

## Hematological Changes post Bariatric Surgery in Saudi Arabia; Single Tertiary Care Center Experience

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Bariatric; Obesity; Gastric bypass

## 1. Abstract

**1.1. Background:** Bariatric surgery is considered a life-saving intervention for treating morbid obesity. The overall reduction in caloric intake accompanied by reduced intake of proteins and several key nutrients, such as iron and vitamin B12 can severely affect various hematological markers, including hemoglobin, hematocrit, and RBC count. This study aimed to investigate the relationship between pre- and postoperative hematological changes that are observed in individuals undergoing bariatric surgery.

**1.2. Method:** A retrospective record-based study was conducted for sequential cohort of patients undergoing bariatric surgery during 2016–2020 at a major tertiary care hospital in Riyadh, KSA. Data on complete preoperative and 6 months' postoperative blood work was collected for 300 adult patients.

**1.3. Results:** The preoperative BMI of the included study subjects significantly reduced from 44 +8.2 kg/m<sup>2</sup> (r= 26.4–87.3) to 30.3 +6.4 kg/m<sup>2</sup> (r= 18.6–68.7), P-value <0.001. Among the hematological parameters, white blood cells, hemoglobin, mean corpuscular volume, and neutrophils showed significant change in the mean value. The commonest type of surgery was sleeve gastrectomy in 274 (91.3%) that showed a mean body mass index drop of 31.6 +8.5, followed by Roux-en Y gastric bypass in 25 (8.4%) with a mean drop of 21.5 +11. No significance of variance was observed between different surgeries with respect to the observed hematological parameters. There was a female preponderance in our cohort (64.3%). Significant difference of mean in pre- and post-body mass index, white

blood cells, platelets, mean corpuscular volume, and neutrophil was observed for females, whereas body mass index, white blood cells, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin and neutrophil with significant difference of mean for pre and post-operation was observed for males. Significant difference in the platelet count was observed only in the female study subjects.

**1.4. Conclusion:** Changes in the hematological profiles are observed in individuals undergoing bariatric surgery before and after surgery. Bariatric surgeries provide the desired outcome by reducing the caloric intake and nutrient absorption that can serve as the basis of several micronutrient deficiencies postoperatively, contributing in turn to anemia. Exogenous supplementation with vitamins, folate, and iron can compensate for this loss and balance the hematological parameters within the desired ranges.

## 2. Introduction

Over 2 billion people were estimated to be overweight and obese in 2015, representing almost 39% of the world's population [1]. Obesity is a major risk factor for non-communicable diseases and reduces the overall life expectancy of the affected individual by 5–20 years [2, 3]. Bariatric surgery is considered a safe, effective, and cost-effective approach for weight loss that can help relieve the health burden of morbid obesity and obesity-associated morbidity [4, 5]. Surgery is usually indicated for patients with a Body Mass Index (BMI) between 35–39.9 kg/m<sup>2</sup> with comorbidities, while it may prove life-saving surgical intervention for those with extremely high BMI >40 kg/m<sup>2</sup> [6]. A total of 394,431 bariatric surgeries were performed in 51 partic-

ipating countries from 2014–2018, according to the report submitted by the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) to the Global Registry (10). It was also reported that for the surgeries conducted between 2012–2016, the mean percentage of weight loss one-year post-op was 28.9%, while 66.1% of type 2 diabetic patients previously on hypoglycemics, reported no more dependence on these medications [7].

Obesity is a metabolic disorder, where BMI has been reportedly directly correlated with hematocrit levels and platelet counts in individuals with metabolic syndrome [8]. Red blood cell count, platelet count, and hemoglobin levels were associated with body adiposity in obese adolescents who were beginning multidisciplinary weight loss therapy [9]. Obesity is recognized as a chronic inflammatory condition and the alterations in the cytokine profiles serve as major mediators of hematological markers associated with cardiovascular events and oxidative metabolism [10]. The insulin resistance and hyperinsulinemia in obese individuals affect the growth of vascular cells, promote atherosclerosis, and stimulate erythropoiesis leading to hematological disturbances [11]. Bariatric surgery often leads to reduced caloric intake accompanied by reduced intake of proteins and several key nutrients, such as iron and vitamin B12 that can severely affect the levels of various hematological markers, including hemoglobin, hematocrit, and RBC count [12]. We, therefore, need to explore the effect of surgery on the absorption of essential vitamins for hemoglobin like iron and vitamin B12.

