Research

Challenges Associated with Managing Pregnancy Following Bariatric Surgery-A Comprehensive Review

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Abstract

The incidence of obesity has reached epidemic proportions. Parallel with that the incidence of the most efficacious and sustainable therapy i.e bariatric surgery (BS) has increased considerably. Over 50% of women who undergo this BS (Including RYGB, LAGB, BPD) are in reproductive age group and hence will encounter the challenges that pregnancy poses in such patients. Here we carried out a systematic review up to 2018 using pubmed search index to analyze the complications one encounters both from maternal and neonatal perspective. Biggest problem till date has been the challenge of diagnosing gestational diabetes mellitus (GDM), as there are complications like dumping syndrome imposed by adding 75gm glucose and falsely high 1h reading and 2nd hr reading coming Very low because of absorption profile alterations. Besides no guidelines exist regarding adequate weight gain in pregnancy following BS, as laid down for different BMI groups without this surgery. Micronutrient deficiency needs to be addressed ensuring adequate supplementation of various vitamins, micronutrients and preventing conditions like precipitation of Wernicke encephalopathy, coagulation disorders. Children born to these mothers were not found to be at higher risk of obesity long-term.

Key Words: Pregnancy; BS; Roux-enY-Gastric Bypass (RYGB); Laparoscopic Adjustable Gastric Banding (LAGB); Biliary Pancreatic Diversion (BPD); GDM; OGTT

Introduction

In our earlier articles we have tried to review various aetiopathogenetic factors, nutrition factors affecting obesity and done an update of various medical therapies, including treatment with thylakoids. Further we elaborated on how Bariatric surgery (BS) is one of the most effective treatments [1-13]. Bariatric surgery (BS has become a common method for treating obesity with an increase in incidence by 800% between1998-2005 [14]. Of these 80% are done in women of whom 50% are of reproductive age group. The report of British registry claimed that 53%of surgeries were in between age18-45 years, of which half of the women had menstrual irregularities [15]. A very dedicated control is required by a team of specialists in women that conceive following BS [16]. Lot of supplements is needed to prevent any nutrient, vitamin deficiencies. As per a survey done recently obstetricians lacked knowledge as per the nutritional recommendations for these women. USA generated data showed that there has been poor screening for any deficiency in almost 50% of women, with much greater rates in pregnancy [17]. In 2013 some guidelines were given regarding these nutritional needs by a combination of American Association of clinical endocrinologists, the Obesity Society and American Society for Metabolic Surgery [18], and an update was described recently by Busetto et al [19]. Thus need has been there regarding an update on managing these women and hence we carried out a review on the effective way of managing pregnancy-an upcoming field and scanty knowledge exists.

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Methods
We did a pubmed search with following MeSH terms, pregnancy, bariatric surgery, neonatal, fetal complications, nutritional recommendations, surgical and medical complications up to 2018.

Results
We found a total of 585 articles on this subject of which selected 100 articles for this review after ruling out duplicate articles. No meta-analysis was carried out.

Fertility in Obese Women
As compared to lean women obese women are less likely to conceive [20]. Reduction in fertility is based mainly on menstrual irregularities/an ovulation. A cross-sectional study reported that 30-47% of overweight/obese women, who present with menstrual abnormalities, have a positive correlation with BMI [21]. In 50% of women sexual life is compromised in severely obese women and men [22]. Also there were longer menstrual cycles [23], which might be secondary to increased circulating Androgens, like testosterone (T), and dehydroepiandrosterone sulphate (DHEAS), which are raised because of increased sex hormone binding globulin (SHBG) production. Hepatic SHBG production is not affected by hyperinsulinemia, that has high correlation with obesity [23,24]. Also hyperinsulinemia stimulates LH mediated androgen production from ovarian theca cells [25]. Thus interaction of these factors causes an imbalance resulting in infertility. Following BS there is a steep rise in SHBG together reduction in T, androstenedione, and DHEAS levels in obese women that might help in normalizing menstrual function along with infertility [26]. There is improvement of quality of sexual life significantly in both genders, along with a satisfaction with the body image [27].

BS and Fertility
Significant reduction in prevalence of type2 diabetes mellitus (T2DM), polycystic ovarian syndrome (PCOS) and menstrual irregularities got seen following BS. Effects of BS usually reported in small number of subjects. Thus larger studies required are to study the effects of BS on fertility along with hormonal values. In some reviews [14,28] a positive effects on weight loss via BS was seen along with hormonal changes. Marked reduction in estradiol (E2), T along with increase in serum follicle stimulating hormone (S.FSH), luteinizing hormone (LH) and SHBG resulted. Also a reduction in thyroid stimulating hormone (TSH) levels were seen, without any changes in T4,Along with increases in serum cortisol and reduction in cortisol binding protein [28]. Normalization of menstrual cycles, regular ovulation and spontaneous conception was published [14,28]. A systematic review that studied gonadal dysfunction in obese subjects along with resolution of this gonadal dysfunction after BS showed that 36%(95%CI22-50) of females had PCOS. PCOS got resolved in 96% (CI 89-100) of women following surgical intervention accompanied by decrease in signs of hyperandrogenism along with reversion of menstrual changes [29].

