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Factors/Mechanisms Affecting Status of Iron & Related Nutrients in RYGB Patients

Arora Beena[1*], Siddhu Anupa[2] and Peters Atul Naveen Christopher[3]

[1]Research Scholar, Lady Irwin College, University of Delhi, India.
[2]Director, Lady Irwin College, University of Delhi, India
[3]Director & Senior Consultant, Apollo Institute of Bariatric & Metabolic Surgery, Indraprastha Apollo Hospitals, Sarita Vihar, Delhi, India

ABSTRACT

Several studies conducted on patients who underwent RYGB have reported deficiencies of iron & related nutrients in the post-operative periods. This review is aimed at to analyze factors or mechanisms contributing to these deficiencies in the bariatric population.

The articles for this review were searched on pubmed and google scholar for the period from 2016 to 2006. The key words used were bariatric surgery, gastric bypass, RYGB, Anaemia, iron deficiency anaemia, iron profile, iron deficiency, TIBC, Ferritin, Folate, folic acid, vitamin B12, 'hemoglobin', 'hematocrit', 'vitamin B12 deficiency', 'folic acid deficiency' and 'folate'. Retrospective, prospective, observational and cohort studies in english language, including laparoscopy and traditional open procedures, conducted on both genders, diabetic as well as non-diabetic were included in this review. Review articles, meta-analysis and studies and articles that covered bariatric procedures other than RYGB were excluded. Studies that compared RYGB with other bariatric procedures and studies done on pregnant or lactating women and below 18 years of subjects were also excluded.

Iron and related nutrient deficiencies are extremely common after RYGB and is linked with multiple risk factors or mechanisms. Pre operative deficiencies must be treated on time, aimed at preventing prolong post op deficiencies. Pre operative oral supplementation is rewarding but in post operative the effect of oral supplementation may be limited as absorption of oral iron supplements is insufficient post RYGB. Intra venous iron therapy is much beneficial in dealing with iron deficiencies.

KEYWORDS: Roux-en-Y Gastric Bypass, RYGB, Gastric Bypass, Iron deficiency, Vitamin B12 status, Folate levels, Ferritin status

*Corresponding author

Mrs. Beena Arora

Research Scholar, Lady Irwin College,

University of Delhi, Delhi - 110002, India

Email: beena_arora@ymail.com, Mob No. – 9899550556

1. INTRODUCTION

Obesity originates illness[1], inferior quality of life[2]and reduces life expectancy[1]. The prevalence of obesity and associated co morbidities are on an exponential escalation worldwide as well as in developing countries like India[3]. Obesity affects more than 135 million persons in India[4].Obesity is a multifaceted metabolic muddle that is often coupled with interrelated co morbid conditions that necessitate therapeutic intervention, including cardiovascular disease, type 2 diabetes mellitus, Blood lipid disorders, degenerative bone diseases, psychological disabilities and nutrient deficiencies[5, 6, 7]. Highly prevalent micronutrient deficiencies in obese individuals are vitamin D, calcium, folate, vitamin B12 an iron[8, 9, 10, 11, 12, 13, 14]. Regardless of high-calorie ingestion, the micro nutrient deficiencies present come into view due to inappropriate diet and impaired micronutrient consumption[15].

Obesity epidemic is a consequence of intricate interactions of nutritional intake, physical activity level, genetics and the environment[6, 16, 17]. Obesity treatment aims at to endorse negative energy balance by cutting back on calorie intake and enhancing calorie consumption.

Studies have indicated that conventional therapies and lifestyle changes, are usually attempt primarily, and if required, medications may be considered, but these methods rarely capitulate reasonable long-term outcomes in obese population[18, 19, 6, 20]. Thus when clinical treatment fails, bariatric surgery appears to be the best choice[18].

Bariatric and metabolic surgery is a reliable and widespread treatment for morbidly obese, defined as weight greater than 100% or 100 pounds above ideal body weight[21] and its associated conditions like cardio vascular diseases, myocardial infarction and stroke and is widely acknowledged as a technique for sustained weight loss[22, 23, 24, 25]. On the other hand several studies reported various nutritional complications after bariatric surgery[23, 26]. In 2011, > 34,04,000 procedures were performed worldwide. In the United States, a leading country for bariatric surgery, there were 160,000 bariatric procedures performed in 2010[7].

