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Laparoscopic ileal interposition with diverted sleeve gastrectomy for treatment of type 2 diabetes

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SUMMARY

Objective: The objective of the present study was to prospectively evaluate the results of laparoscopic ileal interposition (II) with diverted sleeve gastrectomy (DSG) for control of T2DM and related metabolic abnormalities.
Methods: All patients underwent II +DSG. They had T2DM $\geq$ 5 years with poor glycemic control despite adequate dosage of oral hypoglycemic agents (OHAs) and/or insulin. The primary outcome was remission of diabetes (HbA1C < 6.5% without OHAs/insulin), and secondary outcomes were reduction in antidiabetic agent requirement and components of metabolic syndrome.
Results: We report the preliminary postoperative follow-up data of 9.1 $\pm$ 5.3 months (range: 3–21 months). There were 17 patients (male:female = 12:5) with mean age of 50.7 $\pm$ 8.1 (range, 34–66 years), duration of diabetes of 15.1 $\pm$ 5.8 years (range, 5–30 years), and preoperative body mass index of 29.2 $\pm$ 7.5 kg/m^2(range, 22.4–37.5 kg/m^2). Eight patients (45%) had hypertension, while dyslipidemia and microalbuminuria was present in 7 patients (39%) each. Twelve patients (70.5%) had diabetes remission. Seven/eight (87.5%) patients had remission in hypertension. All participants had weight loss ranging between 15% and 30%. Postoperatively statistically significant decline was observed in the glycemic and lipid parameters, microalbuminuria at all intervals ($p < 0.05$). Two patients had vitamin B12 deficiency 1 year after surgery.
Conclusion: Ileal interposition combined with DSG addresses both foregut and hindgut theories and brings about remissions in T2DM patients with reasonable safety. Our preliminary observations demonstrated the feasibility and efficacy of this novel surgical procedure as a promising option in T2DM.

1. Introduction

Diabetes mellitus is a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, both or factors not well understood [1–3]. Chronic hyperglycemia is associated with vascular complications and organ dysfunction. Obesity serves as an additional and important risk factor. Both type 2 diabetes mellitus (T2DM) and obesity are acquiring epidemic proportions [4–7].

In recent years, bariatric surgery has emerged as an effective and well validated treatment to address the metabolic profile in the diabetic population, paving way for the concept of metabolic surgery [8]. A systematic review and Meta analysis of bariatric surgery demonstrated complete resolution of T2DM in 78% of morbidly obese patients [9]. In animal models of T2DM, it has been confirmed that ileal interposition (II) improves glucose tolerance [10] and induces weight loss [11]. Human studies have confirmed the utility of II with sleeve gastrectomy (SG) in remission of T2 DM with high effectiveness in control of metabolic syndrome [12–17]. The combined surgical procedures address both foregut and hindgut theories leading to resolution of T2DM.

We have previously demonstrated that II + SG had better remission results in T2DM and overall metabolic improvement in patients with shorter duration of diabetes, better C-peptide response and higher body mass index [16,17]. Remission rate after II + SG was lower in patients with adverse clinical factors like longer duration of diabetes, poorer C-peptide response and lesser BMI. II with diverted sleeve gastrectomy (II + DSG) addresses both the foregut and hindgut factors in a better way leading to improvements in glycemic control than with classical II + SG. The diverted procedure leads to earlier flux of ileal glucagon like peptide-1 (GLP-1) and hence augments hind gut theory. It excludes duodenal loop and thereby it eliminates role of foregut factor

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(Rubino's factor) in causing insulin resistance. Hence T2DM patients with adverse baseline clinical profile are hypothesized to respond better to this modified procedure of II with DSG. However, data on utility of II with diverted sleeve gastrectomy (DSG) is scarce world over [12,18,19], with no such data published on Indian patients. Both the previous studies were done on poorly controlled T2DM patients with BMI < 35 kg/m^2. The purpose of the current study was to evaluate the safety and efficacy of laparoscopic II and DSG for treatment of T2 DM and related metabolic abnormalities.

2. Methods

The present study is a prospective, nonrandomized case series involving patients with poorly controlled T2DM, who were subjected to laparoscopic II and DSG at Kirloskar Hospital, Hyderabad, India. The study was duly approved by hospital's ethical committee. Informed consent was obtained from all patients participating in the study after explaining the patients about the benefits pertinent to nonobese subjects described in existing literature [17–19] and the potential risks involved.