Pregnancy Planning
Advice regarding postponing conception following BS is essential due to the complications associated with BS post surgery along with nutritional and vitamin deficiencies. Despite correction of an ovulation and chances of conception spontaneously increasing following BS there is need for use of contraception to postpone pregnancy because stabilization of weight changes take time and the effect of various deficiencies occurring in ensuing fetus have not been well studied. As per some publications at least 12-16,18 month or as much as 24mths post BS wait is advised [18-20,30-32]. Comparable rates of gestational DM, pregnancy induced hypertension (PIH), intratere growth retardation (IUGR) or small for gestation age (SGA) offspring [33]. Still optimal time period is not clear. There is very little evidence of conception after 12 months time lapse period. Almost similar results have been seen in some studies. After fasting in pregnancies ketonuria, increased urinary nitrogen excretion along with reduced gluconeogenic acid production were shown and due to physiological insulin resistance (IR) in pregnancy, there is greater incidence of ketonemia and ketonuria is seen [34]. Weight loss immediately following BS markedly effect fetal development in terms of growth, biometry and malformation or future development of the offspring with the aspect of health and disease in terms of neurocognitive, cardiovascular and metabolic parameters that have not been investigated thus far. Once pregnancy ensues in time of maximum weight loss, regular examination of mother and offspring are needed, examining endocrinological and metabolic parameters, documenting general health curve, weight curve, blood parameters, nutritional behavior, intake, and advice regarding mineral, trace element supplementation. Planning further pregnancy and health modalities. Delivery has to be planned in a tertiary centre having an intensive neonatal unit. Importance of nutritional supplements essential in case there is emergency pregnancy, with importance of compliance. Pregnancy planning implies undertaking pregnancy till maximum weight loss along with optimization of nutrients has been completed prior to conception in all women that had BS.

Contraception
A study showed that 4% females tried to conceive in 1st post surgical year, while other 41% had unprotected coitus during this period [35]. Thus comes the importance of post surgical contraception with time lapse between surgery and conception. However oral contraception may not provide sufficient protection post BS, mainly in gastric bypass procedures. Malabsorption along with complications like vomits,
Pregnancy Follow Up

Every short interval examination needs to be done. Higher risks of persistent vomiting, GIT bleeding, anaemia, placental vascular disease, fetal neural tube defects, IUGR or miscarriage might occur [31]. For Post laparoscopic adjustable gastric binding (LAGB), it is essential that immediate follow up start right from 1st trimester, for prevention of complications like vomiting [33,37]. Need for this active gastric band treatment in very experienced hands is there. Trained dieticians having knowhow of bariatric surgery is required for advising diet to these pregnant women [19,32]. There is a recommendation that appointments be given even before pregnancy and every trimester if not more frequently possible. These examinations should be done in specialized centers where facilities for checking nutritional status [18,19,32] along with developmental deficiencies can be picked up and managed at an early stage [19]. Blood sampling at least every trimester for complete blood count, clinical chemistry, coagulation profile, vitamins A,D,E,K,B12,iron status, folic acid, parathyroid hormone along with protein albumin,A1c,glucose and FSH are important concepts further in follow-up [19,38]. As far as mode of delivery is considered BS is not a contraindication for normal delivery. Yet higher incidence of LSCS is reported in operated women while 14-29% in controls [39]. Main reason is previous LSCS as an indication, besides other problems associated with obesity, choice of patient, fetal position and ideation of the treating doctor [39].

