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Correlation of CRP and hypoalbuminemia with morbid obesity: retrospective study at KAUH, Jeddah, Saudi Arabia

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ABSTRACT:

Background:*Obesity is a chronic low-grade inflammation state which lead to increase in C-Reactive Protein (CRP) and many nutrient deficiencies such as Serum albumin (SA). Bariatric surgery is accepted nowadays as the most effective tool in the treatment and control of morbid obesity. Low SA has been shown to correlate with risk for surgical complications and mortality.* ***Aim:*** *Toassess the correlation between obese patients, hypoalbuminaemia and CRP.****Methods:*** *The medical record of 165patients who suffers from obesity and were advised to undergo bariatric surgery at King Abbdulaziz University hospital (KAUH) during 2010 until 2017were examined. CRP and SA were measured using standard methods.* ***Result:****165 patients were studied. There were 44 males (26.66%) and 121 were females (73.33%) with a mean age of 38 years (range 18-62). 50 patients (30.30% of all patients and 32.26% of patients who had pre-operative albumin assessment) had hypoalbuminemia and 105 patients (63.63% of all patients and 67.74 % of patients who had pre-operative albumin assessment) had normal albumin level. 27 patients (16.36% of all patients and 78.1% of patients who had pre-operative CRP assessment) had high CRP and 4 patients (2.42% of all patients and 12.9% of patients who had pre-operative CRP assessment)) had normal CRP.There was no significant correlation between BMI and CRP but BMI was significantly lower in patients who have normal CRP level compared with those who have high CRP level. There was a trend for a negative correlation between CRP and albumin (r = -0.300, p = 0.10). BMI is significantly negatively correlated with albumin level (r = -0.219, p < 0.02). Albumin level is significantly negatively correlated with age. CRP level is strongly significantly positively correlated with lymphocytes percentage (r =0.826, p <0.02).****Conclusion:****In conclusion, our study found an increase in the inflammatory status (as indicated by CRP) and in lymphocyte percentage, whereas albumin levels were decreased in association with obesity and high BMI.***

Keywords: *CRP, Hypoalbuminaemia, Inflammation, Obesity, Protein.*

1. Introduction

Obesity is a chronic condition characterised by an accumulation of body fat [1]. It is a rapidly emerging disease in the developed and developing countries, including Saudi Arabia(SA) [1, 2]. This has prompted the World Health Organisation (WHO) to designate obesity as one of the most important public-health threats [2]. Indeed, obesity is well-recognised to associate with co-morbidities such as cardiovascular complications, metabolic complications and respiratory complications [2].

The aetiology of obesity is multifactorial, including genetic factors, Dietary factors, lifestyle factors and parental factors [1]. In Saudi Arabia (S.A), the socioeconomic status of Saudis has been changed due to the discovery of oil, which led to increase in obesity prevalence among Saudis [3]. There are three levels of obesity

management: lifestyle modification (diet, physical activity and behaviour change), pharmacotherapy and bariatric surgery [4]. However, many patients do not respond to these therapeutic approaches, requiring more effective intervention. In this context, bariatric surgery is nowadays accepted as the most effective tool in the treatment and control of morbid obesity [5]. Among the main benefits of this intervention, loss and weight maintenance in the long-term and improvement or control of associated diseases stand out, with consequent improvements in the quality of life [5]. A study has assessed protein status after bariatric operation, detecting reduction in the dietary intake of proteins and protein intake is often less than the nutritional needs[6]. Other studies have investigated the presence of protein deficiency in morbidly obese [7, 8], which may be aggravated by the surgical procedure, resulting in more serious postoperative complications.

Obesity is associated with a chronic state of low-grade inflammation with progressive immune cell infiltration into obese adipose tissue. Immune cell-derived cytokines and adipose tissue-derived adipokines augment adipose tissue inflammation [9]. C- reactive protein (CRP) is a lowgrade chronic inflammation biomarker that independently predicts high-risk patients for cardiovascular diseases (CVD)[10]. Although many studies showed increased plasma CRP levels in patients with different inflammatory diseases including obesity [11-16]. As the obesity is correlated with CRP andSA (which is used as an index of protein status) has been shown to correlate with risk for surgical complications and mortality, we want to see whetherthere is a correlation between morbidly obese patients, hypoalbuminaemia and CRP.