2.1. Inclusion and exclusion criteria

The inclusion criteria were

- Type 2 DM of ≥5 years duration.
- Inadequate glycemic control with HbA1C > 7% on optimum dosage of insulin ± oral hypoglycemic agents (OHA).
- Age between 25 and 70 years.
- Stable weight for the last 3 months (variation in weight < 3%) [12,15,19].
- BMI ≥ 20 kg/m^2 and stimulated C-peptide level > 1 ng/ml.

The exclusion criteria were

- Type 1 diabetes mellitus.
- Undetectable fasting C-peptide.
- Positive urine ketones, pregnancy.
- Coexisting severe hepatic, pulmonary, renal, cardiovascular, neurological and psychiatric diseases and obesity due to organic illness.

2.2. Subjects and preoperative evaluation

Preoperative evaluation included clinical history of T2DM, co morbidities and complications followed by thorough physical examination. Patients were diagnosed to have type 2 diabetes mellitus on the basis of fasting plasma glucose ≥ 126 mg/dl (Fasting is defined as no caloric intake for at least 8 h) or 2-h plasma glucose ≥ 200 mg/dl during an oral glucose tolerance test after using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water or in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dl [20]. Standing height was measured using a portable stadiometer (Leicester height meter; Child Growth Foundation, UK; range, 60–207 cm). Weight was measured using an electric scale (Salter, India) accurate to 100 g. BMI was calculated as weight in kilogram divided by height in metre^2 [21]. We decided a cut off value for BMI > 25 kg/m^2 to define obesity, as per the consensus statement for diagnosis of obesity, abdominal obesity and metabolic syndrome for Asian Indians [22]. Relevant biochemistry tests, urinalysis, and imaging studies (chest radiograph and ultrasound abdomen) were performed for all patients in a single laboratory accredited by national accreditation board for testing and calibration laboratories (NABL). Fully automated clinical chemistry analyzer (Olympus 2700) was used for biochemical analysis. Fasting and post meal blood glucose were measured by hexokinase method and cholesterol oxidase method was used for estimation of lipid profile. Roshe E 601 analyzer was used for assessment of serum insulin, basal and 1 h post meal C-peptide, thyroid profile and microalbuminuria. Fasting serum samples were subjected to electrochemiluminiscence for insulin level determination. Basal and 1 h post meal C-peptide and thyroid profile were measured by chemiluminiscence method. Immunoturbidometry assay was utilized for detection of microalbuminuria in 24 h urine specimen. Glycated hemoglobin (HbA1C) was checked with high performance liquid chromatography (HPLC) method using Biorad variant D10. Patients with hypothyroidism were prescribed for thyroxine replacement. They were subjected to surgery after achievement of euthyroid state. Glomerular filtration rate was calculated using the modified Cockgroft–Gault equation [23,24]. Insulin resistance (IR) was assessed from the homeostasis model assessment (HOMA) formula (HOMA-IR) using fasting blood glucose and insulin [25].

2.3. Outcomes

The primary outcome measures:

- Remission of T2DM, defined as HbA1c < 6.5% without requiring oral or parenteral hypoglycemic agents.

Secondary outcomes measures:

- Improvement in glycemic parameters (HbA1C, Fasting blood sugar, Post lunch blood sugar).
- Remission in hypertension (blood pressure maintained at <130/80 mm Hg for patients without nephropathy or <125/75 mm Hg for patients with nephropathy without any antihypertensive medications).
- Improvement in other metabolic parameters like lipids, microalbuminuria and uric acid.
- Improvement in weight and BMI in obese patients (BMI > 25 kg/m^2).
- Reduction in insulin and OHA requirement for glycemic control.

As per the evaluation by previous studies [12,15], and ADA proposed criteria [26], the outcomes were planned to be monitored and analyzed at 6 months interval.