Gestational Diabetes Diagnosis

That there is increased risk of Gestational diabetes mellitus (GDM) has been reported following BS in many studies [40-42]. But obese women themselves have an incidence or risk of developing GDM throughout pregnancy in 40%,along with features of metabolic syndrome (MeTS) that might add to pregnancy complications [43,44]. Method of diagnosing GDM is variable. Based on type of BS i.e in Roux-en Y-Gastric bypass (RYGB), fasting glucose absorption occurs during an Oral glucose tolerance test (OGTT) may cause severe post absorptive hypoglycemia [20]. There is difficulty in interpreting results of OGTT as plasma glucose concentrations following a glucose load are changed following a gastric bypass and there is rapidly changing glucose levels besides the high chance of reactive hypoglycemic episodes after a glucose load [45-48]. Thus there is misinterpretation of GTT as 1hour sugar appears very high and 2hours very low therefore there is need for finding other ways of diagnosing GDM following BS. Also there might be side effects like dumping syndrome following OGTT in patients having had RYGB, Omega loop or sleeve gastrectomy [47]. So no recommendations are there for diagnosing GDM between 24-28gestation weeks. Thus in an alternative given by ACOG it is advised to check home glucose tests as an alternative [32] for a number of days like say a week. Other alternative is measuring capillary glucose from 14-16 weeks and continue it throughout pregnancy [47]. There are other tests like concomitant glucose monitoring (CGM) or flash glucose monitoring (FGM) systems that are being developed which are more implementable. These devices might be of more use in settings of hypoglycemia at regular intervals and may be of help in achieving glycaemic control. FGM proved to be safe as well as accurate in pregnant ladies having diabetes [49]. Recently in a case report successful use of FGM was reported in pregnancy following RYGB and complicated with GDM and nocturia [50]. Still more studies are needed for checking the reliability of FGM in Pregnancy post BS. Diagnostic criteria suggested following metabolic surgery using capillary blood glucose for GDM are fasting >=95mg/dl, while for overt diabetes >=126mg/dl and HbA1C >=6.5% and postprandial (PP) 2hrs >=120mg/dl for GDM in early pregnancy <20weeks [40]. In pregnancy it is postprandial glucose levels that are important for diagnosis of GDM since they are related to fetal hyperinsulinemia, fetal growth, birth weight and abdominal circumference. As there are changes in absorption of glucose following BS risk for dumping increases in many cases. In pregnancy following RYGB post prandial hypoglycaemia occurred in around 55%, going up to 90%in pregnant women getting a 75gm OGTT between 24-28 weeks gestation [45,48]. Greater occurrence of SGA fetus association with postprandial glucose nadir with fetal growth was published [45,48]. Hence use of increased glucose values but for diagnosis and starting insulin therapy is not recommended, with fasting and 2hr postprandial glucose check appear to be better and safer for diagnostic decision making. Similarly for diagnosis of overt T2DM prior to 20weeks diagnosis should be based on fasting and HbA1c values. Once dumping syndrome is there one need to carry more postprandial measures beyond the 2h measurement. In pregnancy, be it GDM/overt DM one needs to develop more severe controls and individualization of diabetic treatment. Perinatal outcomes are similar in GDM with bariatric surgery or without [20]. Managing dumping syndrome/other complications like flatulence, diarrhea, constipation, dehydration, reviewed in [52,53]. Briefly in early dumping proportion of food per portion requires be decreased and breaking up in six meals a day [52]. Liquid intake delay by at least 30’ following the meal is advocated. Dumping management occurring late includes avoiding foods that are readily absorbable and refined carbohydrates [52]. As per a case report the good effects of acarbose in pregnant ladies following RYGB surgery with severe pro-
gressive hypoglycemic events were not successful like other interventions [52]. There was marked decrease in postprandial hypoglycaemia and a healthy baby at term having normal development was the outcome.

**Weight Gain in Pregnancy**

This should follow the institute of medicine (IOM) recommendations i.e for underweight <18.5kg – recommended weight gain 13-18kg throughout pregnancy, with .5kg gain per week in 2nd and 3rd trimester. For normal weight 18.5-24.9 recommended weight gain 11-16kg throughout pregnancy, with .5kg gain per week in 2nd and 3rd trimester, for overweight 25-29.9kg is the recommended weight gain 7-11kg throughout pregnancy, with .3kg gain per wk in 2nd and 3rd trimester and for obesity >=30kg/m² recommended weight gain 5-9kg throughout pregnancy, with .2kg Gain per week in 2nd and 3rd trimester as no other evidences for weight gain in pregnancy following BS exist [32,54]. Till now data has shown lower weight gain in such pregnancies as compared to no operated controls [33]. In a small study done recently following RYGB surgery, mean gestational weight gain of 3.8±12kg were found with no significant difference seen compared to those who became pregnant immediately or following surgery within 1st year [55]. If weight gain doesn't match the IOM criteria more intense control measures need to be done as per individualized approach. If there is time lapse between surgery and pregnancy occurrence there may be affect on gestational weight gain and postpartum loss [20]. Recently in a systematic review it was revealed that weight gain below or above the IOM recommendations for the particular weight class correlated with bad perinatal outcomes [56]. Greater risk of SGA and preterm birth were shown in weight gain below these IOM recommendations.