2. METHODOLOGY

The articles for this review were searched on pubmed and google scholar for the time period from 2016 to 2006.The key words used were bariatric surgery, gastric bypass, RYGB, Anaemia, iron deficiency anaemia, iron profile, iron deficiency, TIBC, Ferritin, Folate, folic acid, vitamin B12, 'hemoglobin', 'hematocrit', 'vitamin B_{12} deficiency', 'folic acid deficiency' and 'folate'. Retrospective, prospective, observational and cohort studies in english language, including laparoscopy and traditional open procedures, conducted on both genders, diabetic as well as non diabetic were included in this review. Review articles, meta-analysis and studies and articles that covered bariatric procedures other than RYGB were excluded. Studies that compared RYGB with other bariatric procedures and studies done on pregnant or lactating women and below 18 years of subjects were also excluded.

Table 1: Overview of Reviewed Articles

S. No.	Author	Year	Country	Study Type	Procedure	Case No.'s	Intended follow up (Months)	Mean Age (years)	Male	Female	Mean BMI	Nutrition Management
1	Haoyong Yu et al	2016	China	Prospective	RYGB	84	24	-	-	-	-	-
2	Gesquiere I et al	2016	Belgium	Prospective	RYGB	54	12	48	21	33	40.4	Daily micronutrient Supplement intake
3	Haleigh James et al	2016	USA	Retrospective	RYGB	287	-	-	-	-	-	SC Vitamin B12 and Standard Vitamin and Mineral Supplement
4	Sigrid Bjerge Gribsholt et al	2016	Denmark	Survey	RYGB	1429	-	47.1	286	-	-	-
5	Flavia Andria Marin	2016	Brazil	Prospective	RYGB	45	6	>= 35	-	45	-	Supplementation 1 RDA, 2 RDA
6	Jens Homan et a	2016		Follow up Cohort	RYGB	148	36	-	-	-	-	WLS Forte, sMVS
7	Careaga M et al	2015	Spain	-	BS	947	-	-	-	-	-	-
8	Van der Beek ES et al	2015	Netherlan ds	Retrospective	RYGB	427	-	-	-	-	-	-
9	Aaseth E et al	2015	Norway	Retrospective	RYGB	441	60	41.5	24.90 %	75.10%	46.1	Oral multivitamin, calcium/ vitamin D, Iron and IM B-12 three monthly
10	Del Villar Madrigal E et al	2015	Mexico	Retrospective	RYGB	486	12	39.9	195	291	42.4	Daily Supplements
11	Kotkiewicz A et al	2015		Prospective	RYGB	319	56	45	50	269	-	-
12	Karefylakis C et al	2015	Sweden	Retrospective	RYGB	431	120	51.3	-	-	-	-
13	Molin Netto BD et al	2015	Brazil	Observational	RYGB	41	6	39.4	2	39	44.6	-
14	Worm D et al	2015		Prospective	RYGB	835	24	43.3	-	-	47.2	Ca, Vit D and Multivitamin and Iron B12
15	Ramon NM et al	2015	Brazil	Retrospective	RYGB	137	48	18-60	-	-	-	Multivitamins and Minerals
16	Obinwanne KM et al	2014	La Crosse WI	Retrospective	RYGB	959	120	43.8	15.10 %	84.90%	47.4	IV Iron Therapy

17	Gesquiere I et al	2014	Belgium	Retrospective	RYGB	164	-	43	41	123	-	Oral challenge test with 100 mg FeSO4 . 7H20 was performed
18	Gobato RC et al	2014	Brazil	Prospective	RYGB	36	6	-	-	-	-	-
19	Wilson Salgado Jr. et al	2014	Brazil	Retrospective	RYGB	-	48	-	-	-	-	-
20	Mercachita T et al	2014	Portugal		RYGB	60	12	-	-	-	-	-
21	Marambio A et al	2014	Chile	Prospective and Analytical	RYGB	13	6	44.1	1	12	40.4	Multivitamin
22	Miller GD et al	2014	USA	Prospective	RYGB	17	12	-	-	-	-	-
23	DeFilipp Z et al	2013	USA	Retrospective	RYGB	23	>=12	-	-	-	-	2 g Iron Dextran IV
24	Malone M et al	2013	USA	Observational	RYGB	125	45.7	44.7	11%	89%	47.3	Oral or IV Iron therapy or blood transfusion
25	Margerat Malone et al	2013	USA	Observational	RYGB	125	45.7	44.7	11%	89%	47.3	Oral and IV
26	Lee YC et al	2012	Taiwan	Retrospective	RYGB	442	24	30.8	-	-	40.7	-
27	Custódio Afonso Rocha V	2012	Brazil	Prospective	RYGB	22	2	-	-	22	-	-
28	Candriatta Blume et al	2012	Brazil	Retrospective	RYGB	170	36	-	34	136	-	Standard Vitamin and Mineral Supplement
29	Ramsey M Dallal et al	2012	USA	Longitudinal	RYGB	590	398 days	-	-	-	-	-
30	Christian T Cable et al	2011	USA	Retrospective	RYGB	1009	36	-	-	-	-	-
31	Dimitrios V Avgerinos et al	2010		Retrospective	RYGB	206	86 weeks	40.8	41	165	>40	Ferrous Sulphate X 2 weeks