2.4. Procedure

The operation was performed under general anesthesia with a standard six-port laparoscopic technique. A variable sleeve gastrectomy was performed after devascularization of the greater curvature from the antrum to the fundus area. Fig. 1 depicts diagrammatic representation of the procedure. The lumen of the stomach was adjusted by a 32–60 French calibrator (Romsons International, New Delhi, India) that was placed along the lesser curvature. The endo-GIA stapler with 60-mm cartridges was used for resection. Non obese patients were subjected to only fundectomy, leaving a good volume of residual stomach for normal food intake. After that, the devascularization along the greater curvature of the stomach continued to the duodenum, 2–3 cm beyond the pylorus. The duodenum was transected using a 60-mm linear stapler. The gastric pouch and proximal duodenum then were transposed to the lower abdomen through a hole created at the root of mesocolon. A distal ileal segment of 170 cm was transected along with its mesentery pedicle, measured from

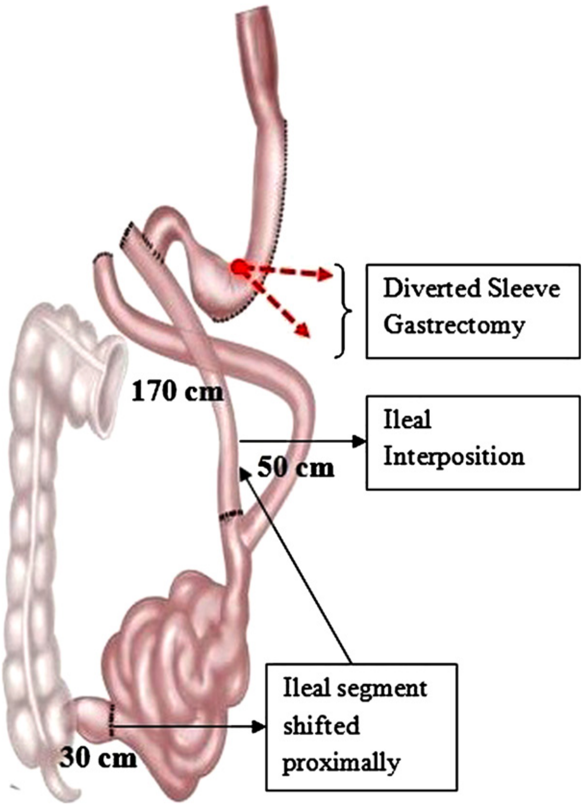

Fig. 1. Diagrammatic representation of ileal interposition with diverted sleeve gastrectomy.

30 cm proximal to the ileocecal valve. Continuity of small bowel is restored by ileo-ileal anastomosis using stapler. The proximal end of this transected ileal segment was interposed and anastomosed peristaltically to the proximal duodenum. This anastomosis was done in 4 layers using intracoporeal hand suturing. A point in the jejunum 50 cm from the ligament of Treitz was measured and anastomosed to the distal part of the interposed ileum side to side to it using stapler. All anastomoses were performed functionally using 45-mm linear staplers, with care taken to close mesenteric defects using interrupted 3–0 polypropylene sutures (Fig. 1). The trocar openings were closed.

2.5. Postoperative follow up

Postoperatively the diabetes and hypertension medications were adjusted according to the plasma glucose and blood pressure record levels respectively. The patients were kept on a liquid diet for 5–7 days, followed by semisolid diet for another 7 days, and finally a solid diet, always in small quantities. The patients were discharged between the fourth and sixth postoperative day with vitamin supplements. Routine upper gastrointestinal endoscopy was done after 1 month of surgery. They were asked to come for follow-up visits at 1, 3, 6 and 9 months and every 6 months then after. Outcomes measures were collected prospectively. The main parameters included fasting and postprandial glucose, HbA1c, diabetes medication usage (agents, doses, frequency), weight loss (expressed in BMI and percentage of weight loss), resolution or improvement of associated metabolic abnormalities and complications, the reoperation rate, and the morbidity–mortality of the procedure. Patient and laboratory evaluation was scheduled for every 3 months until 18 months after the operation. Tests for malabsorption including serum iron, vitamin B12, protein and calcium too were done at 3 monthly intervals.

2.6. Statistical analysis

All outcome measures were evaluated prospectively from the third month onward at every visit. Online Graphpad Quickcalcs software (Graphpad. Software Inc, La Jolla, CA, USA, available at http://www.graphpad.com/quickcalcs/index.cfm) was used for statistical calculations. Continuous data were analyzed by student's t test. The categorical data were analyzed by using two tailed Fisher's exact test, in view of the small sample size. The sample size during later periods of follow up was small. Still we were stimulated to do the statistical analysis with an intention to compare the outcomes among different group of patients. *P* values less than 0.05 were considered significant.

