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Iron Deficiency Anemia and Its Effect on Comorbidities Post Roux-en-Y Gastric Bypass in Pakistani Population: A Single Center Cohort Study

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Abstract: This single-center prospective cohort study was conducted from May 2015 to May 2020 at Shifa International Hospital, Islamabad, Pakistan. It included all patients above the age of 18 undergoing Roux en Y gastric bypass (RYGB) surgery for weight loss. All patients included had a body mass index above 40 kg/m^2 without co-morbidities and a body mass index between 30-35kg/m^2 with comorbidities. Iron studies, complete blood count, and lipid profile were done pre-operatively and post-operatively at 12, 24, and 36 months. There were 134 (67%) females and 66 (33%) males. A total of 110 (55%) people were iron deficient preoperatively. The mean age calculated for iron deficient participants was 42.25 while that for iron-sufficient was 46.13. Also, the mean preoperative BMI for iron deficient patients was 45.5 while for iron sufficient was 46.2. Overall, the mean hemoglobin before surgery was 13.5 which decreased to 12.9 at 12 months, 12.5 at 24 months, and 11.7 at 36 months postoperatively. There was an improvement in all comorbidities such as hypertension, type-2 diabetes, sleep apnea, quality of life, depression, osteoarthritis, gastroesophageal reflux disease, and dyslipidemia after RYGB surgery. Iron deficiency increases after RYGB, the deficiency is more profound in pre-menopausal women and people with baseline iron deficiency.

Keywords: Anemia, Bariatric Surgery, Iron Deficiency, Obesity, Roux en Y

1. Introduction

As obesity reaches epic proportions, candidates for bariatric surgery are increasing day by day. A number of studies have provided high-quality evidence that bariatric surgery is superior to medical management in the treatment of obesity [1]. Despite being the most popular surgical procedure for weight loss, Roux en Y gastric bypass (RYGB) leads to many micronutrient deficiencies that concern surgeons and patients alike. One of the many micronutrient deficiencies is iron [2, 3].

Iron deficiency (ID) in the context of bariatric surgery is multifactorial; ID exists in patients both pre-operatively as well as post-operatively. Pre-operatively patients can be anemic and/or iron deficient due to their obesity as it is a low-grade inflammatory state. This inflammatory state, by mechanisms currently unknown, results in anemia. Post-operatively decreased absorptive surface due to surgery, aversion to iron-rich foods, and resumption of regular menstrual cycles in pre-menopausal women are the key reasons leading to anemia. The top risk factors for post-bariatric surgery anemia are young age, female gender, and premenopausal status [4].

Hence it is important to check the iron status of high-risk individuals before surgery and all patients after surgery. The main objective of this study was to investigate the pre-operative and post-operative characteristics of Patients who are at risk of developing iron deficiency.

2. Methods

This single-center prospective cohort study was conducted at Shifa International Hospitals, a tertiary care hospital in Islamabad, Pakistan. All patients above the age of 18 undergoing Roux en Y gastric bypass (RYGB) from May 2015 to May 2020 were included in the study after written informed consent. All patients included had a BMI above 40 kg/m^2 without co-morbids and BMI between 30—35kg/m^2 with comorbids. Patients who had undergone bariatric surgery such as sleeve gastrectomy before RYGB and those with known causes of anemia such as hemolytic anemia were excluded from the study. Shifa International Hospital Ltd Institutional Review Board and Ethics Committee gave institutional approval for the study with reference number IRB #407-1227-2020.

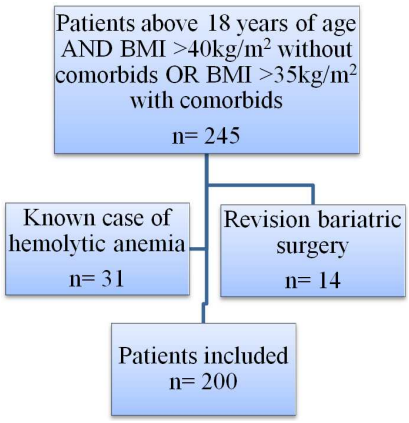

Figure 1. *Flowchart depicting the inclusion and exclusion criteria.*

All the eligible patients underwent detailed assessment with a team consisting of a bariatric surgeon, internal medicine specialist and nutritionist. Pre-operatively demographics, and physical and laboratory parameters including complete blood count, lipid Profile and iron profile were recorded on a pre-formed questionnaire completed by the study team. Patients were labeled as anemic if hemoglobin was less than 12mg/dl in females and 14mg/dl in males. Patients were labeled as iron deficient if serum ferritin was less than 50 ng/L and iron-sufficient if serum ferritin was more than 50ng/L.