3. ROUX-en-Y GASTRIC BYPASS (RYGB)

American Society for Metabolic and Bariatric surgery had mentioned that "The Roux-en-Y Gastric Bypass – often called gastric bypass – is considered the 'gold standard' of weight loss surgery", against which other procedures are compared, with most patients losing 50% to 75% of their excess weight[21]. RYGB is a surgical technique in which the distal stomach, duodenum and proximal jejunum are bypassed precluding exposure of the food bolus to these sites in the postoperative bilio-pancreatic limb[22].The newly made stomach pouch in RYGB is significantly smaller and enables substantially smaller meals, which in turn allow less calorie consumption. Food bolus contact to the normal gastric acid gradient along the fore-gut is also changed which restricts absorption of macro and micro-nutrients[27].

The redirecting of the food stream yields alterations in gut hormones that produces early satiety, conquer appetite, and reverse one of the primary mechanisms through which obesity persuades type 2 diabetes[27].

RYGB in long term can lead to long-term vitamin/mineral deficiencies particularly deficits in vitamin B12, iron, calcium, and folate[27].

3.1 Iron & Related Nutrients

3.1.1. Iron:

Iron is a vital micro nutrient in humans, makes up 0.005% of the body weight and is involved in heme and non-heme proteins occupied in oxygen and electron transportation[7]. Iron deficiency is prevalent in developing countries, as well as in developed countries, particularly in menstruating women (up to 16%)[28]. Obesity increases the risk of iron deficiency. Iron deficiency is therefore prevalent before any bariatric procedure and several studies have reported it's exacerbation following RYGB, the mechanism behind is multifactorial (Table 2).

3.1.2 Ferritin:

Assessment of Ferritin deficiency was low in the pre op as compared to post surgery follow up periods. Only six studies[29, 30, 31, 32, 33, 34] conducted pre op serum ferritin assessment before surgery and the cut off levels referred to define it ranged from <6ng/ml[28] to <30ng/ml[34]. In all of these studies subjects were found deficient ranged from 9% to 100%. Pre-operative low serum ferritin level and female gender were associated with higher possibility to suffer iron deficiency anemia 2 years after RYGB[35].

Post op assessment was conducted in 12 studies[29, 36, 37, 38, 30, 32, 26, 39, 40, 33, 34, 41]. Out of all these studies only two studies showed improvement in serum ferritin levels[34, 41] at 3.8 years and 1.7

years follow up periods respectively. Rest all studies showed degradation of serum ferritin levels at different follow up periods ranged from 6 months to 48 months[29, 36, 38, 30, 32, 26, 32, 26, 39, 40, 33].

3.1.3 Vitamin B12 & Folate:

Vitamin B12, also known as cobalamin, helps in the production of healthy red blood cells that carry oxygen around the body. Folate, also called as Vitamin B_9 or folic acid, also serves the same function. Vitamin B12 and Vitamin B9 deficiency is called megaloblastic or macrocytic anaemia (larger than normal red blood cells).