The estimation of preoperative hematological parameters in individuals seeking bariatric surgery for weight loss can thus provide an important insight into the overall health status of the individuals. Post-operatively, the hematological profile can serve as an indicator of the success of the intervention and can help clinicians to timely predict any cardiovascular or hematological complications. Although hematological markers have been reported to be perturbed in obese individuals with increased inflammatory biomarkers and some hematological markers like ferritin [13]. Few studies have investigated the direct relationship between obesity and various hematological parameters of complete blood count, such as White Blood Cell (WBC) count, Red Blood Cell (RBC) count, platelet count, hemoglobin, Mean Corpuscular Volume (MCV) Mean Corpuscular Hemoglobin (MCH), and hematocrit [14]. This study aims to investigate the relationship between pre- and postoperative hematological changes in individuals undergoing bariatric surgery.

### 3. Methodology

After acquiring Institutional Review Board (IRB) approval, a retrospective record-based study of patients undergoing bariatric surgery from 2016–2020 at a major tertiary care hospital in Riyadh KSA was conducted. We included a sequential cohort of 300 adult patients who underwent bariatric surgery with complete preoperative and 6 months postoperative blood work, and follow-up based on international protocols with no missing data.

### 3.1. Statistical Analysis

Categorical data were summarized as frequencies and percentages. Continuous data were presented as mean and standard deviation. For comparison of categorical and continuous variables, we used the Chi-square test and Student t-test, respectively. Analysis of variance (ANOVA) was used to compare continuous variables across multiple groups). The significant level was set at P-value  $\leq 0.05$ . The statistical analyses were performed using STATA software, version 23.

### 4. Results

Our study included 300 bariatric surgery patients with the mean age of 36.8 +12.3 years (range  $r^2=14-77$ ), and preoperative BMI of 44 +8.2 kg/m<sup>2</sup> ( $r= 26.4-87.3$ ), which significantly reduced postop to 30.3 +6.4 kg/m<sup>2</sup> ( $r= 18.6-68.7$ ), P-value <0.001. There was a female preponderance in our cohort (64.3%). Among hematological parameters, WBC, Hgb, MCV, and Neutrophils showed significant change in the mean value. The results are summarized in Table 1.

The commonest type of surgery was sleeve gastrectomy in 274 (91.3%), followed by Roux-en Y gastric bypass in 25 (8.4%). We compared the difference between sleeve gastrectomy & gastric bypass with respect to the drop in the BMI, and found a significant drop from 44.2 +8.1 kg/m<sup>2</sup> to 30.2 +6.4 kg/m<sup>2</sup> in sleeve gastrectomy and 43.2 +9.1 kg/m<sup>2</sup> to 33.4 +6 kg/m<sup>2</sup> in gastric bypass surgery (P-value <0001). All surgery types showed a significant drop in the mean BMI of the subjects. Next, we computed the BMI drop through ANOVA between surgeries and found the difference of drops to be significant (F (9.88), (prob > F): <0.00001). The mean drop of 31.6 in BMI with sleeve gastrectomy was more pronounced than a drop of 21.5 observed with gastric bypass. However, we would like to mention here that in our study, the number of patients undergoing gastrectomy was approximately 14 times more than those going for gastric bypass. There was no significance of variance between different surgeries when compared to hematological parameters.