**Pregnancy Outcome**

Generally greater incidence of GDM, PIH, abortion, LSCS rate and still birth have been reported in pregnancy in obese women. Once pregnancy follows Post BS, maternal complications were shown to be reduced by approximately 10% risks of normal weight women and improved neonatal outcomes as compared with obese ladies without any intervention [14,18,20,31,57]. Lower incidence of GDM, hypertension, preeclampsia along with abortions were seen in pregnancies after BS as compared to no operated obese ladies [30,33,39,57]. Lower incidence of preterm birth was seen, although there has been conflicting data with some studies showing LGA or SGA infants [20,33,39]. Though no difference in prematurity rate and perinatal deaths have been shown in most studies [33]. In a Swedish study based on 627,693 singleton pregnancies in Swedish medical birth register from 2006-11, of these 670 pregnancies occurred in women who had undergone BS.5 control pregnancies were matched for the mothers presurgery BMI, with early pregnancy BMI's in the controls went by the above results and showed a lower risk of GDM (OR 1.9% vs 6.8%; odds ratio 0.25,95%CI-0.13-0.47;p<0.001), LGA infants (8.6% vs 22.4%,95%CI,0.24-0.44;p<0.001). Rather there were higher incidence of SGA infants (15.6% vs 7.6%, odds ratio, 2.20,95%CI,1.64-2.95;p<0.001) and shorter gestation (273 vs 277.5 days; mean difference -4.5 days ;95%CI-2.9 to 6.0;p<0.05 although risk of preterm birth was not significantly different (10.0% vs 7.5%, odds ratio,1.95 CI 0.92-1.78;P=0.15). Still birth or neonatal death was 1.7% vs 0.7% (odds ratio 2.39;95%CI 0.98-5.85;P=0.06). No group difference was found in congenital malformations. Thus Johansson et al concluded that BS was associated with decreased risk of GDM and excessive fetal growth, shorter gestation, an increased risk for SGA infants and possibly increased mortality. However for diagnosing GDM, capillary blood glucose 4-6times during pregnancy and plasma glucose levels 8.0mmol/L (144mg/dl) or higher or women who belonged to a risk group like (e.g., women with obesity, previous gestational diabetes or macrosomia, or a family history of diabetes) undergo an oral glucose-tolerance test conducted with a loading dose of 75 g. The diagnosis of gestational diabetes is generally made (and was made in this study) on the basis of a 2-hour plasma glucose level of 10.0 mmol per liter (180 mg per deciliter) or higher during such a glucose-tolerance test (range among Swedish counties, 8.9 to 12.2 mmol per liter [160 to 220 mg per deciliter]) or a fasting plasma glucose level of 7.0 mmol per liter (126 mg per deciliter) or higher. If oral glucose-tolerance testing is deemed unsafe (e.g., owing to the risk of the dumping syndrome [i.e., rapid gastric emptying]), fasting glucose levels and preprandial and postprandial glucose values are assessed instead [40]. In a retrospective study carried out by Weintraub et al in Israel, perinatal outcomes of women delivering following BS in a tertiary medical centre from 1988-2006,301 deliveries preceded BS and 507 followed it. A marked decrease in incidence of DM (17.3% Vs11.0;P=0.009), hypertensive disorders (23.6%vs 11.2%;p<0.001) and fetal macrosomia (7.6%vs 3.2%;p=0.004)were noted in BS. BS was found to be independently associated with a decrease in DM (OR 0.42,95%CI0.26-0.67;P<0.001), hypertensive disorders (OR 0.38,95%CI0.59;P<0.001) and fetal macrosomia (OR0.45,95%- CI0.21-0.94;P=0.033), thus concluding that maternal complications like DM, hypertensive disorders of pregnancy (HDP), along with reduction in fetal macrosomia was achieved following BS [58]. Ducarme et al found a significantly lower mean weight gain during pregnancy in the LABG group than controls (5.5kgvd7.1kg; p<0.05). Pre eclampsia, GDM, low birth, weight and fetal macrosomia was less in the LABG group (p<0.05) and incidence of LSCS deliveries during labor were half in LABG group (15.5%vs 34.4%; p<0.01), with no difference in the neonatal outcomes in the 2 groups [59du]. The same group analyzed pregnancy outcomes following a sleeve gastrectomy in a retrospective study done from 2001-11 in a centre in France. 63 pregnancies occurring in 54 patients were included, of which 52 (89.9%) occurred in 1st post operative year and 26(41%) in women who remained obese. As compared to women that were no longer obese at conception, those who were still obese delivered neonates of significantly lower gestation...
age at birth (p=0.02) and birth weight (p=0.001). Odds of preterm delivery was also increased (Odds ratio 4.37,95%CI 1.17-16.27, P=0.03). There was no significant differences in maternal and neonatal outcomes as per the interval between LSG. Thus women remaining obese following LSG have increased risk of adverse outcomes [60]. They did not give any diagnostic criteria for GDM diagnosis. Burke et al in an American study, studied babies before and following BS, found lower chance of GDM (OR 0.23,95% CI 0.15-0.36) and lower chance of LCS (OR 0.53,95% CI 0.39-0.72). They used ICD code-9 to define GM [30]. In a very recent meta-analysis done by Kwong et al to 20 cohort studies, those included 2.8 million subjects, who had BS. Decreased rates of GDM (OR 0.2,95%CI 0.11-0.37; number needed to benefit 5), LGA infants (OR 0.31,95%CI 0.17-0.59; number needed to benefit 6), Gestational hypertension (OR 0.38,95%CI 0.19-0.76; number needed to benefit 11), hypertensive disorders (OR 0.38,95% CI 0.27-0.53; number needed to benefit 8), postpartum haemorrhage (OR 0.32,95%CI 0.08-1.37; number needed to benefit 21), and lower segment caesarian section (LSCS) rates (OR 0.50,95%CI 0.38-0.67; number needed to benefit 9), though groups of patients showed SGA infants (OR 2.16,95%CI 1.3-4.3; number needed to harm 21), IUGR analysis (OR 2.16,95%CI 1.34-3.48; number needed to harm 66), and preterm deliveries (OR 1.55,95%CI 1.02-1.79; number needed to harm 35), when compared with controls, subjects matched for pre pregnancy BMI-no difference was seen in preeclampsia, neonatal intensive care unit admissions , stillbirths , malformations and neonatal deaths [61].