2. Material and Methods

2.1 Study population.

After obtaining approval from Unit of Biomedical Ethics Research Committee we conducted a retrospective chart review of male and female patients who suffers from morbid obesity and were advised to undergo bariatric surgery. Patients' body mass index (BMI) was calculated and only those with BMI > 40 kg/m² or BMI between 27-40 kg/m² with comorbid conditions were included in the study. Their preoperative albumin and CRP levels were studied. The patients are seen at King Abdul-Aziz University (KAU) Hospital between January 2010 until now. There are no exclusion criteria.

Measurements of albumin level and hs-CRP was conducted in laboratory of KAU hospital. Albumin was measured using Dimension Vista® System. Levels of < 35 mg/dl were considered low. One hundred and fifty-five patients had a pre-operative serum albumin assessment. Hs-CRP was measured using BN II / BN ProSpec® System and CardioPhase® hs-CRP reagents. Levels of hs-CRP > 3.0 mg/l were considered high. Thirty-one patients had a pre-operative CRP assessment. CRP ≥ 3.0 mg/dl was recognized as high.Data recorded included gender, age, BMI, albumin level, WBC count and automated lymphocyte.

2.2 Statistical analysis.

Data was analyzed using SPSS software (version 21). Difference in BMI and CRP levels between albumin groups was determined using independent T-test. Difference in BMI between CRP groups was also determined using independent T-test. Relationships between BMI, CRP, albumin and lymphocytes' continuous data was analysed using Pearson's correlation. Statistical significance for the difference in the frequency between groups was determined by Pearson chi-square χ^2 test. The continuity correction in R was computed for 2x2 tables. A Two-sided *P* values of 0.05 or less was considered statistically significant. Data was represented as mean ± SE and as frequencies and proportions. All missing data was classed as missing at random and only available data were analysed.

3. Result

One hundred and sixty-five patients were studied. There were forty-four males (26.66%) and one hundred and twenty-one females (73.33%) with a mean age of 38 years (range 18-62). Fifty patients (30.30% of all patients and 32.26% of patients who had pre-operative albumin assessment) had hypoalbuminemia and one hundred and five patients (63.63% of all patients and 67.74 % of patients who had pre-operative albumin assessment) had normal albumin level. Twenty-seven patients (16.36% of all patients and 78.1% of patients who had pre-operative hs-CRP assessment) had high hs-CRP and four patients (2.42% of all patients and 12.9% of patients who had pre-operative hs-CRP assessment)) had normal hs-CRP.There were no differences between genders in BMI, albumin, CRP, lymphocyte percentage, lymphocyte count and WBC counts (Table 1).

Table 1. Means of different factors in both genders.

	Female	Male
BMI	42.11 ± 0.55	42.63 ± 1.17
Albumin	35.43 ±0.28	37.71 ± 0.59
CRP	13.38 ± 1.79	10.05 ± 1.57
Lymphocyte %	35.61 ± 1.00	35.46 ± 1.31
Lymphocyte	2.7 ± 0.07	2.72 ± 0.09
WBC counts	7.99 ± 0.21	0.35 8.30

3.1 Relation between BMI, age and CRP

There was no statistically significant correlation between BMI and CRP level; however, BMI was significantly lower in patients who have normal CRP level compared with those who have high CRP level (P <0.05, student's t-test) (Fig. 1). There was no relationship between age and CRP.

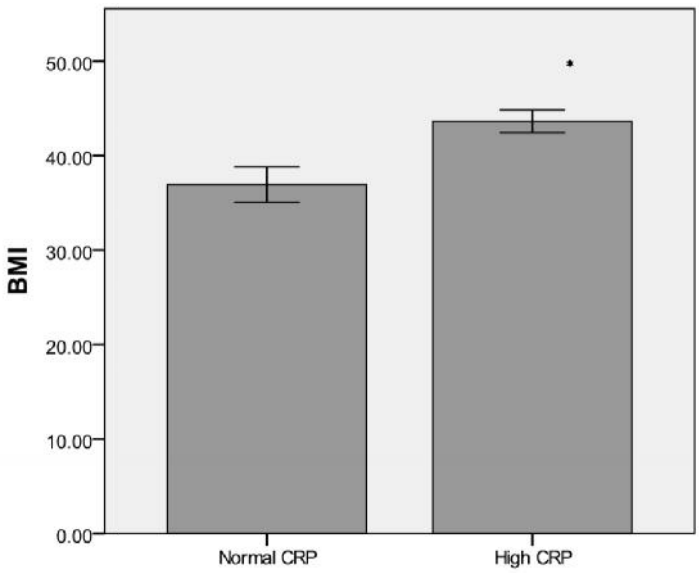

Figure 1. BMI in patients with normal CRP and high CRP, * p < 0.05.