Gender-wise, percentage of BMI dropped significantly in males 33.3% +7.9 (95%CI= 31.8–34.8) than in females 29.4%+9.5 (CI= 28–30.7). With a cut-off of 40 years, there was a significantly less BMI drop in older patients postoperatively at 27.6% +9.2 (95%CI=25.8–29.4) than their younger counterparts at 32.5% +9.2 (95%CI= 31.2–33.6) (Figures 1 and 2). The gender-specific difference was observed in the t-test. Table 2 summarizes the t-test for pre-and postop hematological parameters for females, showing a significant difference of mean for BMI, WBC, platelets, MCV, and neutrophils. Female patients showed a significant difference in the platelet count, while in males it was not significant. On the contrary, males show significant difference in hematocrit, which was not observed in females (Table 3).

Age-specific t-test of hematological parameters for patients aged less than or equal to 40 years (n=196, 65.3%) showed pre-and postop BMI, WBC, platelets, MCV, MCH and neutrophils showing significant difference of mean (Table 4), just like in those aged more than 40 years (n=104, 34.7%), except for MCH (Table 5).

**Table 1:** Basic descriptive analysis of pre and post variables and comparison of their means using student t-test.

| Variable                        | Mean±SD (PreOp) | Mean±SD (PostOp) | Range (PreOp) | Range (PostOp) | P-value |
|---------------------------------|-----------------|------------------|---------------|----------------|---------|
| Age(years)                      | 36.8±12.3       | -                | 14-77         | -              | -       |
| BMI(kg/m <sup>2</sup> )         | 44±8.2          | 30.3±6.4         | 26.4-87.3     | 18.6-68.7      | <0.001  |
| WBC(×10 <sup>9</sup> /L)        | 7.8±2.2         | 6.9±2            | 2.8-16.2      | 2.9-16.4       | <0.001  |
| Hgb(mg/dL)                      | 132.3±16.3      | 131.2±17.1       | 79-178        | 70-179         | 0.0479  |
| Hematocrit(%)                   | 40.0±4.4        | 39.4±4.8         | 23.6-54       | 19.8-52.5      | 0.05    |
| Platelet(×10 <sup>9</sup> /L)   | 277±70.7        | 265.7±73.9       | 163-616       | 155-182        | <0.001  |
| MCV (fL)                        | 81.9±6.4        | 84.6±6.7         | 54.7-96.1     | 52.7-100.5     | <0.001  |
| MCH (pg)                        | 27.8±2.7        | 28.3±4.4         | 15.1-39.9     | 3.7-87.8       | <0.001  |
| Neutrophil(×10 <sup>9</sup> /L) | 4.5±1.9         | 3.7±1.9          | 1-19.1        | 0.7-13.9       | <0.001  |

**Table 2:** Basic descriptive analysis of pre and post variables and comparison of their means using student t-test for Females.

| Variable   | Mean and Std (PreOp) | Mean±SD (PostOp) | Range (PreOp) | Range (PostOp) | p-value  |
|------------|----------------------|------------------|---------------|----------------|----------|
| Age        | 36.4±12              | -                | 14-66         | -              | -        |
| BMI        | 43.3±7.5             | 30.5±6           | 26.4-87.3     | 18.6-68.7      | < 0.001* |
| WBC        | 7.7±2.1              | 6.8±2.1          | 2.8-15.4      | 2.9-16.4       | < 0.001* |
| Hgb        | 124.5±12.7           | 123.7±14.7       | 79-173        | 70-149         | 0.1892   |
| Hematocrit | 37.9±3.5             | 37.4±4.3         | 23.6-47.6     | 19.8-49.6      | 0.074    |
| Platelet   | 287.5±76.2           | 273.2±79.6       | 16.3-616      | 15.5-638       | 0.0002*  |
| MCV        | 80.9±6.6             | 83.8±7.2         | 54.7-96.1     | 52.7-100.5     | <0.001*  |
| MCH        | 26.6±2.8             | 27.7±3.0         | 15.1-39.9     | 3.7-37.0       | <0.001*  |
| Neutrophil | 4.3±1.7              | 3.7±1.98         | 1-19.1        | 0.7-13.9       | 0.0012*  |

**Table 3:** Basic descriptive analysis of pre and post variables and comparison of their means using student t-test for Male Gender.

