

Original Article

## EFFECT OF METABOLIC SURGERY ON TYPE 2 DIABETES REMISSION: A MATCHED GROUP ANALYSIS

LEENA MATHEW\*<sup>1</sup>, D. KILIMOZHI<sup>2</sup>, S. PARIMALA KRISHNAN<sup>2</sup> MOHAMMED ISMAIL<sup>3</sup>

<sup>1</sup>Chemist's College of Pharmaceutical Sciences, Varikoli p. o, Puthenkruz, Kerala, India, <sup>2</sup>Department of Pharmacy Annamalai university, Annamalai Nagar 608002, <sup>3</sup>Tamilil Nadu, India, <sup>3</sup>Bariatric and Metabolic Department, Moulana Hospital, Madavana, Pathaikkara p. o Perinthalmanna, Malappuram, Kerala pin 679322  
Email: leenageorge1@rediffmail.com

Received: 28 May 2015 Revised and Accepted: 15 Jul 2015

### ABSTRACT

**Objectives:** In this study it is proposed to analyse the effect of bariatric metabolic surgery on diabetes remission in obese type 2 diabetic patients compared to conventionally treated similar patients.

**Methods:** A retrospective review, of prospectively collected data base of conventionally treated group and metabolic group were screened from the year 2010-2013 at the study centre for patients satisfying the inclusion criteria. Three follow up data at an interval of three months and a base line value for both group were collected. Primary outcome measures the percentage of patient achieved diabetes remission, i.e. glycosylated haemoglobin (HbA1c)<6 % without active pharmacological therapy at one year and percentage of patients who achieved excess weight loss more than 60 % at one year.

Secondary outcome includes percentage reduction in medication use. Statistics used in the study is student 't' test, Chi-square and ANOVA (Analysis of Variance). The treatment effects were found to be significant to the least significant difference (LSD) at 5% level of significance.

**Results:** The patients underwent bariatric surgery had a significant improvement in glycemic status (HbA1c<6 %). In conventionally treated group less than 5% achieved HbA1c less than 6.5 % level with active pharmacological therapy. There was an increased use of antidiabetic medication with 2-5% increase in mean body weight in conventional group.

**Conclusion:** Compared to conventional therapy bariatric surgery markedly improves diabetes and results in discontinuation or marked reduction of anti-diabetic medications in majority of patients treated. So bariatric surgery seems to be a better option for the obese diabetic patients.

**Keywords:** Bariatric metabolic surgery, Glycosylated hemoglobin, Obesity, Type 2 diabetes, Body Mass Index, Weight loss.

### INTRODUCTION

The growing incidence of obesity and type 2 diabetes is one of the most challenging contemporary threats to the public health as changing lifestyle leads to reduced physical activity and increased obesity. The rise in the prevalence of obesity is associated with the increase in type 2 diabetes mellitus (DM), hyperlipidemia, hypertension, obstructive sleep apnoea, heart disease, polycystic ovary, stroke, asthma, several forms of cancer and depression [1]. The initial treatment for type 2DM associated with obesity is lifestyle modification involving dietary modification and increased physical activity with or without active pharmacological therapy [2]. To maintain glycemic status and average weight loss for a long period of time with lifestyle intervention alone is difficult to achieve. Except metformin most glucose lowering drugs causes weight gain [3]. The introduction of glucagon-like peptide-1 (GLP-1), dipeptidyl peptidase inhibitors and sodium dependent glucose transporter-2 inhibitors has altered the management of type 2DM because these agents do not cause weight gain [4, 5].

However there are limited data on the long term efficacy of these drugs. Both consensus meeting and international Diabetes federation have recommended consideration of bariatric surgery for control of type 2DM when obesity is severe and/or available medical therapies fail to control diabetes. Evidences from different studies suggest that bariatric surgery can improve type 2 diabetes [6]. A high profile Meta analysis by Buchwald *et al.* reported that 78% resolution in type 2DM following bariatric surgery [7]. This study changed clinician's focus of bariatric surgery for weight loss to cure of diabetes gave rise to the term "metabolic surgery" [8].

Present study was done with an objective to investigate the impact of bariatric metabolic surgery on excess weight loss and diabetes remission at one year of treatment in obese type 2 diabetes patients compared to a conventionally treated matched patient group.

### MATERIALS AND METHODS

This retrospective observational study was conducted at the bariatric and metabolic surgery department of Moulana hospital after receiving the institutional ethical committee approval. The study population who had undergone medical treatment and metabolic surgery for diabetes were retrospectively identified from the medical records of the hospital. Medical records between the years 2010 January to 2013 December were screened for selection of patients. Patients satisfying the criteria, age between 25-60 years, BMI>32.5 kg/m<sup>2</sup> with type 2DM for more than 2 years and HbA1c not less than 7.5% at base level with a minimum follow up of 18 months were selected for the study. A total of 150 patients of which 85 females and 65 males who met the inclusion criteria were selected for metabolic surgery group and in the conventional group there was 155 patients of which 70 females and 85 males.