3.2 Relation between CRP, BMI, age and albumin

There is a trend for a negative correlation between CRP and albumin (r = -0.300, p = 0.10) (Fig. 2). In addition, there is a trend for higher CRP level in patients with hypoalbuminemia compared to patients with normal albumin level (P = 0.052, student's t-test) (Fig. 3).

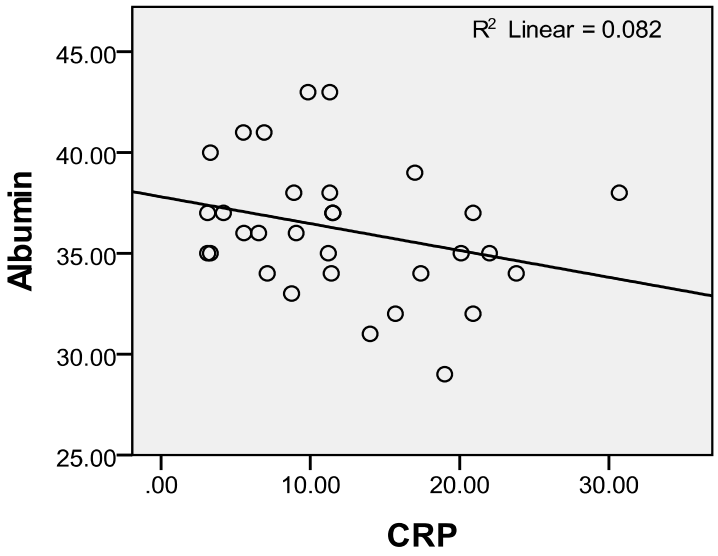

Figure 2. The relation between albumin and CRP.

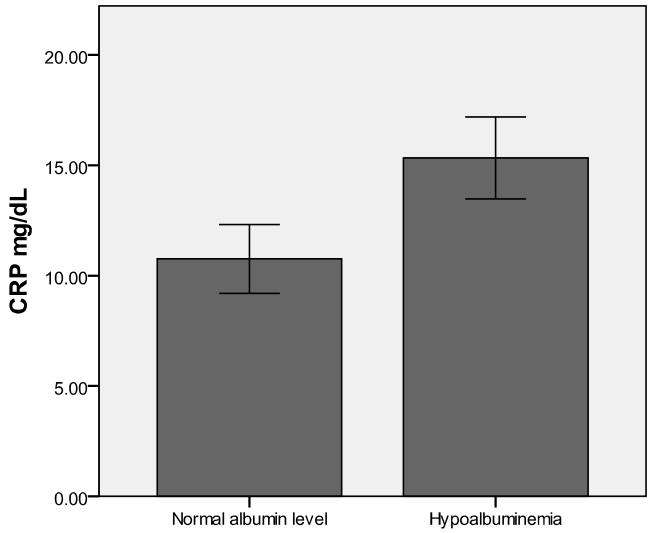

Figure 3. CRP level in patients with normal and low albumin level.

100% of patients who had normal CRP level had a normal albumin level. In patients with High CRP level, 66.7% had normal albumin level and 33.3% had Hypoalbuminemia. The association between Albumin and CRP here did not reach statistical significance (Chi-square test) (Table 2).

Table 2. Calculations on patients' number regarding CRP and albumin level.

	Normal albumin level		Hypoalbuminemia	
	n	N %	n	N %
Normal CRP	4	100.0%	0	0.0%
High CRP	18	66.7%	9	33.3%

n, number of patients, N %, patients' number percentage.

BMI is significantly negatively correlated with albumin level ($r = -0.219$, $p < 0.02$) (Fig. 4). In addition, the BMI for patients with hypoalbuminemia is significantly lower than the BMI for patients with normal albumin level ($P < 0.01$, student's t-test) (Fig. 5).