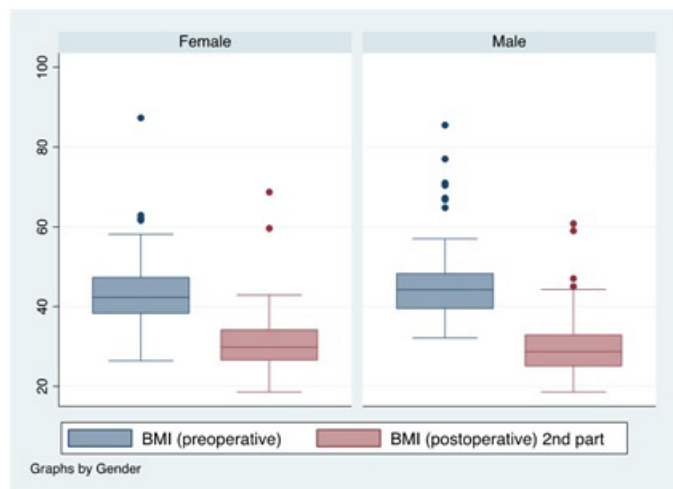
| Variable   | Mean ±SD (PreOp) | Mean±SD (PostOp) | Range (PreOp) | Range (PostOp) | P-value  |
|------------|------------------|------------------|---------------|----------------|----------|
| Age        | 36.4±12          | -                | 15-77         | -              | -        |
| BMI        | 45.3±9.2         | 30.1±7           | 32.1-85.5     | 18.6-60.8      | < 0.001* |
| WBC        | 8.2±2.3          | 7.1±2            | 3.9-16.2      | 3.5-13.4       | < 0.001* |
| Hgb        | 146.5±12.3       | 144.8±12         | 113-178       | 105-179        | 0.0922   |
| Hematocrit | 43.9±3.4         | 43.2±3.3         | 34.6-54       | 32.9-52.5      | 0.0101*  |
| Platelet   | 259.5±55.2       | 267.6±162.9      | 150-426       | 87-1820        | 0.607    |
| MCV        | 83.7±5.7         | 86.2±5.6         | 67.2-95.8     | 68.3-97.2      | <0.001*  |
| MCH        | 27.9±2.4         | 29.4±6.2         | 20.7-32.5     | 20.2-87.8      | 0.0089*  |
| Neutrophil | 4.8±2.3          | 3.9±1.9          | 1.6-14.8      | 1-9.8          | <0.001*  |

**Table 4:** Basic descriptive analysis of pre and post variables and comparison of their means using student t-test for ≤40 years of age

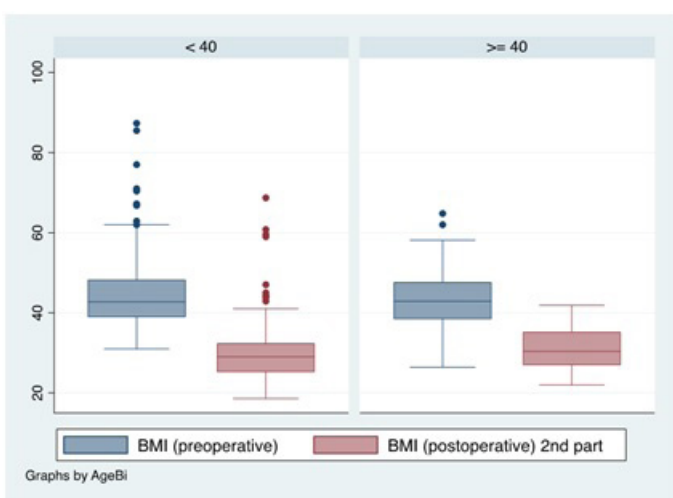
| Variable   | Mean±SD (PreOp) | Mean±SD (PostOp) | P-value  |
|------------|-----------------|------------------|----------|
| BMI        | 44.4±8.7        | 29.9±7           | < 0.001* |
| WBC        | 7.9±2.2         | 7±2.1            | < 0.001* |
| Hgb        | 132.1±18.1      | 131.3±19.6       | 0.406    |
| Hematocrit | 40±4.3          | 39.6±4.8         | 0.097    |
| Platelet   | 281.4±67.7      | 273.1±129.5      | 0.36     |
| MCV        | 81±8.5          | 84.5±8.6         | <0.001*  |
| MCH        | 26.9±2.9        | 28.4±5.3         | <0.001*  |
| Neutrophil | 4.3±1.8         | 3.7±2.1          | 0.004*   |