3. Results

Total of 17 patients underwent II + SG (5 female and 12 male) from March 2010 to September 2011. Their baseline demographic parameters are mentioned in Table 1. Preoperatively 8 patients required $\geq$2 OHAs and 10 required insulin $\pm$ OHA for glycemic control.

The mean operative time was 387.7 $\pm$ 84.3 min and the mean postoperative hospital stay was 8.8 $\pm$ 5.4 days. Intraoperative complications were noted in 4 patients (23%). One patient had dusky duodenal stump leading to application of drain. Another patient's tip suture broke into abdominal wall which was extricated by C arm. A 2 cm opening at gastric antrum in another patient was closed with PDS because of faulty stapling and 4 cm segment of bluish proximal ileal segment had to be resected in the same patient. On 3rd post operative day 1 patient complained of pain abdomen and distension, diagnostic laparoscopy revealed no abnormality. In view of persisting pain abdomen on 7th day with gas under diaphragm, patient was subjected to exploratory laparotomy followed by closure of ileal perforation and appendectomy. Inflamed appendix adherent to uterine fundus was an incidental finding. Nausea and loss of appetite was observed in 3 patients (18%), which improved over a period of 2 weeks. At 3 months postoperative follow up, none of these patients had any complications with regards to the intraoperative and immediate postoperative events.

Mean follow up period was 9.7 $\pm$ 5.3 months (range: 3–21 months). The post operative follow-up data is summarized in Table 2. Diabetes remission data is depicted in Fig. 2. Over all at the end of the study, 12 patients (70%) had remission in diabetes with rest showing significant reduction in antidiabetic agent requirement. Glycemic control with HbA1C < 7% was achieved in 14 (85%) patients.

Table 1
Baseline data of the study group.

N (men/women)	17 (12/5)
Obese patients (BMI > 25 kg/m^2) – *N* (%)	13 (72%)
Non obese patients (BMI $\leq$ 25 kg/m^2) – *N* (%)	5 (28%)
Hypertension – *N* (%)	8 (45%)
Dyslipidemia – *N* (%)	7 (39%)
Microalbuminuria – *N* (%)	7 (39%)
Age (years)	50.7 $\pm$ 8.1 (34–66)
Duration of DM (years)	15.1 $\pm$ 5.8 (5–30)
BMI (Kg/m^2)	29.2 $\pm$ 7.5 (21.5–30.2)
HbA1C (%)	9.8 $\pm$ 1.8
Fasting C-peptide (ng/ml)	3.1 $\pm$ 1.8
Post meal C peptide (ng/ml)	4.2 $\pm$ 2.2
HOMA-IR	17.1 $\pm$ 8.1
LDL-Cholesterol (mg/dl)	97.4 $\pm$ 41.7
Triglyceride (mg/dl)	184.8 $\pm$ 85.8
Microalbuminuria (mg/24 h)	42.5 $\pm$ 30.1

Data expressed as N or mean $\pm$ SD (range).
N: Number of patients, SD: standard deviation, BMI: Body Mass Index, HbA1C: glycosylated hemoglobin, HOMA-IR: homeostasis model assessment-insulin resistance, LDL: low density lipoprotein.

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Table 2
Post operative metabolic parameters in 17 patients.

Parameter / Follow up	FBS (mg/dl)	PLBS (mg/dl)	HbA1C (%)	BMI (kg/m^2)	Cholesterol (mg/dl)	LDL-C (mg/dl)	Trigly. (mg/dl)	Micralb. (mg/24 h)
Preop	236.52 ± 88.4	305.1 ± 124.3	9.8 ± 1.8	29.2 ± 7.5	164.2 ± 52.7	97.4 ± 41.7	184.8 ± 85. 8	42.5 ± 30.1
1 month	*121.6 ± 21.5	*160 ± 23.5	*9.7 ± 1.0	*22.3 ± 6.4	*128.6 ± 22.1	*74.9 ± 12.8	*89.1 ± 10.5	*33.9 ± 25.3
3 months	*111.8 ± 38.1	*169.6 ± 33.5	*7.8 ± 0.9	*23.7 ± 3.5	*144.7 ± 18.3	*83.8 ± 23.2	*130.5 ± 22.5	*43.2 ± 16.8
6 months	*126.1 ± 31.2	*173.2 ± 54.2	*7.3 ± 0.8	*22.4 ± 3.1	*139.1 ± 29.5	*76.6 ± 24.8	*96.9 ± 32.3	*27.2 ± 13.3
12 months	*103.1 ± 18.2	*138.4 ± 38.9	*6.6 ± 0.6	*22.1 ± 2.9	*135.3 ± 18.2	*83.1 ± 15.1	*88.5 ± 27.7	*16.0 ± 7.8
18 months#	114	134	6.4	23.4	140	94	90	10