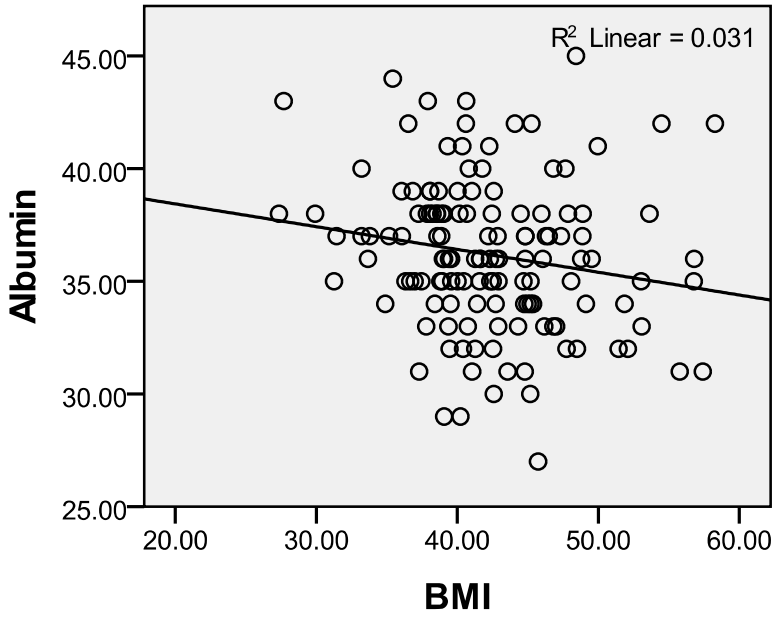

Figure 4. The relation between albumin level and body mass index (BMI, kg/m²)

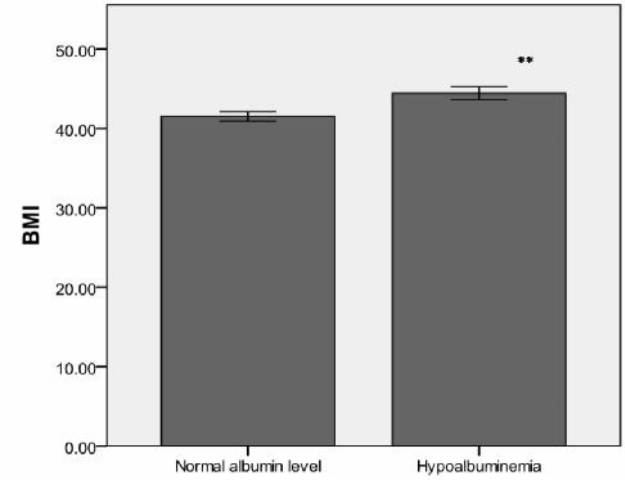

Figure 5. BMI in patients with normal and low albumin level, ** p < 0.01.

3.3 CRP and lymphocytes

CRP level is strongly significantly positively correlated with lymphocytes percentage (r =0.826, p <0.02) (Fig. 6).

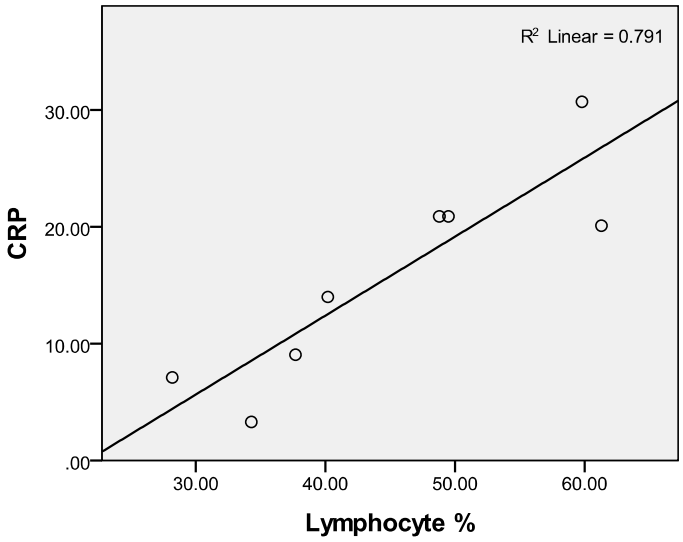

Figure 6. The relation between CRP and lymphocyte percentage

4. Discussion

The current study shows that BMI is significantly lower in patients who have normal CRP level compared with those who have high CRP level (Fig. 1). *Seishi Yamada* et al 2001 have carried a cohort study on the Japanese population and stated that anthropometric indices including BMI are correlated with CRP [17]. Expansion of WAT in obesity lead to infiltration of macrophages in WAT which is the major source of TNF-α produced by WAT and contribute in 50% of WAT deliveredIL-6 [18]. Also, adipokines, cytokines, and other factors produced and released by WAT are responsible for the inflammation [18]. However, in the current study, results showed no correlation between BMI and CRP level. The reasons behind this could be due to BMI limitation in determining the actual fat levels. A study showed that people with same BMI could differ in the level of body fat [19]. Also, it is largely attributable that Asian population have a higher proportion of body fat comparing to western population. The fact that Asian population have high risks of CAD and T2DM at lower BMI has been documented by many studies [20, 21]. The other reason is because of the small sample size which also cause the absence of relationship between age and CRP. Although, the cohort study of the Japanese population documented a correlation between age and CRP [17].