**Table 5:** Basic descriptive analysis of pre and post variables and comparison of their means using student t-test for >40 years of age.

| Variable   | Mean±SD (PreOp) | Mean±SD (PostOp) | P-value  |
|------------|-----------------|------------------|----------|
| BMI        | 43.2±7          | 31±5.1           | < 0.001* |
| WBC        | 7.8±2.1         | 6.8±1.9          | < 0.001* |
| Hgb        | 132.7±16.5      | 129.1±20         | 0.0166   |
| Hematocrit | 42.1±19.7       | 39.1±4.95        | 0.069    |
| Platelet   | 268.7±78.1      | 266.2±88.6       | 0.599    |
| MCV        | 82.3±9.4        | 84.1±6.9         | 0.0074*  |
| MCH        | 29.6±23.03      | 30.3±25.9        | 0.8425   |
| Neutrophil | 4.7±2.0         | 3.7±1.6          | <0.001*  |



**Figure 1:** Gender-wise Box and Whisker plot for BMI



**Figure 2:** Age-wise Box and Whisker plot for BMI, at 40 years cut-off

## 5. Discussion

Modern bariatric surgical procedures provide substantial and durable weight loss and have proven to be more effective in terms of durability and safety compared to alternative optimal medical regimes for weight loss [15, 16]. The hematological profiles are usually severely perturbed in morbidly obese individuals. This retrospective study aimed to investigate the hematological profiles of the included study subjects from a single center in Saudi Arabia who underwent bariatric procedures.

In our study cohort, there was a female preponderance. The prevalence of obesity is higher in females compared to males in all age groups [1]. In KSA, although the rates of obesity are higher in males in urban areas, the overall data is in concordance with global reports indicating an increased prevalence of obesity among females [17].

The results of this study showed that the postsurgical BMI drop was greater in males compared to females. This is similar to a previously reported meta-analysis that has highlighted that men show relatively higher weight loss compared to females following obesity treatment [18]. Additionally, males showed better satisfaction and psychological well-being scores than females despite higher complication risk [19].

Obesity also follows an age-wise pattern with increased prevalence in individuals aged from 20 to 65 years [1]. This increased tendency of gaining body weight is associated with the body composition and hormonal changes that occur with aging along with lifestyle changes. The fat-free mass declines by about 40% from 20–70 years of age. The overall physical activity decreases with age with an inclination towards a sedentary lifestyle, increasing the risk of obesity [20, 21]. The decreased expression of growth hormone, testosterone, and dehydroepiandrosterone and increased resistance of insulin and leptin also occur with aging that can lead to increased weight gain with age [22]. These factors are also responsible for determining the success of bariatric procedures in older individuals with morbid obesity. The results of our study showed significantly less drop in BMI in older patients compared to the younger ones. The aforementioned factors responsible for the increased tendency of weight gain and obesity in the elderly population are probably also responsible for this decrease in the drop of BMI in the older population.