Preoperative comorbidities were recorded as well as the medications used by the patient for each comorbidity. Patients were labeled hypertensive and diabetic by an experienced internal medicine specialist according to local hospital protocols. Gastro-esophageal reflux disease (GERD) was defined as episodes of reflux more than three times a week in a patient with no pre-existing esophageal disorder. A patient was labeled as having sleep apnea if the Apnea-Hypopnea Index (AHI) score was equal to or more than five per hour on a sleep study. Osteoarthritis was diagnosed using knee X-rays, dyslipidemia using lipid profile, and depression using a Patient Health Questionnaire (PHQ-9) score (score of five or more labeled as depression).

Post-operatively, patients were followed up at 12, 24, and 36 months postoperatively with repeated complete blood count, lipid profile, and iron profile. Their co-morbid status, medications, and weight were also reviewed at each visit using the same protocol mentioned above.

3. Results

The study included 200 patients undergoing Roux-en-Y gastric bypass surgery from May 2015 to May 2020, in the surgical department at Shifa International Hospital. The sample consisted of 134 (67%) females and 66 (33%) males. A total of 110 (55%) people were iron deficient preoperatively out of which 37 were male and 73 were female. 90 out of 200 patients were iron-sufficient. The mean age calculated for iron deficient participants was younger, around 42.25 years whereas that for iron-sufficient was 46.13 Also, the mean preoperative BMI for iron deficient patients was 45.5 while for iron sufficient was 46.2 as shown in Table 1.

Table 1. *Preoperative Characteristics of patients undergoing sleeve gastrectomy.*

Variable	Iron deficient	Iron-sufficient	P-value
Demographics			
Sex, n (%)			
Women	73 (54.4)	61 (44.6)	
Men	37 (56.1)	29 (43.9)	
Mean age	42.25	46.13	
Mean preoperative BMI (kg/m^2)	45.5	46.2	
Co-morbidities, n (%)			
Sleep apnea	94 (47.2)	106 (52.8)	0.046
Diabetes mellitus	97 (48.5)	103 (51.5)	0.475
Hypertension	93 (46.4)	107 (53.6)	0.012
Coronary artery disease	88 (43.8)	112 (56.2)	0.363
Gastro-esophageal reflux disease	105 (52.4)	95 (47.6)	0.072
Menstrual status, n (%)			
Premenopausal	62 (83.6)	22 (16.4)	0.001
Postmenopausal	13 (32.8)	37 (62.6)	

Table 2. *Laboratory Values over Follow-up Period (for Patients with Ferritin <50 ng/mL vs Those with Ferritin ≥50 ng/mL).*

	Overall			Iron-deficient (Ferritin <50 ng/mL)		Iron-sufficient (Ferritin ≥50 ng/mL)		p value
	N	Mean Hb (g/dL)	SD	Mean Hb (g/dL)	SD	Mean Hb (g/dL)	SD	
Preoperative hemoglobin	133	13.5	1.31	13.32	1.11	13.7	1.21	0.001
1 year postop hemoglobin	102	12.9	1.54	12.43	1.42	13.5	1.42	0.001
2 years postop hemoglobin	74	12.5	1.84	12.44	1.64	13.4	1.64	0.001
3 years postop hemoglobin	49	11.7	2.14	11.31	2.03	12.3	1.93	0.001

Overall, the mean hemoglobin before surgery was 13.5 which decreased to 12.9 at 12 months, 12.5 at 24 months, and 11.7 at 36 months postoperatively. Patients were again divided into two groups, iron deficient and iron sufficient using the same criteria. As shown in Table 2, hemoglobin consistently decreases as time passes after surgery. This drop in hemoglobin was more profound in patients with baseline iron deficiency than those with sufficient iron stores at baseline. This drop was statistically significant.

We correlated baseline co-morbidities with iron status pre-operatively. Interestingly, more co-morbidities were found in the iron-sufficient group than in the iron-deficient group on the baseline with the exception of GERD which was more in the iron-deficient group. The biggest impact on iron stores was the menstrual status. Significantly more women had low iron stores in the premenopausal group than the post-menopausal group.

Table 3. *Co-morbidities pre and post-operative status.*

Sr No	Co-morbidities	Pre-Operative	Post-Operative
1	Hypertension	83%	56%
2	Type -2 Diabetes	79%	48%
3	Sleep apnea	51%	18%
4	Quality of Life (Poor)	81%	23%
5	Depression	76%	39%
6	Osteoarthritis	63%	24%
7	GERD/Reflux	75%	69%
8	Dyslipidemia	65%	34%

We also analyzed the incidence of co-morbidities before surgery and their change after the procedure. The most common co-morbidity was hypertension followed by Type-2 diabetes. There was a significant change in all co-morbidities such as hypertension, and type-2 diabetes. sleep apnea, quality of life, depression osteoarthritis, GERD, and dyslipidemias after RYGB surgery.