Pre op assessment of Vitamin B12 and Folate was considerably low. Only two studies of all reviewed articles assessed vitamin B12[29, 39]and Folate[29, 32] and the subjects were found deficient from 21.30% to 100%. Post operative rate of assessment was better, 8 studies assessed vitamin B12[29, 37, 42, 38, 32, 25, 26, 43] and 6 studies assessed folate levels[29, 42, 38, 25, 26, 43]. Out of 8 studies, 3 studies[42, 38, 25] showed improvement in vitamin B12 concentration from 2 years to 10 years after surgery. Remaining 5 studies reported decrease in Vitamin B 12 levels. 5 studies out of 6 reported improvement in folate status post operatively[42, 38, 25, 26, 43] at 2 years to 10 years follow up periods.

3.2 Pre operative and Post operative Status

Assessment of pre op and post op iron and related nutrient status was low among patients underwent RYGB. Only seven studies conducted pre operative iron status in patients underwent RYGB[30, 31, 32, 39, 40, 33, 34], even the rate of post operative follow up was low[30, 25, 26, 39, 44, 34]. In a recent retrospective study (total 21,345 patients) the medical insurance claims of a large population of RYGB patients (17,930 patients) who had undergone nutritional testing for Iron deficiency was found to be only 21% preoperatively which improved at 12 months post surgery (53%) which declined over 13 – 24 months (39%) and 25 – 36 months (31%)[24]. The strong point of this study is large sample size and limitation was methods to define iron deficiency were not specified. The authors may have included serum iron which is not sensitive or serum ferritin which can be elevated during obesity because of systemic inflammation. On the other hand, the results of this study are consistent with others that show exacerbation of iron deficiency when followed from pre op and upto 120 months post RYGB where rates of deficiency were reported preoperatively ranged from 8.7% - 100%[31, 32, 40, 33, 34]. Post operatively reported rate of deficiency were found between 20% - 42%[25, 29, 44]. However, not all studies have reported deterioration of iron status following RYGB, same or improved iron status was found mainly in male candidates[30, 26, 34].Pre menopausal women who had undergone RYGB were at increased risk of iron deficiency[39, 40]. Iron deficiency may or may not be symptomatic.

Table 2: Factors/ mechanisms responsible for poor status of iron and related nutrients in bariatric surgery candidates (pre operative and post operative)

S. No.	Pre Operative	Post Operative
		Pre op operative micronutrient deficiencies[32, 22]
1.	Poor Dietary Habits[26, 40, 34]	Gastric resection[24, 41]
2.	Menstrual bleeding/ Reproductive age[35, 45, 46, 22, 18, 47]	Low Dietary Intake[29, 18, 47, 48, 44, 34]
3.	Systemic inflammation[46, 48]	Achlorhydria[37, 47, 41]
4.	Increased hepcidin[29]	Intrinsic factor reduction[26]
5.	Increased CRP[29, 48]	Peptic ulcers[34, 47]
6.	Indirect inflammatory markers[46, 48]	Bleeding[34, 47]
7.	Elevated Ferritin[22, 30, 41]	Menstruation[18, 44, 49, 50]
		Inflammation induced by erythropoietin response and malabsorption[46, 48]
		Exclusion of duodenum and proximal jejunum[18, 34, 43]
		Changes in iron transporter DMT -1[22, 47]
		Length of Roux limb[22, 47]

***3.3 Pre operative Factors/Mechanisms*:** Pre operative Iron deficiency is often asymptomatic[42], and sometimes may lead to anemia and fatigue[26, 34]. Other symptoms which may be present include muscle weakness, dyspnea, chest discomfort, pica and pagophagia[34].

Pre op iron and related nutrients deficiencies are an independent risk factor for post operative iron deficiency, increase in mortality and results in reduced QOL[32, 26].

3.3.1 Poor Dietary Habits:

Dietary factors such as low caloric diet, which is one of the conventional methods for weight loss in obese population[26], meat intolerance[40] or diminished intake of red meats[24] or less intake of heme iron and its absorption[26] are common concerns related to iron deficiency in the obese population[26].

3.3.2 Menstrual Bleeding:

Iron and related nutrients deficiencies are common in women of fertile age, adolescents and pregnant women[47]. Rates of anemia and iron deficiency are reported highest in menstruating women[22] and losses in menstruation also exacerbate the condition[22, 30, 40].

3.3.3 Systemic Inflammation:

Systemic inflammation is commonly encountered in morbid obesity disturbs iron homeostasis[31]. Inflammatory status is measured by hs- CRP[31].When hs- CRP as inflammatory marker and ferritin as iron index are considered, impaired iron status could be identified in approximately two thirds of BS candidates[31]. The vital role of ferritin is storing iron in the body, however elevated levels indicate inflammation[26].