Among the hematological factors, we have observed statistically significant changes in the values of WBCs, hemoglobin, hematocrit, MCV, and neutrophil count. Obesity has been characterized as a chronic inflammatory condition [23]. An increased WBC count is a very basic indication of inflammatory changes in the body. In a study conducted on 15,000 healthy women, obesity has been found to be associated with a higher WBC count [24]. Some evidence suggests that WBC count falls with weight loss [25]. This can be due to the reduction in the expression of proinflammatory cytokines [26]. The results of our study also show that WBC counts are higher preoperatively and dropped significantly postoperatively, suggesting a marked suppression of the inflammatory pathways with BMI reduction. Neutrophil count also increases in response to inflammatory processes. A study conducted on a cohort of African American males showed a strong correlation between the increased neutrophil count and obesity [27]. In our sample set, the neutrophil count decreased postoperatively. This is in concordance with previously published data. An 11.7% decrease in neutrophil count was observed in a 2-year follow-up study whereby the changes in the WBC and neutrophil count were being explored with sustained weight loss in obese individuals [27].

The levels of hemoglobin, hematocrit, and MCV reduced significantly postoperatively in our study. All of these hematological parameters are markers of anemia, in particular iron deficiency anemia, and the changes observed hereby show that anemia is a characteristic hematological feature observed following surgical intervention. Bariatric surgical procedures usually limit the intake and absorption of nutrients and have thus frequently been associated with several micronutrient deficiencies such as vitamin B12 (cobalamin), folate, and iron [28]. This can lead to a generalized suppression of the hematopoiesis following these surgical procedures. This can partly explain the hemoglobin deficiency and reduction in the red blood cell mass postoperatively [29]. Timely supplementation with vitamin B12, folic acid,

and iron can help in improving hemoglobin levels postoperatively to compensate for the reduced micronutrient intake and absorption [30].

Several types of bariatric procedures are in practice, including sleeve gastrectomy and Roux-en Y gastric bypass surgery. Sleeve gastrectomy surgery was the most opted for surgical procedure in our cohort, followed by gastric bypass and Roux-en Y. Although no clear evidence exists to suggest the relative effectiveness of these surgical procedures in terms of weight loss and BMI reduction, our results showed the difference of drop to be significant ( $F(9,88)$ , ( $\text{prob} > F$ ):  $<0.00001$ ) between surgeries. A higher BMI drop was observed with sleeve gastrectomy ( $31.6 \pm 8.5$ ) than with gastric bypass ( $21.5 \pm 11$ ) in our cohort. A recent meta-analysis based on multiple Randomized Controlled Trials (RCTs) suggests that Roux-en Y surgery and sleeve gastrectomy yielded similar weight-loss effect, and both were superior to laparoscopic adjustable gastric band surgery. The meta-analysis further indicates that various other factors, such as complications and patient preference, may also influence surgical consultation [23]. While the differential impact of these surgical procedures on hematological markers has not been studied, our study showed no significance of variance between different surgeries with respect to hematological parameters. Not all patients in our cohort were compliant with the postop supplementation, even though it was mandated as per protocol.

## 6. Conclusion

Our study provides important insights into the changes in the hematological profiles observed in individuals undergoing bariatric surgery in Saudi Arabia. Several factors might account for these changes. Bariatric surgery usually leads to the reduction in BMI, and thus the inflammatory processes are significantly reduced following weight loss and adiposity reduction. This is responsible for the reduction in the number of WBCs and neutrophils postoperatively. On the other hand, bariatric surgeries provide the desired outcome by reducing caloric intake and nutrient absorption, both of which can serve as the basis of several micronutrient deficiencies postoperatively, contributing in turn to anemia. Supplementation with exogenous vitamins, folic acid and iron can compensate for the reduced nutrient intake and absorption and improve the prognosis following surgical intervention.

## 7. Recommendations

The pre-and postop assessment of hematological profiles of morbidly obese individuals highlights the success of the procedure and helps identify any complications impacting the outcomes. The assessment of these profiles must be included in the list of tests that are routinely performed before surgery and in the follow-up laboratory checks. Further studies are needed to evaluate the differential impact and effectiveness of various weight-loss surgical procedures on hematological profiles.

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