Even in this Meta-analysis no diagnostic criteria for diagnosing GDM was given. Although no congenital malformations were seen in this study, some very old case reports from late 1980’s had published neural tube defects (NTDs) following gastric bypass surgery [62,63]. Thus some research regarding the occurrence of these NTDs needs to be done.

In long-term outcomes in women having biliopancreatic diversion (BPD) showed that overweight and obesity risk up to 18 years after birth and no increase in underweight, improved insulin sensitivity, lipid metabolism and ghrelin levels, lower inflammatory parameters and less hypertension as compared to offspring from nonoperated women [64,65]. Still age difference between the 2 groups i.e. 10 yrs 16 years needs to be considered a relevant confounder [64]. Weight was comparable at ages 1 and 6 years, though at 12 years, a greater percentage of those born before BPD were considered overweight (42% vs 33%) and obese (22% vs 3%; p<0.009) as compared to their counterparts born after BPD, with only 21-25 yrs subjects considered in study group, with body weight and BMI in subjects born before BPD was greater (p<0.02 and p<0.12 respectively, than in those born after BPD (79.5 KG V+16.5 KG vs 66.7 +11.8 kg and 27.5 +3.9 kg/m2 vs 23.4 +3.7 kg/m2 respectively [barisone m]). Though other studies do not show any differences at age of 10 yrs or preschool age [66,67]. In study by Guenard et al it was found that a total of 5698 genes were differentially methylated between BS and siblings born after maternal gastric bypass surgery (AMS), who exhibited a preponderance of glucoregulatory, inflammatory and vascular disease genes. There was a statistically significant correlation between gene methylation and gene expression and plasma markers of improvement of insulin resistance that were consistent with metabolic improvements in AMS offspring’s, that reflected the genes involved in DM related cardiac metabolic pathway, showing treatment of a maternal phenotype is durably detected In methylome and transcriptome of subsequent offspring [68]. However in a case control retrospective Danish study where micronutrient deficiencies was investigated following 151 post RYGB pregnant women followed up for 3 years. Risk of SGA birth (OR=2.67,95% CI 0.4-6.82) and maternal anemia (OR=3.0,95% CI 0.9-8.25) were significantly increased for RYGB group as compared to non RYGB group. No difference was found in gestational weight gain (p=0.169) between history of RYGB (11.51 KG +8.97 SD) and non RYGB operated women (12.18 +6.28 SD). Thus following RYGB there is increase in risk of SGA birth and anemia, with no difference in gestational weight gain. Micronutrient deficiency seems to be the etiology of decreased gestational wt gain than reduced gestational weight gain in post RYGB surgery, Hammamaken et al found greater rates of reduced cord blood levels below the 2.5 percentile for calcium, zinc, iron and vit A and B12 in RYGB offspring [69]. Once offspring’s of RYGB with a mean age of 46 months of women who had gastric bypass surgery, inadequate fiber intake was seen in all children who had deficiencies of Vitamin A and folic acid [70].

