Original Article

Prevalence and Incidence of Iron Deficiency in Patients Undergoing Bariatric Surgery: A Teaching Hospital Experience in Thailand

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Background: Bariatric surgery currently plays an important role in the treatment of obesity. However, iron deficiency and iron deficiency anemia are long-term complications after bariatric surgery. There have been no studies of prevalence and incidence of iron deficiency and iron deficiency anemia after bariatric surgery among Thai population.

Objective: To evaluate the incidence and prevalence of iron deficiency and iron deficiency anemia in Thai post-bariatric surgery patients.

Materials and Methods: The present study was a retrospective study. The data were collected from the medical records of 78 patients that underwent bariatric surgery, 12 for laparoscopic sleeve gastrectomy (LSG) and 66 for laparoscopic Roux-en-Y gastric bypass (LRYGB), at Phramongkutklao Hospital between January 2008 and December 2016. Demographic and laboratory data were obtained prior to surgery and at 3, 6, 12, and 24 months after the surgery.

Results: The prevalence and incidence of iron deficiency 24 months after LRYGB were 25.8% and 18.7%, respectively. The prevalence and incidence of iron deficiency anemia 24 months after LRYGB were 19.7% and 16.0%, respectively. Increasing time after surgery was also associated with significant abnormal iron profiles ($p<0.001$); whereas, there were no signs of iron deficiency and iron deficiency anemia among patients who underwent LSG.

Conclusion: At 24-month follow-up, the prevalence and incidence of iron deficiency and iron deficiency anemia have significantly increased among the patients who underwent LRYGB. Therefore, serum iron, hemoglobin, and hematocrit should be monitored to prevent and initiate the treatment of iron deficiency anemia.

Keywords: Sleeve gastrectomy, Roux-en-Y gastric bypass, Iron deficiency, Anemia

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Obesity is a chronic health problem. Overall, about 13% of the world's adult population were obese in 2016[1]. The prevalence has been reported in many countries, including Asian countries[2]. Morbid obesity can be the cause of chronic diseases, such as type 2 diabetes mellitus, hypertension, dyslipidemia, cardiovascular disease, obstructive sleep apnea, and some cancers. Furthermore, it is affecting the quality of life and death due to these co-morbidities[3].

Bariatric surgery has been accepted as the most effective procedure for treating obesity, due to providing sustain weight loss and improving the co-morbidities[4]. Nevertheless, long-term complications may occur after this type of surgery such as micro-nutrient deficiencies, which iron deficiency (ID) is an

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important issue. Iron is an essential mineral that plays a key role in cell metabolism and enzyme cofactors[5,6]. ID is thought to be the most common cause of this population[7-9]. Many studies have reported a high incidence of ID and iron deficiency anemia (IDA) after surgery, with up to 40% of the patients having ID, within one to two years after surgery[10-13].

Nowadays, bariatric surgery has become an important surgery in Asian countries[14]. Laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) are the most commonly performed bariatric surgery in Thailand. There have been no studies on incidence and prevalence of ID in Thai population as most research studies were based on Western populations[11-13]. Therefore, the authors sought to evaluate the incidence and prevalence of ID and IDA in Thai post-bariatric surgery patients.

Materials and Methods

The Institutional Review Board approval (Q008h/61_Exp) was obtained to retrospectively review treatment record of patients that underwent LSG and LRYGB at Phramongkutklao Hospital between January 2008 and December 2016 and received a follow-up period of 24 months. The inclusion criteria were patients who have undergone LSG and LRYGB. The patients who were not followed up within one year after surgery, were excluded. All patients in the present study had received an iron-free multivitamin supplement.

Demographic data were collected on gender, age, and height. Baseline weight and follow-up after surgery were recorded. The biochemical tests included hemoglobin, hematocrit, and iron indices, which included serum ferritin and transferrin saturation (TSAT), were collected. All data were recorded preoperatively and at 3, 6, 12, and 24 months after surgery. The start time of iron supplement was documented.

Primary outcome was an ID. In the present study, the authors used criteria based on serum ferritin of less than 30 µg per L and TSAT of less than 20% because it has a good performance characteristic[15,16]. IDA were diagnosed when patients had ID with hemoglobin level of less than 12 g per dL for female and less than 13 g per dL for male, which is recommended by the World Health Organization[17].