Iron deficiency cannot be defined solely on the basis of serum ferritin levels because serum ferritin is a critical phase reactant which is generally high in obese population, assuming secondary to underlying prolonged inflammation[22, 30].

Ferritin <12ng/ml in females and <15ng/ml in males irrespective of hs-CRP level was classified as absolute –iron deficiency, whereas ferritin between these thresholds and 100ng/ml is categorized as Functional – iron deficiency if hs-CRP is >3mg/l. In a study conducted on inflammation and iron status in bariatric surgery candidates, prevalence of absolute and functional iron deficiency was found 8.7% and 52.5% respectively. In addition to this anemia was found in 11.2% of the cohort, 80% of which were associated with iron deficiency. Transparent saturation less than 20% along with ferritin less than 30 ng/ml are reported as practical cut offs to identify patients with functional iron deficiency and larger iron status impairment[31].

The inflammation condition is supported by increase in pro- inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-alpha), interleukin-1 beta (IL-1beta), interleukin-6 (IL-6) and from acute phase protein, such as C-reactive protein[30].

In low grade systemic inflammatory conditions, hepcidin is stimulated by inflammatory cytokines IL-6 and synthesized by hepatocytes and adipocytes[30].Increased hepcidin concentrations in obesity have been linked to low grade chronic inflammation and seems to contribute to reduced iron availability and mineral deficiencies in this condition[30]. Hepcidin plays a key role in the regulation of iron metabolism acting as a negative regulator of iron absorption in the intestine and stimulating iron retention in macro phages when higher systemic concentrations occur[30]. Iron metabolism is affected by hepcidin, a hormone that promotes the inhibition of intestinal iron absorption, iron recycling by macrophages and iron mobilization from the liver[30]. Studies reported that HS-CRP and hepicidin were high during pre op and decreased significantly at 12 and 6 months respectively[29] and decrease in low grade inflammation and hepcidin levels improved iron metabolism 6 months after RYGB[30].

3.4 Post operative Factors/Mechanisms

Numerous factors/mechanisms affect iron and related nutrients intake and absorption after RYGB.

3.4.1 Gastric Resection:

Gastric resection or reduced gastric capacity[24] restricts the intake of nutrients by reducing the volume of food intake[18] which may lead to nutritional complications like anemia. Dietary intake of iron from plant[18] as well as animal sources[18, 26] is related to the pathophysiology of iron deficiency. The non-heme iron is highly bioavailable and is mainly found in red meats. Its absorption mechanism is not completely clear, but heme carrier protein 1 (HCP-1) has been suggested as the iron transporter at the brush border. The non heme iron is widely distributed and is absorbed in its ferrous state[47].

3.4.2 Ulceration:

In the early stages of Gastric Bypass the stomal ulceration reported rate varied from 3% - 8%. Their development is reported mainly in patients who had large proximal gastric pouches (more than 50 ml). It has also been reported that by reducing the pouch size, acid secretion from the pouch decreases hence the rate of ulceration lowers down. With this reduction the rate of stomal ulcers reported still remains 2%. Stomal ulceration occurs due to reflux of acid from the distal bypass stomach into the proximal pouch and thus affects the acid sensitive jejuna mucosa of the roux limb. Very small proximal pouch structured from Gastric cardia leads to absence of acid secretion into the pouch. Altered acid secretion secondary to gastric bypass may lead to Vitamin B12 deficiency and devastating neurological complications in the long term. Vitamin B12 deficiency after gastric bypass is multifactorial such as:

1. Maldigestion of foods containing vitamin B12 (inadequate release of protein bound Vitamin B12 secondary to decreased acid/ pepsin production from the proximal pouch.
2. Decreased availability of intrinsic factor caused by either degradation of unprotected free intrinsic factor secreted into the bypassed distal stomach by luminal acid (IF-Vitamin B12 complex is acid/ pepsin stable), or poor mixing of IF from the distal stomach with the orally ingested Vitamin B12.
3. Inadequate mixing of Vitamin B12 with R-protein or the incomplete release of Vitamin B12 from the Vitamin B12 – R-protein complex.
4. Decreased formation of an IF – Vitamin B12 complex owing to decreased or absent secreted into the proximal gastric pouch.