**Surgical Complications**

Intestinal obstruction, or hernia, gastric ulcer, band or staple line complications have been published [33] that need immediate action for minimizing both maternal and fetal risks. In a national cohort study where data from Swedish medical birth registry and Swedish national patient registry was merged to obtain the incidence of abdominal surgery during pregnancy after BS. Stuart & Kalle 2017 found that during first pregnancy after BS, rate of surgery for intestinal obstruction was 1.5% (3/2,543; 95%CI 1.1-2.0%) in women in a case group as compared with 0.02% (4/21,909; 95%CI 0.0-0.04%) among women in the control group (adjusted OR 34.3; 95%CI 11.9-98.7). Rate of diagnostic laparoscopy or laparotomy was 1.5% (37/542, 95% CI 1.0-1.9%) in women in a case group as compared with 0.1% (18/21,909; 95% CI 0.0-0.1%) among women in the control group (adjusted OR 11.3; 95% CI 6.9-8.5), concluding increased risk of abdominal surgery during pregnancy exists post BS [71]. Also small intestinal obstruction or inner hernia was described in a case series [72]. Kushner reported that in a case of persistent vomiting, i/v supplementation of vitamins and trace elements needed to be considered, as especially after RYGB and BPD-DS are at high risk in pregnancy, which might get aggravated by hyper emesis gravidarum in pregnancy [73]. Thiamine deficiency
symptoms are Wernicke's encephalopathy, oculomotor dysfunction, and gait ataxia. Once Wernicke's encephalopathy is suspected giving IV solutions containing glucose might further deplete thiamine that is available, precipitating Korsakoff syndrome [73]. Intravenous thiamine infusion 100mg that is followed by consecutive i/m injection (100mgx5days) and then oral maintenance of 50-100mg need to be given [73]. Lakhani et al recommended giving antibiotics in the form of amoxicillin for 7-10days/month over 2 months as they hypothesized that small intestinal bacterial overgrowth occurs because of alteration in GIT micro biome following BS which may be the cause of thiamine deficiency [74]. Once nutrient intake has been inadequate for a longtime, it should be gradually reintroduced, preferably after admission with close monitoring of electrolytes which include potassium, and phosphorus, in view of a potentially life threatening feeding syndrome might occur. In case of a gastric band, there is need for assessing the band position early in pregnancy by a bariatric surgeon. Reports of earlier studies showed band migration =>consequent complications like vomiting, disturbances in fluid and electrolyte disturbances along with band leakage occurred in nearly 29% of cases [40]. In a systematic review a report of 5 neonatal deaths with 3 maternal deaths, with requirement of urgent surgery because of inner hernia occurring following RYGB surgery was reported [14]. In another study by Gudbrand et al., 23 women post BS, who were collected from a Danish National register needed urgent surgery secondary to internal hernia although no death was reported in this study [65]. Laparoscopic surgery was done as late as 31st gestational week, concluding a good prognosis and that surgery can be done sub acutely or electively depending on patient's condition and that of fetus, and clinical assessment is straightforward, not needing a CT Scan [75]. Petruccianni Net al reported a case report where acute bowel ischemia that followed thromboses of superior mesentry artery in pregnancy following RYGB surgery caused loss of the fetus and needed various laparotomies and subtotal enterectomy though 1st 20cm of jejunum got preserved [76].

**Protein Supplementation**

Though for routine pregnancy criteria laid by German-Austrian – Swiss (DACH) nutritional recommendations i.e 0.9gm protein/kg body weight in 2nd trimester and 1.0g/Kg in the 3rd [78]. Calculations done based on normal wt, including overweight/obese. In lactation 1.2g/kg recommended [78]. For BS individualization needed as per the surgery done till any specific recommendations are given.

**Micronutrients Supplementation**

i) **Iron**-Since ther 1 gm is expansion of blood volume, increase in Fe demand occurs from 15 to 30mg/d. By WHO definition anemia is defined as Hb<11.0gm/l. Regular iron level checkups needed along with Hb, that decides the intensity of iron supplementation. Supplementation needs to be done orally. i/v iron is not recommended in 1st trimester [79]. Since oral calcium and iron interact the 2 should not be given together. In RYGB, greater than 4yrs time of conception significantly lower Hb 9.6gm vs 11.1g/dl; p=0.047, with higher requirement of i/v iron supplementation or PCV transfusion identified (30.8%vs0%p=0.026) as compared to women with less than 4yrs time to conception[80]. Other than anemia no problems seen in mother or child [38].

**Calcium**

Calcium homeostasis is markedly influenced by BS as well as pregnancy. For absorption of calcium to occur an acidic surrounding is needed for its absorption and demands both in pregnancy and lactation are increased, that is critical for bone density and dental state [81]. Mainly in last trimester a significant shift occurs from mother to fetus, for increasing fetal mineralization. Thus mainly from bone to main reservoir of calcium it gets mobilized and renal calcium retention that increases risk of osteoporosis [81]. Doses recommended are higher in pregnancy following BS. In 1st st to 3rd and 2nd trimester 15.2% deficiency was reported and 20% in 3rd trimester in pregnant women following RYGB [82]. PTH excursions were found in 19.6%, 30.4% and 32.6% from 1st st to 2nd and 3rd trimester.