BMI: Body mass index; FBS: fasting blood sugar; PLBS: post lunch blood sugar; LDL-C: low density lipoprotein cholesterol.
Statistical analysis could not be done as only 1 patient has completed 18 months follow up.
* $p < 0.05$ (student's t test), data expressed as mean ± SD values.

Percentage reduction in HbA1C was higher compared to corresponding fall in BMI at all intervals (over mean decline in BMI 20% versus mean fall in A1C 35%, (Fig. 3). Seven patients (86%) had remission in hypertension.

We looked for impact of the surgical procedure on malabsorption profile and included serum calcium, protein, iron and vitamin B12 levels for periodic assay. Table 3 depicts the evaluation of these parameters. Two patients at 12 months and 1 patient at 18 months developed vitamin B12 deficiency, though all of them were asymptomatic. Patients were given additional intramuscular vitamin B12 supplements.

Patients were divided according to their duration of postoperative follow up periods. Group A had 8 patients with follow up ≥ 12 months (14.8 ± 2.8 months) and group B had 9 patients with follow up < 12 months (5 ± 1.6 months). Postoperative clinical and biochemical data in comparison to preoperative parameters in these 2 groups of patients are shown in Table 4. Remission was seen in all 8 patients in group A and 4 patients from group B. The remaining 5 patients had a significant decrease in antidiabetic agent dosage with 4 patients requiring only metformin and 1 patient requiring 2 OHAs (with short follow up period of 2 months) for glycemic control. Patients from both group had significant weight loss to the tune of 15–30% with group A subjects showing greater decline (28% vs 22%), reflecting time bound fall in weight. Statistically significant reduction in lipid parameters and microalbuminuria was seen in patients in both groups.

4. Discussion

T2DM in morbidly obese is usually attributed to increased body weight besides other factors. American Diabetes Association in their 2009 guidelines [27] has recommended bariatric surgery in T2DM patients with BMI > 35 kg/m^2. However, in a country with large number of diabetic patients in world [28,6], a recent consensus statement [22] has established high adiposity at lower BMI amongst Indians [28,6]. This results in higher co-morbidity association at lower BMI levels. Hence the definition of obesity has been modified in Indian subcontinent to BMI ≥ 25 Kg/m^2 [22], calling for the need to aggressively address the issue of obesity.

Bariatric surgery has proved its worth in improving diabetes and other associated metabolic abnormalities. Previous studies have shown that II added to SG offers good remission rate in diabetes without causing side effects related to gastric bypass and other malabsorptive procedures [12–15]. However it is reported that in patients with long standing diabetes with lesser BMI and lower C peptide reserve, remission rate is less [16,17]. In this study we have shown that DSG with II offers good remission rate in this subgroup of patients. Improvement in other metabolic parameters is also significant with this procedure. To the best of our knowledge, this is the first report from India about laparoscopic surgical procedures of II + DSG for control of T2DM, hypertension and other associated metabolic derangements. Our study results have indicated II and DSG as a safe procedure without any