Several studies have reported decrease in Ferritin levels or increase in its rate of deficiency during the post op periods[29, 36, 37, 38, 30, 32, 26, 39, 40, 47]. Only a few studies revealed improvement in ferritin levels after RYGB[34, 41].

3.4.3 Low Dietary Intake:

The most obvious effect of all Bariatric surgical procedures is an alteration in the dietary pattern[18]. Sequential changes in dietary intake following one year post RYGB including specific food groups and nutrients[44, 48], surgically induced alterations in meal size[30, 48] and food intolerances present after surgery are responsible factors for potential nutrient deficiencies[48]. Mercharita T et al 2014 reported a significant reduction in (p<0.05) iron intake at one year after RYGB. Less micronutrient intake (dietary and supplement) leads to micro nutrient deficiencies[29]. A significant reduction was observed in intake of calories and macro nutrients. Intake of carbohydrates and lipids differed from baseline, however, no significant difference was observed for protein intake. In addition to this a significant reduction was found in consumption of unhealthy foods six months post RYGB. Reduction in red meat[34] (a major natural source of iron) or beef intake[18]. The decrease in calorie intake is found to be associated with decreased intake of protein, iron and calcium, with a decline in hemoglobin hem autocrat and red blood count after surgery[44].Servings of vegetables and grains were lower at 12 months post RYGB, thus the intake of Vitamin C and folate[48].

Changes in food choices after RYGB are due to following factors[18]:

- Food intolerances[40]
- Prevention of dumping syndrome symptoms
- Optimization of weight reduction
- Alteration of neuroendocrine regulation
- Nutritional counseling and education about healthy choices.

3.4.4 Exclusion of Duodenum and Proximal Jejunum:

The duodenum and the proximal jejunum are excluded in RYGB Surgery and are the main sites of Iron absorption[18, 30, 34, 47].

3.4.5 Menstruation:

Absence of evaluation of menstrual blood loss contributes for the changes in the bio chemical markers such as ferritin and hemoglobin[18]. In some studies after surgery, the incidence of anemia substantially increased only in pre menopausal women from 16% to33%[44, 49, 50].

3.4.6 Intrinsic Factor Reduction:

Inappropriate secretion of intrinsic factor after RYGB leads to Vitamin B12 and Folic acid (38%) deficiency[26].

3.4.7 Changes in Iron Transporter DMT -1:

DMT 1 is a trans-membrane protein found on the apical membrane of the entrecote that, by the proton motive force, transports ferrous iron in to the cells.DMT 1 is mainly found in the duodenum and its expression decrease along with digestive tract. DMT 1 is responsible for absorption of non heme iron in its ferrous state[22, 47].In conditions of iron deficiency the duodenal mucosa is the mucosa that adapts the most and is capable of adapting by over expressing DMT 1 and in overload conditions by diminishing its expression[47]. The authors also reported increased DMT 1 expression in patients 6 months after RYGB, in the cytoplasm of entrecotes located in the apex of the villi of the proximal jejunum. It is a compensation mechanism as it is associated with a decrease of total quantity of the receptor in the mucosa mainly due to cellular changes experienced by the intestinal villi in RYGB patients.

3.4.8 Bleeding:

Anemia may result from bleeding due to the operation itself such as oozing from the staple or suture lines, gastritis, anastigmatic bleeding or due to mal absorption of compounds important for metabolism of hemoglobin such as iron, folate, vitamin B12 and vitamin C[34, 47].

3.4.9 Length of Roux Limb:

The longer the roux limb the higher the incidence of iron and related nutrients deficiency, because of the eventual increase in malabsorption[22, 47].

4. POST OPERATIVE SUPPLEMENTATION

In a prospective study conducted on RYGB patients who were followed until 12 months, association between total micronutrient intake and status markers were analyzed . All subjects were advised to take standard multivitamin supplement. At 12 months post RYGB levels of iron, vitamin B12 and vitamin C were higher than baseline except for zinc[29].

Study conducted at Mayo Clinic, USA assessed patient reported adherence to and efficacy of Vitamin/ Mineral supplement protocol and reported excellent (> 92%) patient adherence to a standardized multivitamin/ mineral and vitamin B12 regimen. Prevalence of Vitamin D deficiency continued on the other hand anemia and iron deficiency were observed at lower rates than previously reported[36].

