolic syndrome.[27] We therefore recommend further prospective cohort studies to determine the clinical course of obese patients with leukocytosis.

Conclusion

The positive correlation between obesity and leukocytosis proves the relationship but does not establish causation. Although most obese patients in this study had a WBC count within the normal range, their counts were higher than the non-obese group due to prominent neutrophilia. Therefore, work-up of patients to rule out the common causes and subsequently treating the cause is essential. The association highlighted will have an impact on patients during the pre-operative work up for bariatric surgery, as neutrophilia is a risk factor for metabolic and cardiovascular complications that needs detection and treatment to minimize this risk. The incidental detection of leukocytosis in any obese patient is not yet rationalized and further research looking into the inflammatory and metabolic biomarkers are warranted to explain the etiology of this association.

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Conflict of interest

The author declares no conflict of interest.

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