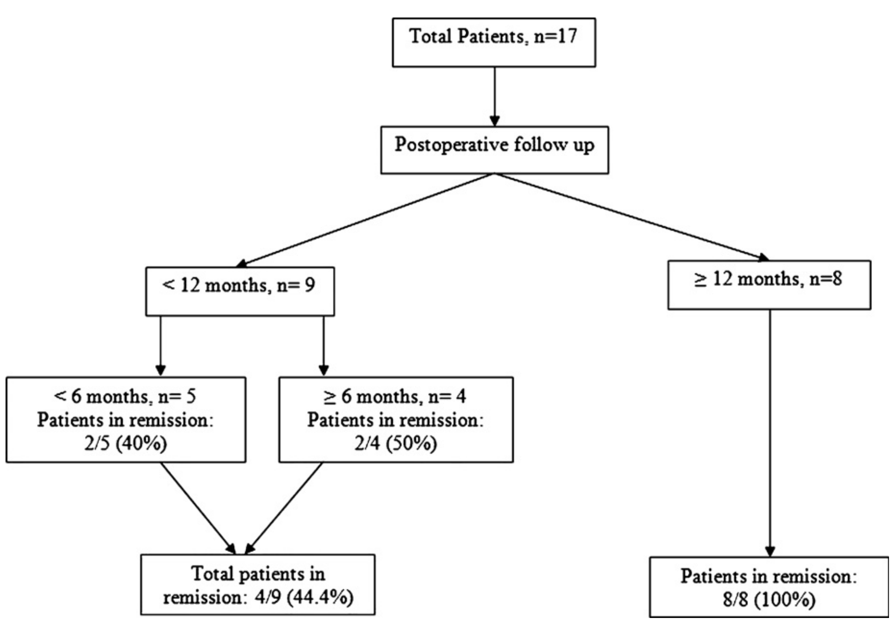

Fig. 2. Diabetes remission data of the study population at different intervals.

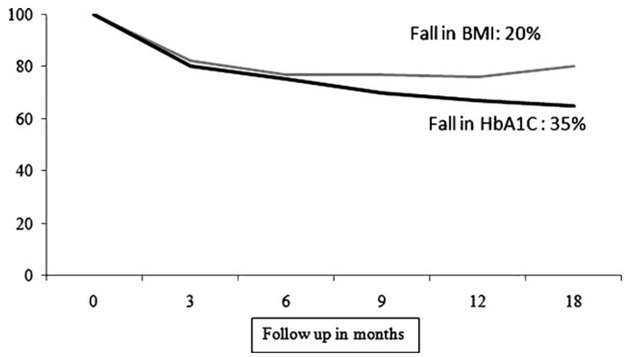

Fig. 3. Postoperative comparison of percentage (%) fall in BMI and HbA1C.

mortality or reoperation and with complication rates comparable to other reports on similar bariatric procedures.

Overall at the end of the study, 12 patients (70%) had remission in diabetes with rest showing significant reduction in antidiabetic agent requirement. Glycemic control with HbA1C < 7% was achieved in 14 (85%) patients. The remission rate was higher as the duration of follow up was higher (100% in patients with follow up ≥ 12 months and 44% in patients with follow up < 12 months). We could witness a gradually increasing remission rate at successive subsequent follow up visits [2 (40%), 4 (44.4%) and 12 (70%) patients at 6, 12 and 18 months respectively]. The study by De Paula et al. has reported that 76.3% patients had HbA1C < 6.5% and 91% patients had HbA1C < 7% [19]. The lower remission in our study population might be attributed to shorter follow up and higher insulin resistance in Indian patients as compared to Caucasians.

Normalization in hypertension was observed in 86% patients compared to 87% in the study by De Paula et al. [19]. The observed beneficial effects on hypertension can be explained by weight loss and improved insulin sensitivity [29]. The associated metabolic parameters like microalbuminuria and lipid profile showed statistically significant reduction at all follow up intervals. This further justifies the usage of the terminology metabolic surgery for this novel procedure.

The combination of II and DSG addresses both the foregut and hindgut hypotheses implicated in pathogenesis of T2DM leading to resolution of the accompanying metabolic milleu. The SG component restricts calorie intake and reduces ghrelin (a potent orexigenic substance that contributes significantly toward impaired glucose homeostasis) [30]; it also speeds up gastric transit of food, reaching the ileal segment faster. Glucagon-like peptide 1 (GLP-1), the incretin responsible for the first phase of insulin secretion, is defective in T2DM. In the ileal interposition component of II + DSG, rapid stimulation of interposed ileal segment by ingested food leads to augmented GLP-1 secretion [31]. Only fundectomy was carried out in nonobese patients for the metabolic benefits of ghrelin withdrawal. Postprandial glucose homeostasis is determined not only by stimulation of insulin secretion and suppression of hepatic glucose production, but also by the velocity of gastric emptying. GLP-1 also influences glucose metabolism by inhibiting glucagon secretion, decreasing hepatic gluconeogenesis, delaying gastric emptying, promoting satiety, suppressing appetite, and stimulating glycogenesis [32–38]. The diverted procedure scores over the conventional II + SG procedure with regards to following 2 points:

- Apart from standard SG induced reduction of ghrelin produced by gastric fundus and calorie restriction, the diverted procedure also excludes the duodenum known to produce Rubino's factor, which is hypothesized to promote insulin resistance [39].
- Exclusion of duodenum further attenuates the GIP secretion from K cells. GIP is demonstrated to cause dose dependent stimulation of glucagon secretion [40]. Disruption or attenuation of GIP action is associated with diminished weight gain, resistance to diet-induced obesity, and improved insulin sensitivity in preclinical studies [41,42], whereas genetic variation within the human *Gipr* gene is linked to control of postprandial glucose and body weight [43,44].
- In comparison to standard II + SG, in II + DSG, the interposed ileal segment is shifted more proximally than in the standard SG procedure, leading to earlier and rapid stimulation of transposed ileal segment by ingested food leading to augmented glucagon-like peptide (GLP-1) hormone secretion.

All patients had weight loss amounting to 15–30%. The fall in HbA1C was higher than fall in BMI, which reaffirmed the basic aspect of weight loss independent glycemic benefits of this metabolic surgery. Possible mechanisms explaining the benefits of this procedure in nonobese subjects could be:

(a) Calorie restriction induced decreased stimulation of duodenum leading to attenuated secretion of unknown culprit foregut factor (Rubino's factor) [39].
(b) Earlier exposure of food to ileum leading to better incretin response [45].
(c) Ileal brake: Food entering into ileum modulates gastric and intestinal motility to reduce food intake and absorption [46].
(d) Enhanced postoperative serum bile acid levels have been proposed to play a role in improved insulin sensitivity (correlated with high adiponectin levels) and increased incretin induced insulin secretion [47–49].

In II + DSG, since duodenum and part of jejunum are bypassed, it can potentially cause some malabsorption. All patients are advised regular intake of iron, calcium, B12, and multivitamins. The more extensive the intestinal bypass, the greater are the chances of nutritional and metabolic complications [9]. However, iron deficiency was observed in 4.5% patients despite routine iron supplementation in the study by De Paula et al. [12]. We did not find any iron deficiency in our group of patients. Albumin levels were routinely measured and were always normal. The increased levels of GLP-2 leading to intestinal growth and improvement of nutrient absorption may eventually explain the absence of malnutrition in this series [50]. Two patients developed vitamin B12 deficiency during later follow up visits 1 year after surgery. Subsequent monitoring for these nutritional elements and vitamins seems essential after the surgery and would address

Table 3
Postoperative nutritional profile of patients.

Parameters	Normal values	3 months	6 months	9 months	12 months	18 months
Serum iron (μg/dl)	50–170	75.5 ± 12.5	80.6 ± 14.5	70.3 ± 29.5	63.4 ± 30.9	65.5
Serum vitamin B 12 (pg/ml)	500–1300	955.5 ± 78.2	784.5 ± 67.8	675.6 ± 65.9	450.5 ± 97.5	398.5
Serum protein (gm/dl)	6–8	6.4 ± 2.1	6.9 ± 2.8	6.7 ± 2.4	7.6 ± 4.1	6.1
Serum calcium (mg/dl)	9–10.5	10.1 ± 2.4	9.8 ± 1.9	9.5 ± 1.8	9.1 ± 3.5	9.2

Table 4
Clinical and biochemical data before (preop) and after (postop) surgery.

Parameters	Group A (*n* = 8)			Group B (*n* = 9)		
	Preop	Postop	*P* value	Preop	Postop	*P* value
BMI (Kg/m^2)	30.1 ± 4.5	23.4 ± 2.9	0.0084	29.0 ± 3.9	21.9 ± 2.7	0.0004
FBS (mg/dl)	226.7 ± 81.2	99.5 ± 19.2	<0.0001	238.5 ± 90.2	105.4 ± 21.2	0.0035
PLBS (mg/dl)	310.5 ± 134.5	132.5 ± 32.6	<0.0001	298.4 ± 129.5	143.5 ± 39.7	0.0003
HbA1C (%)	9.9 ± 1.9	6.2 ± 0.5	<0.0001	9.7 ± 1.6	7.1 ± 1.1	0.0049
LDL-C (mg/dl)	92.4 ± 35.6	79.5 ± 12.1	0.035	102.5 ± 45.4	92.5 ± 20.1	0.051
Tg (mg/dl)	180.5 ± 78.8	78.5 ± 22.8	0.0032	192.1 ± 90.6	95.5 ± 32.1	0.042
Microalbuminuria (mg/24 h)	45.5 ± 29.1	15.5 ± 12.5	0.0405	40.2 ± 33.2	29.8 ± 14.5	0.052