Table 4. *Mean weight (kg).*

Mean Weight (kg)		
Pre Operative	Post Operative	Weight Regain
93.4	56.7	3.1

The mean weight of the patients before the surgery was 93.5kg while the post-operative mean weight was 56kg showing an average loss of 36.7 kg after the surgery. The weight regained stood at 3.1kg.

4. Discussion

Bariatric surgery is the most effective therapy for obesity, and the number of individuals who undergo this is steadily increasing every year [5]. Iron deficiency, detected by low ferritin levels, occurs in 2% to 50% of individuals who undergo Roux-en-Y gastric bypass (RYGB). Duodenum is the primary site of iron absorption is subverted in this procedure, posing a risk of nutritional deficiencies. One of the major nutritional complications is iron deficiency anemia. Anemia can be caused by bleeding from the surgery itself, such as leaking from staple or suture lines, marginal ulcers, gastritis, anastomotic bleeding or by malabsorption of hemoglobin-metabolizing chemicals such iron, folate, thiamine, vitamin B12, niacin, riboflavin, vitamin C, zinc and copper.

Identifying the characteristics of patients who develop postoperative iron deficiency anemia is crucial to tailoring patient care. We included patients with pre-operative iron deficiency anemia as its prevalence in our population is high. We wanted to see how RYGB impacts the iron status in patients with already low iron stores. According to Castanha *et* al, bariatric surgery patients are mostly female (89.3%). The leading comorbidity in their study was hypertension (44.4%), and diabetes (18.2%) [6]. A study by Kelles *et* al., also identified that 79% of patients were female, 60.8% were hypertensive and 22.3% were diabetic. In our sample, we had similar results; our sample consisted of majority (66%) females but our sample had more comorbidities with 83% having hypertension and 79% having diabetes [7].

Iron deficiency was more commonly seen in the subset of women who were actively menstruating or had a history of abnormal uterine bleeding in a study done by Brolin et al [8] the same was reflected in our study. Melissa T et al., found that 71% of women with amenorrhea or oligomenorrhea regained normal menstrual cycles after bariatric surgery [9]. Unfortunately, our questionnaire did not include asking women about their menstrual cycles after surgery, this question can be answered in future research. Most women in our study were premenopausal, this was supported by earlier studies, such as the Obinwanne *et* al. cohort study, which found that premenopausal status is a major risk factor for iron deficiency [10]. Most studies have reported greater than 40% incidence of iron deficiency and 50% of anemia postoperatively [11].

Toh and colleagues previously published the most comprehensive post- RYGB findings, reporting on 149 patients for up to 12 months after surgery. In their research, they revealed that 21% of patients were iron deficient and 16% were anemic [12]. In a research including obese individuals undergoing RYGB, Salgado et al. reported that 21.5% of the 102 patients had pre-surgical anemia and 20% had iron deficiency. There was no change in the number of anemic patients throughout the course of the research,

although serum ferritin levels dropped considerably. Females have a higher frequency of iron deficiency, and patients who have lost weight have a higher rate of anemia [13].

When we examined ferritin, we focused on how it relates to iron deficiency. Five years following bariatric surgery, Alexandrou et al. observed ferritin insufficiency in up to 30% of patients, with no differences between those who had RYGB. During the follow-up phase, our study showed a rise in the number of ferritin-deficient patients [14].

Current guidelines suggest routine screening of iron before metabolic surgery. In the general population, oral iron supplementation is considered the first-line therapy for iron deficiency. Brolin et al [8] showed that preventive oral administration of 320mg iron twice a day reduced iron deficiency in menstruating women following RYGB in a double-blind, randomized controlled trial [15].

5. Conclusion

To conclude, bariatric surgery is an excellent tool for people struggling with the metabolic side effects of obesity. Iron deficiency is a side effect that can easily be monitored and curtailed. Patients with risk factors of developing iron deficiency post-operatively must be screened prior to surgery and followed up in a timely manner to avoid anemia-related complications.

6. Recommendations

It is more common in pre-menopausal women and patients with pre-existing anemia. Pre-operative and post-operative comprehensive screening by iron studies will help detect iron deficiency. By identifying at-risk patients before surgery, we can liaise with nutritionists and significantly improve the patients' quality of life.

7. Limitations

There are several limitations to this study. First, nutritional deficiencies can develop years after bariatric surgery, and although compliance with postoperative laboratory testing was high, testing extended to just 12 months postoperatively. Secondly, we did not assess the regularity in patients' menstrual cycles after RYGB. Researchers can ponder over these areas in future research.

Disclosure Statement

The authors declare no conflict of interest. The research was not funded by any organization and did not receive any grant.

Abbreviations

BMI; Body mass Index. *RYGB;* Roux en Y gastric bypass; *ID* Iron deficiency, *GERD;* Gastro-esophageal Reflux Disease*, AHI;* Apnea-Hypopnea Index.

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