Statistical analysis was performed by the Stata, version 14.0 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). Descriptive data were presented as percentage, median, or mean, with their standard deviation. The generalized estimating equations (GEEs) compared proportions over time. The time to the first primary outcome event was analyzed with the use of a Cox proportional model to compare the hazards between groups. Time to event curves were calculated with the use of the Kaplan-Meier method. The significant level was set at p-value less than 0.05.

Results

Baseline characteristics are shown in Table 1. Data from the 78 patients who met the inclusion criteria were collected, 12 patients (15.4%) had LSG and 66 patients (84.6%) had LRYGB. Most patients were female (69.2%), mean age of 35±9 years, and mean body mass index (BMI) of 44.6±10 kg/m^2. Before surgery, most of patients had normal hemoglobin and hematocrit.

Table 2 shows that after 24 months follow-up, 17 patients (25.8%) developed ID, all of them were in the LRYGB group. Moreover, 13 out of 17 patients (19.7.0%) were diagnosed as IDA. Conversely, ID and IDA were not found in the LSG group. The incidence of ID in the LRYGB group was 18.7%. Twelve (16%) of these patients were classified as IDA. The time to occurrence of IDA is shown in Figure 1.

At the 3, 6, and 12 post-operative-month follow-ups, the post LRYGB patients who had anemia based on hemoglobin levels were increasing over time, as 20.4%, 27.7%, and 33.3% of the patients, respectively. Additionally, 10.9%, 21.1%, and 27.1% of patients, respectively, had ID defined by ferritin level (Table 3). Likewise, 22.2%, 16.7%, and 25% of the patients, respectively had non-IDA in the LSG group (Table 4).

Discussion

Gastric bypass and gastric resection may affect the absorption of numerous micronutrients, especially iron. ID is a common nutritional deficiency that develops early in the patients who underwent bariatric surgery[7-9]. The authors found that the ID prevalence was 25.8% at 24 months post-operative in the patients after LRYGB surgery. The prevalence of IDA after surgery increased over time. According to a study of micronutrient deficiencies following LRYGB[18], the development of iron deficit after 24 post-operative months reached the rate of 23.7%. Many studies have found that the prevalence of ID increased after surgery[11-13,19]. A systematic review and meta-analysis about anemia after LRYGB surgery found that the frequency of ferritin deficiency increased two-fold in patients six months after surgery, and this trend became substantial at 24 months. Serum ferritin is

Table 1. Baseline characteristics of the patients undergoing bariatric surgery

Characteristics	Total (n=78) n (%)	LSG (n=12) n (%)	LRYGB (n=66) n (%)
Female	54 (69.2)	10 (83.3)	44 (66.7)
Age (year); mean±SD	35.1±9.2	34.2±8.2	35.3±9.4
BMI preoperative; mean±SD	44.6±10.3	38.1±9.2	45.8±10.1
Comorbidity			
T2DM	24 (30.8)	2 (16.7)	22 (33.3)
Hypertension	41 (52.6)	2 (16.7)	39 (59.1)
Dyslipidemia	32 (41.0)	3 (25.0)	29 (43.9)
Fatty liver	16 (20.5)	4 (33.3)	12 (18.2)
Chronic kidney disease	2 (2.6)	1 (8.3)	1 (1.5)
Obstructive sleep apnea	40 (51.3)	5 (41.7)	35 (53.0)
Hb preoperative (g/dL); mean±SD	13.8±1.4	13.0±1.0	13.9±1.4
Hct preoperative (%); mean±SD	41.7±3.7	39.5±2.4	42.1±3.7
Ferritin preoperative (µg/L); median (IQR)	111.5 (82.8, 195.8)	105.6 (98.7, 182.3)	118.2 (82.8, 195.8)
Preoperative iron deficiency	3 (3.8)	0 (0.0)	3 (4.5)
TSAT (%); mean±SD	24.8±11.9	25.9±8.6	24.6±12.4
Iron supplement			
Preoperative	2 (2.6)	0 (0.0)	2 (3.0)
At 3rd month	13 (16.7)	2 (16.7)	11 (16.6)
At 6th month	21 (26.9)	2 (16.7)	19 (28.7)
At 12th month	26 (33.3)	2 (16.7)	24 (36.4)
At 24th month	36 (46.2)	4 (33.3)	32 (48.5)
EWL at 12 months (%); mean±SD	62.4±22.6	62.4±28.5	62.4±21.6

BMI=body mass index; T2DM=type 2 diabetes mellitus; Hb=hemoglobin; Hct=hematocrit; TSAT=% transferrin saturation; EWL=excess weight loss; SD=standard deviation; IQR=interquartile range