Magnesium-5-30% pregnant women develop nocturnal calf cramps. There is a association with lower Mg levels. Oral Mg might also help in preventing uterine contractions [83,84]. High doses of Mg might cause osmotic diarrhea.

**Zinc**

Low levels of zinc seen in pregnant women without BS have been associated with early child birth, low birth weight and spina bifida. Ec-
zema, dermatitis and failure to thrive have been shown in offspring’s [85] during lactation. For preventing further copper deficiency ensure at least 1 mg of Cu is given per each 8-15mg zinc substitution. Inadequate Zn was reported in 20% pregnant women following RYGB surgery though no association was found with birth weight/neonatal anthropometry [86].

**Iodine**

Deficiency is commonly encountered in Middle Europe and deficiency has been shown in normal pregnancies [87]. 13.8% of the women who participated had normal recommended range of 150-249µg/l iodine urinary concentrations deficiency despite availability of iodine table salt commercially. Upper iodine urinary concentrations should not exceed the 250 µg/l due to significant association of subclinical hypothyroidism, while WHO recommendations are Upper l iodine urinary concentrations not exceed 500 µg/l in pregnant women [88]. After BS limited resorption occurs in women planning to become pregnant /in pregnant women it might be associated with lower urinary concentrations. Mainly after malabsorptive intervention limited evidence is there especially considering that resorption of iodine occurs in stomach and small intestine. In no pregnant women following malabsorptive events increased urinary iodine concentrations was found 3-18mths after BS [89,90]. No I2 deficiency was seen 10 years after gastric bypass or vertical banded gastroplasty [91]. Till now no adverse fetal or maternal outcome has been seen following Fe, Ca, Zn, Mg, iodine deficiency after BS [38].

**Vitamins**

**Vitamin A**

Cruz et al studied nutritional status of Vitamin A per trimester of pregnancy influence on prpregnancy BMI, total gestational weight gain (TWAG) and presence of anemia in women who had previously undergone RYGB. They conducted an analytical retrospective study in 30pregnant women. In all trimesters of pregnancy serum concentrations of retinol, β-carotene, stages of vitamin A deficiency (VAD), night blindness (NB),anemia and anthropometric variables were assessed .VAD in pregnancy affected 90%of women,86.7%deeloped NB and 82.8%had mild VAD,TWAG above/below the recommend ed range was related to the low serum concentration of β-carotene (p=0.045)in the 2nd trimester and women with TWAG above the recommended range showed 100%of inadequacy of this nutrient in the 3rd trimester. Among pregnant women with anemia 90.9%had VAD and 86.4% had NB. Thus concluding that this study highlights improving Vit A nutritional status in prenatal care, because of relationship with TWAG and high percentage of VAD and NB found since the beginning of pregnancy. It also reaffirmed the use of cutoff value of<1.05µmol/L Rather than 0.7 µmol/L for determining VAD [92]. An upper limit of 5000IU (1600µg retinol equivalent is given by American literature for preventing congenital malformations [32,85,93]. Similarly European Food Safety Agency (EFSA) quoted that most recent recommendation is tolerable upper limit of 3000µg/d retinol equivalent [94]. β- carotene form of vit A is the recommended form over retinol [53]. 2 Brazilian studies agreed with these findings following RYGB [86,95]. Marked association of VAD with UTI and dumping syndrome was found. In a case of severe maternal VAD deficiency following BPD, premature birth and ocular and renal malformations were noted [96].

**Vitamin B12**

Levels need regular checking. Deficiency of this vitamin has been shown in 50%of pregnant women following BS [97,98]. It can be given parenterally or orally if available in that form. Neonatal deficiency of this vitamin might =>irreversible deficits and hence needs to be detected early [38,99].

**Vitamin D**

In normallyealthy adults 800IU is the recommended amount as per DACH criteria [78]. Basic aim is to achieve a target level of 25(OH) D serum levels of above 50nmol/l. Endocrine society recommends maximal dose of 4000iu/day in pregnancy or while planning for the same [100]. In post BS populations up to 6000 IU/d have been recommend ed as for no pregnant women [19]. In a study where vitamin D status along with its relation with ionic calcium and Parathyroid hormone in pregnant women and RYGB was done, it was found that vitamin D deficiency (20µg/ml) or insufficiency (20-30µg/ml) was found in above 70% patients in all trimesters [100]. Also there is a negative correlation between calcium and PTH along with association of vitamin D with higher risk of urinary tract infection (UTI).