Another study compared two supplementation regimes (Group 1: One RDA pre and 2 RDA after vs Group 2: one RDA after) on RYGB patients uptil six months. Group 1 resulted in reduction in iron deficiency but not for Group 2.Incidence of anemia was found same in both groups at 6 months (9%). Both groups had significant reductions in hs-CRP and ferritin levels. The study concluded that group 1 supplementation scheme was more efficient in controlling iron metabolism[30]. Findings of a cohort study of a triple – blind randomized controlled clinical trial concluded that three years post RYGB an optimized multivitamin supplement (WLS forte) was more effective in reducing anemia and ferritin, vitamin B12 and zinc deficiencies compared with a standard multivitamin supplement and control[37].

In a retrospective study use of multivitamin and B12 supplements was reported by 1% - 9% of patients before surgery, 79% - 84% of patients at one year and 52% - 83% of patients 5 years after

RYGB. At 5 years mean concentrations of folic acid, vitamin B12 and vitamin C were significantly higher as compared to before surgery[42].

In a retrospective study conducted over RYGB patients who completed atleast 1 year follow up, effect of daily supplements as suggested by the AACE/TOS/ASMBS Guidelines were assessed over iron profile, folic acid and vitamin B12 and frequency of anemia 1 year after RYGB was found low[46].

In another 2 year follow up study, effects of daily supplement of a multivitamin, a vitamin B12 injection (1 mg) every third month and oral or intravenous iron (only in subjects with low ferritin and Hb) were assessed. The study concluded decrease in Hb and ferritin levels at 24 months in both genders whereas concentrations of folic acid and vitamin B12 increased[38].

In a retrospective analysis of RYGB patients 48 months post surgery decrease in serum ferritin levels was reported in both genders, on the other hand improved serum iron was found only in males. In spite of using multivitamins and minerals supplements, vitamin B12 levels dropped at 48 months post-surgery in females, whereas at the same stage folic acid levels scaled[26].

In a mono-centric retrospective study conducted upon RYGB patients, assessed impact of oral iron challenge test with 100 mg $FeSO_4.7H_2O$ in iron deficient patients (n = 23). Out of 23 only one patient showed sufficient iron absorption[39].

In a post RYGB study outcomes of IV iron therapy using standardized 2 giron dextran infusion wereestimated. The study declared that intravenous therapy with 2 g of iron dextran rectifies anemia and restores iron for >= 1 year in maximum patients[33]. Another study evaluated impact of IV iron therapy after oral iron failure andfound increased Hb and ferritin levels[41].

170 RYGB patients were retrospectively assessed for nutritional profile before and after RYGB upto 3 years. Out of all subjects only 6% had used standard vitamin and mineral supplements pre operatively, whereas 77.1% and 72.4% at 24 and 36 months respectively. Vitamin B_{12} level showed no significant difference whereas folic acid levels increased significantly at the end of the study[43].

Iron substitution did not prevent anemia after RYGB, which especially affected premenopausal women[38].

After 5 years of RYGB 52-83% of patients were complaint to multivitamin supplementation and estimated mean concentrations of vitamin B_6, folic acid and vitamin B 12 and vitamin C were significantly higher[42].

Post operative oral supplementation of anaemia was only successful in 62.5% of the patients in contrast to oral treatment for Vitamin B_{12} deficiency which was more than 80% of the patients[9].

Daily supplements as suggested by the AACE/TOS/ASMBS guidelines were routinely prescribed. Blood count, iron profile, folic acid and B12 measurements 1 year after surgery were reviewed and only 4% of patients were found with anaemia[46].

Clinical recommendations include prophylactic iron supplementation with ferrous-sulphate to prevent iron deficiency anemia. Ferrous sulfate is a well-established cause of constipation possibly resulting in low patient tolerability and subsequent low adherence rates. Patients treated with IV iron (400-1400mg), experienced increase in Hb and ferritin[26].

5. CONCLUSION

Iron and related nutrient deficiencies are extremely common after RYGB and is linked with multiple risk factors or mechanisms. Pre operative deficiencies must be treated on time, aimed at preventing prolong post op deficiencies. Pre operative oral supplementation is rewarding but in post operative the effect of oral supplementation may be limited as absorption of oral iron supplements is insufficient post RYGB. Intra venous iron therapy is much beneficial in dealing with iron deficiencies.

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