Table 2. Prevalence and incidence of iron deficiency and iron deficiency anemia in 24 months

Event	Prevalence; n (%)		Incidence; n (%)	
	LSG (n=12)	LRYGB (n=66)	LSG (n=12)	LRYGB (n=63)
Iron deficiency	0 (0.0)	17 (25.8)	0 (0.0)	14 (18.7)
Iron deficiency anemia	0 (0.0)	13 (19.7)	0 (0.0)	12 (16.0)

LSG=laparoscopic sleeve gastrectomy; LRYGB=laparoscopic Roux-en-Y gastric bypass

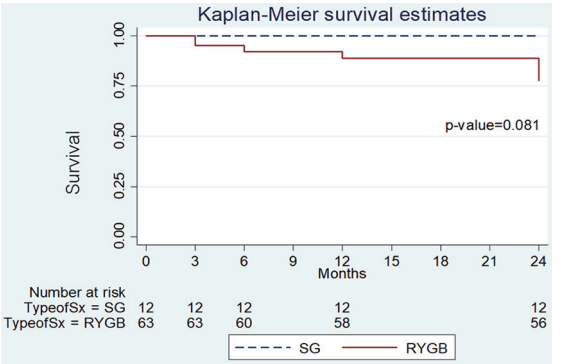

Figure 1. Cox regression analysis of survival in iron deficiency patients diagnosed between LSG and LRYGB group.

a more specific and earlier indicator for ID[20]. The present study also found that hemoglobin, ferritin, and TSAT significantly decreased over study period. The incidence of ID in the present study is interesting. The authors found that the incidence rate of ID increased to 18.7% at 24 months post LRYGB surgery. Previous reports stated a range of incidence from 20% to 47%[11,21-23]. As mention previously, Obinwanne et al found that 53.1% of the patients included were ID[24]. Furthermore, the authors found that ID may have occurred since the third post-operative month similar to the report by Monaco-Ferreira et al[25]. The reasons for ID can be attributed to the bariatric procedure of LRYGB, which is done by restricting

Table 3. The proportion of patients with anemia and abnormal iron profiles in LRYGB group of 24 months follow-up

Time/parameters	Preoperative n (%)	3 months n (%)	6 months n (%)	12 months n (%)	24 months n (%)
Hemoglobin†* (p<0.001)					
Adequate	60 (92.3)	43 (79.6)	47 (72.3)	44 (66.7)	42 (63.6)
Deficiency	5 (7.7)	11 (20.4)	18 (27.7)	22 (33.3)	24 (36.4)
Ferritin‡* (p<0.001)					
Adequate	31 (91.2)	41 (89.1)	45 (78.9)	43 (72.0)	37 (59.7)
Deficiency	3 (8.8)	5 (10.9)	12 (21.1)	16 (27.1)	25 (40.3)
TSAT§* (p<0.001)					
Adequate	30 (57.7)	35 (70.0)	53 (81.5)	51 (78.5)	46 (70.8)
Deficiency	22 (42.3)	15 (30.0)	12 (18.5)	14 (21.5)	19 (29.2)

TSAT=% transferrin saturation

† Hemoglobin <13 g/dL (male) & <12 g/dL (female), ‡ Ferritin <30 µg/L, § TSAT <20%

* Generalized estimating equations (GEEs), using a significant level at p<0.05

Table 4. The proportion of patients with anemia and abnormal iron profiles in LSG group of 24 months follow-up

Time/parameters	Preoperative n (%)	3 months n (%)	6 months n (%)	12 months n (%)	24 months n (%)
Hemoglobin†* (p=0.02)					
Adequate	9 (75.0)	7 (77.8)	10 (83.3)	9 (75.0)	10 (83.3)
Deficiency	3 (25.0)	2 (22.2)	2 (16.7)	3 (25.0)	2 (16.7)
Ferritin‡#					
Adequate	9 (100)	8 (100)	9 (100)	9 (100)	10 (100)
Deficiency	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TSAT§* (p=0.02)					
Adequate	8 (80.0)	6 (75.0)	7 (70.0)	8 (72.7)	8 (72.7)
Deficiency	2 (20.0)	2 (25.0)	3 (30.0)	3 (27.3)	3 (27.3)

TSAT=% transferrin saturation

† Hemoglobin <13 g/dL (male) & <12 g/dL (female), ‡ Ferritin <30 µg/L, § TSAT <20%

Not evaluation; * Generalized estimating equations (GEEs), using a significant level at p<0.05

food intake and malabsorptive component, resulting from the bypass site of the duodenum and proximal jejunum that affects iron absorption[26].