In the current study, the correlation between CRP and albumin was negative(r = -0.300, p = 0.10) (Fig. 2). Several studies have showed similar outcomes, that the presence of hypoalbuminemia in inflammatory diseases [22-25]. In inflammatory disorders, the albumin synthesis decreased and its degradation increased [26]. Also, in systemic inflammatory response in kidney failure, Cytokines impact on nutritional status by modulating protein catabolic rate [27]. In support to this finding we found that there is a trend for higher CRP level in patients with hypoalbuminemia compared to patients with normal albumin level (Fig. 3). We found also 100% of patients who had normal CRP level had a normal albumin level and in patients with High CRP level, 33.3% had Hypoalbuminemia (Table 2). Although, the association between Albumin and CRP here did not reach statistical significance in our study, a limitation must be pointed out which is the small sample size.

In the current study, a negative correlation between BMI and albumin was found (Fig. 4). In addition, the BMI for patients with hypoalbuminemia is significantly lower than the BMI for patients with normal albumin level(Fig. 5). A study on the micronutrient status of morbidly obese women before bariatric surgery has showed similar outcomes, that high prevalence of albumin deficiency is present which is associated with intake of a poor-quality food which is rich in fats and carbohydrates but low levels in proteins [7]. On the other hand, Schweiger et al 2013 found no hypoalbuminemia in morbid obesity [5]. Other study showed that baseline hypoalbuminemia appears to be uncommon in the United States, but was reported in up to 15.6% of subjects undergoing RYGB in Brazil [28]. This could be due to the differences in dietary habits in between countries and the contents of food from proteins.Albumin level had a negative correlation with age in the current study. A retrospective study of 1683hospital discharged patients with an average age of 79 years documented the presence of hypoalbuminemia in 973 patients [29]. CRP increases by age due to the increased production of interleukin-6 (IL-6) with aging which stimulate the hepatic production of CRP[30, 31]. The increase in CRP level by age explain the presence of hypoalbuminemia in old people.

A strong positive correlation between CRP level and lymphocyte percentage has been found in the current study (Fig. 6). This relationship was consistent with a cohort study that found an association between leukocytes and cancer (inflammatory disease) [32]. Another study showed an elevation of CRP and WBC values in 72.8% of patients with acute appendicitis (inflammatory disease) [33]. The various cytokines that is produced during inflammatory disease resulted in attract a diverse leukocyte population that is capable of producing different mediators like TNF-α and IL-6. IL-6 is a strong inducer of acute-phase response, which can result in elevation of acute-phase proteins such as CRP [32].

5. Conclusion

Our study found an increase in the inflammatory status (as indicated by CRP) and in lymphocyte percentage, whereas albumin levels were decreased in association with obesity and high BMI (Fig. 7).We recommend carrying more in vitro and in vivo studies to clarify the pathophysiology of serum albumin level derangements in inflammation and obesity. Studies are also needed to identify any association between preoperative CRP and albumin levels with patient surgical outcomes.

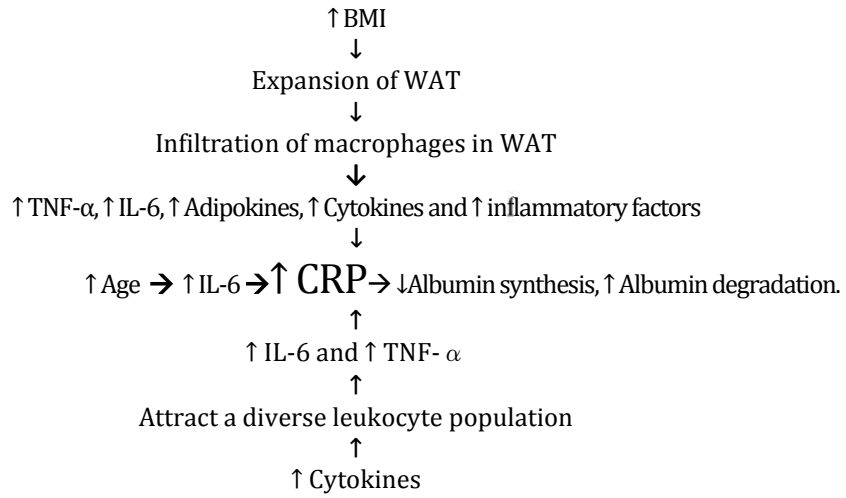

Figure 7. The relation between BMI, age, CRP level, lymphocyte percentage and inflammation

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