Data are mean ± SD values.
Group A: patients with follow up ≥ 12 months (mean follow-up 14.8 months, range, 12–20 months); Group B: patients with follow up < 12 months (mean follow-up 5.0 months, range, 2–11 months).
FBS, fasting blood sugar; PLBS, plasma blood sugar.

this concern in a better way. Micronutrient deficiency needs to be looked at in the long term.

The averaging operative time was 387.7 ± 84.3 min, which is quite similar to previous such reports on current procedure [12,18,19]. De Paula et al. have reported 7.7% intraoperative complications including resection of an ischemic transposed ileum, cardiac arrhythmia and hypertensive crisis [12]. We had intra-operative complication in 4 patients (23%) as mentioned in the results. This figure is variable across different units performing this surgery. It leads to the suggestion that the surgery should be done only in specialty centres, till more data and experience is available on this procedure. Exclusion of high risk cases and proper preoperative control of cardiac morbidities would serve the purpose. Overall postoperative complication rate in our series was low with mainly nausea and loss of appetite in about 18% patients. No major long term or delayed surgical complications were noted in any of the patients. De Paula et al. have demonstrated 15.4% minor early postoperative complication and 21.1% late clinical complications like gout attack, prolonged emesis, urinary tract infection and fungal esophagitis [12]. Tinoco et al. have demonstrated ketoacidosis and urinary infection in 3.3% cases and diarrhea in 6.6% cases. Three months postoperatively there was 3.3% incidence of cholecystolithiaisis and bowel obstruction caused by adhesions [15]. Three patients developed urinary tract infection at 3 months postoperatively and were treated with oral antibiotics. None developed other surgery or related complications including cholecystolithiasis or other infective episodes. We found a low rate of complications and no mortality in our study group. So II + DSG appear to be reasonably safe procedures. Hypertrophy of the pancreas with nesidioblastosis [51] has been reported in post gastric bypass patients, though no causal relationship has been established. Various hypotheses have been proposed to explain this condition. Proliferative effect of GLP-1 on β cells is also considered. Only a long term follow up of these patients will be able to establish this possibility.

The limitations with our study were

(a) The brevity of the study.
(b) Report from single center with follow up of only 20 months.
(c) Relatively small number of patients with absence of control group.
(d) Non randomized cross sectional data.
(e) We did not study the effects of this procedure on diabetic complications. De Paula et al. have demonstrated objective improvement of retinopathy in 36.4%, symptomatic improvement in neuropathy in 62. 5% and some improvement in erectile dysfunction in 62.5% cases following IISG [12].

Multicentre studies on larger number of patients with longer follow up period would strengthen our observations. Nevertheless, the data of our current report adds value to the limited information available on this procedure [12,18,19]. Another important limiting factor is the technical expertise required for the laparoscopic ileal interposition, which requires extensive training and referral to highly skilled surgeons with adequate experience. Long term data is needed to establish its efficacy as some recent results have shown recurrence rate close to 50% following bariatric surgery (R-n-Y gastric bypass) [52,53]. Similarly more long term data needs to be collected regarding safety and complications before it can rolled out as a routine procedure for diabetes therapy.

Conflict of interest

It is submitted with the full knowledge and approval of our institute and there is no conflict of interest to disclose from any of the authors with regards to publication of the manuscript or an institution or product that is mentioned in the manuscript. There are no competing interests to disclose, due to any reasons, with whom so ever concerned.

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Contribution of authors. All the four authors have made substantial contribution to the intellectual content of the paper and fulfill at least 1 condition for each of the following categories of contribution i.e., category 1 (conception and design, acquisition of data, analysis and interpretation of data), category 2 (drafting of the manuscript, critical revision of the manuscript for important intellectual content) and category 3 (final approval of the version to be published).

Declaration. The manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met, and that each author believes that the manuscript represents honest work.

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