A study of impacts of LSG on iron indices found low incidence of anemia (1.6%) and ID (4.9%) in patients that underwent LSG after 12 months follow-up. The incidence of ID one year after surgery in LSG was lower than previously reported among the other types of bariatric surgery[27]. Similarly, the study of Ferraz et al found that the prevalence of ID at the end of 24 months of follow-up in the patients that underwent LSG was lower to the ones that underwent LRYGB[18]. The present study found that there was no ID and IDA in the LSG group.

Remarkably, the number of patients with low hemoglobin levels in the LSG group was more than in the LRYGB in the first period, but the number of patients with low hemoglobin levels decreased over time. All patients were non-IDA in the LSG group, as we found that none of the patients had low ferritin level. At any rate, iron homeostasis changes related to LSG were due to decrease in food intake and a reduction of secretion of hydrochloric acid in the stomach[27]. Therefore, it did not affect the site of iron absorption in the small intestine. The received iron supplementation in the post-operative period, related with maintenance of iron absorption at the duodenum and proximal jejunum, may give the explanation for this increase in the level in the patients who undergone LSG[27].

Pathogenesis of ID in the obese patients through the action of legion adipocyte, responsible for the production of pro-inflammatory adipokines such as tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6), leptin, and hepcidin results in chronic systemic inflammation in these patients. Furthermore, it decreased red blood cell synthesis in erythropoiesis process. As hepcidin also inhibit iron excretory mechanism that results in functional ID[9,28].

Ferritin is an intracellular protein responsible for storage and releasing of iron. Ferritin was used to correlate with ID, but in these obese patients, it may display high value as a result of the related chronic inflammatory process[12,28]. The study of Monaco-Ferreira et al found that iron overload was found in 30.6% of the patients before surgery and the 120-month follow-up also had iron overload[25].

According to the American Society of Metabolic and Bariatric Surgery (ASMBS) guideline, they recommend at least 45 to 60 mg for the patients who underwent LSG and LRYGB[7]. The hyperferritinemia is the result of the inflammatory effect of obesity[12,28]. In addition, oral iron supplement was generally associated with gastrointestinal disturbance, which could further complicate non-compliance to diet intake, especially food rich in protein[27]. High protein diet could preserve muscle tissue when the patient loses the weight. The reason that all the post-bariatric patients did not receive iron supplement until the markers had tendency to depreciate over time was to prevent an iron overload. However, all patients in LSG group did not develop an ID during the study period. In addition, the patients in the present study had low prevalence of ID after being followed for 24 months.

The present study has several limitations. First, as retrospective review research, inadequate diet pattern that affect ID and adherence in vitamin supplements were unknown. Second, there are many difficulties associated with following the patients. Additionally, the medical record may not have been collected completely due to loss to follow-up. However, the present study is the first research to report on the incidence and prevalence of ID and IDA in Thai populations who undergone LSG and LRYGB. Additionally, the highlight of the present study was to be able to know the onset of the disease. As this present study discovered, occurrence of the ID could be found during the third post-operative month in the LRYGB group. Finally, the time of occurrence of ID in post-bariatric surgery could be applied as a practice guideline for management of ID and IDA among these populations.

Conclusion

At the 24-month follow-up, ID was not seen in the patients that underwent sleeve gastrectomy, but was found in the Roux-en-Y gastric bypass surgery. ID increased over time. Therefore, the monitoring of iron status parameters should be done as early as three months after surgery. Early detection of ID is the role to the successful management among these group of patients, and all of post-bariatric surgery patients should be monitored for ID and IDA.

What is already known on this topic?

ID is frequently found after bariatric surgery. It is associated with various factors, such as dietary restrictions, hypochloridria, and malabsorption, resulting from the bypass site of the duodenum and proximal jejunum. Many research studies have reported high incidence and prevalence of ID and IDA after bariatric surgery. However, most of the results were based on Western populations.

What this study adds?

There have been very limited studies evaluating iron status in Asian post-bariatric surgery patients. None of the research studies have been conducted among Thai population. The present study is the first study to investigate the prevalence and incidence of ID among Thai post-bariatric surgery patients.

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Conflicts of interest

The authors declare no conflict of interest and this project was not sponsored.

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