**Vitamin E**

Elimination of free radicals is associated with vit E deficiency. DACH recommends daily intake of 13mg tocopherol equivalent (=19.4IU) [38], and EFSA recommendations suggest a daily intake of 11mg for women having no additional needs in pregnant/lactating women and a 300mg/d (=447IU) upper tolerable intake levels [101].

**Vitamin K**

A daily intake of vitamin K is 60µg as per DACH Recommendations. In view of lack of evidence the EFSA could not define a tolerable upper limit level of vitamin K [102]. A daily intake of 70µg of phylloquinone is recommended [102]. Following BS vitamin K shows decreased absorption and thus reduced transfer across placenta. Hence it might be important to monitor its levels. One can either directly measure...
vitamin K levels or indirectly by prothrombin time. Deficiencies reaching practically 90% in 1st trimester have been shown following BS with practically 50% up to birth. In one study no complications got reported [103]. Though 5 cases of intra cranial bleeding associated with vitamin K deficiency and malformations were described [104]. Following BPD, a case of vitamin K deficiency associated with maternal coagulopathy with vaginal haemorrhage and fetal hypercoagulability was shown [105]. Chronic complications like oculomotor and mental retardation from bleeding including neonatal death have been described [38].

Folic Acid

Folate (vitamin B9) has important roles in DNA and RNA synthesis and single carbon transfer reactions. Deficiency can cause megaloblastic anemia, thrombocytopenia, leucopenia, glossitis and increased homocysteine levels. Adequate folate intake is essential to prevent NTD. In the fetus, Folic Acid (FA) deficiency can occur following BS due to low gastric pH and reduced capacity of intestinal absorption [106]. Folate can be absorbed in the remaining small intestine and widespread fortifications of food like breakfast cereals means that folate deficiency following BS is relatively uncommon [107]. However, fetal myelo menigocele has been reported in post a post gastric bypass patient who was non compliant with supplementation [108]. Preconception supplementation with 400 microg/day of FA and continuing until the 12th week is recommended [109]. This increases to 5 mg in women at high risk including those with obesity and/or diabetes and those with history of prior pregnancies complicated by NTD’s. Women who have undergone BS should be deemed as high risk.

Lactation

Regular examination needed every 3 months in post BS patients. In pregnancy with hyperglycemia, fasting glucose or HbA1c control is advised for 4-12 weeks to document glycaemic control postpartum. FBS and HbA1C is recommended to control and diagnosis is indicated once FBS > 126mg or HbA1c 6.5%. Due to high variability continuous glucose monitoring (CGMS) is recommended [110]. CGMS detected high rise of postprandial hyperglycemia in patients who were following guideline recommendations and had shown a normal fasting glucose and HbA1c [41,110]. Thus capillary glucose monitoring with several time points postprandial is the ideal. CGMS and FGM may be offered additionally to collect same and postprandial glucose for few days if uncertainty exists. Micronutrients deficiencies have to be identified as in pregnancy. WHO recommends all mothers do breastfeeding until 6th after birth while quality of intake of mother affects breast milk delivered to infants [111]. A significantly higher, fat and energy and slight increase in carbohydrates in mothers after BS as compared with milk macronutrient with nonoperated controls is seen [112]. There are no excess known for mothers after BS, though concerns with micronutrient and vitamin deficiency in exclusively breast fed infants have been raised [53]. Maternal intake has a big influence on breast milk nutrients after BS as compared to controls. Mainly Vit B12 deficiency can cause megaloblastic anemia and developmental delay in offspring [58,111,113,114]. Previously Vit B12 deficiency in breast milk following RYGB surgery was reported with pancytopenia and long term developmental delay [113,114]. Calcium deficiency might lead to decreased calcium in the breast milk and hence undersupply and mineralization of fetal bones [110]. There are no suggestions of increased vitamins and trace elements as per DACH recommendations.

Conclusions

Thus we have tried to highlight the complications one encounters once a patient tries to undertake pregnancy following BS. Ideal time for pregnancy is after some wait, with contraception like OC might not prove much efficacious. Still lacunae exist regarding the ideal method of diagnosing GDM, in view of the limitations and complications associated with OGTT, and newer ways are being found. Currently CGMS, FMS are the once recommended. Another thing is no ideal weight gain criteria laid till date for pregnancy following BS. Gradually with more time passage and experience of handling these pregnancies these guidelines will get introduced. Additional nutrient and macronutrient supplementation along with vitamins addition has been highlighted although the occurrence of neural tube defects following surgery still remains controversial but excessive folate supplementation is essential. Although there is no contraindication to normal delivery still incidence of LSCS remains high in view of limitations with pregnancy in obese, operative scar, awareness of obstetrician and choice of the patient. Lactation also has to be monitored for good neonatal outcomes.

References

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