The patients of both groups were matched for age, gender, BMI and glycosylated haemoglobin. Diagnosis of type 2DM was made according to American Diabetes Association guidelines and surgery followed fulfilment of the Consensus in Asia-Pacific 2005 criteria [6, 9]. The initial data collected at base line includes height, weight, HbA1c, co-morbidities, and medications for both groups. Similarly follow-up data were collected at three months interval which includes change in BMI, weight loss, HbA1c, and medication use pattern. BMI is calculated using the formula weight in kilogram divided by height in meter square. Weight loss is reported as the mean percentage of excess weight loss which is the standard in bariatric procedures. The formula used for finding percentage excess weight loss is equal to weight loss divided by excess weight multiplied by 100. Ideal body weight is calculated from the standard table which has ideal weight corresponding to each BMI.

### Outcome measure

Primary outcome was the percentage of patients achieved diabetes remission (HbA1c<6 % without active pharmacological therapy) and percentage of patients who lost>60% excess body weight. Secondary outcome includes percentage reduction of medication use in both groups.

### Statistics

Statistical analysis was done using independent't' test for comparison of means chi-square for goodness of fit of ratios and 2 factor ANOVA for comparison of parameters between groups.

### RESULTS AND DISCUSSION

Table1 gives the mean, standard deviation (SD) and the't' values of the baseline data for conventional and surgical groups. There is no significant difference in glycemic status and gender between groups, but the mean age, duration of diabetes and BMI between groups differ significantly. The mean age of conventional group was 47.5±9.15 and bariatric group it was 41.47±7.72, duration of diabetes in conventional group 11.65±6.75 and in bariatric group it was 7.67±5.24, BMI in conventional group was 37.24±6.18, bariatric group 42.13±7.24 and in conventional group excess mean % weight was 20.06±13.89, in bariatric group 63.60±23.85. From

the table it is clear that obesity is dominant among people in the age group between 36 to 45years. Similar report was published by Unni et al. [10].

### BMI and excess weight loss%

Tables 2 and 3 give a comparison of means of BMI, excess weight loss%, Glycosylated haemoglobin, and insulin units per day and oral hypoglycemic agents (OHA) in the three follow ups of the conventional and bariatric groups. The bariatric surgery produced significant and desirable excess weight loss%. At baseline, patients in the bariatric group weighed more BMI average (42.13±7.24) compared to conventional group BMI 37.24±6.18. At the end of the study period there was an increase in mean BMI from 37.24±6.18 to 37.45±4.56 in the conventional group. The second parameter excess weight loss showed a sharp reduction in bariatric group whereas it showed no reduction in conventional group. Weight loss is the most important parameter of bariatric surgery. The fig. 1 shows the graphical representation of excess weight loss% in bariatric group. Here the average weight loss per follow up was>20% and excess weight loss at the end of the study was>60%. In our study more than sixty percent patients lost their excess body weight by 60%. More than 50% excess weight loss indicates success of bariatric surgery [8]. Retrospectively reviewed 102 patients and a similar result were published.

**Table1: Preoperative parameters of study population**

Parameter	Conventional group			Bariatric group			Significance		
	n	mean	SD	n	mean	SD	t	df	p-value
Age	155	47.5	9.15	150	41.47	7.72	13.458	303	P<0.01
DM duration	155	11.65	6.75	150	7.67	5.24	5.762	303	***P<0.001
BMI	155	37.24	6.18	150	42.13	7.24	16.448	303	P<0.01
Excess % wt	155	20.06	13.89	150	63.60	23.85	16.504	303	P<0.001
Glycosylated haemoglobin	155	8.01	1.23	150	7.9	1.80	8.277	303	NS
Insulin	130	51	6.24	78	49.5	7.71	8.697	183	P<0.05
Metformin+combination	25	1533.33	561.74	72	1071.43	305.12	7.340	188	P<0.001

\*pvalue<0.05 p \*\*<0.01,\*\*\*p value<0.001 df (degree of freedom),NS-not significant, \*pvalue<0.05(significant) p\*\*<0.01, (more significant) \*\*\*p value<0.001 (highly significant)

**Table 2: Follow up parameters in conventional group (CG)**

parameters	No of patients	First follow up	Second follow up	Third follow up	P value
BMI (mean±SD)	155	37.37±4.68	37.33±4.08	37.45±4.56	NS
Excess weight loss%	155	nil	nil	nil	NS
Glycosylated haemoglobin	155	8.01±0.78	7.9±0.75	7.5±0.8	NS
Insulin+OHA units/day	130	44±6.24	40±21	45±26	>0.05
OHA alone(mg)	25	1554±250	1255±365	1583±345	>0.05
				N=135	
				N=20	

OHA-Oral hypoglycaemic agents, BMI-Body Mass Index

**Table 3: Follow up parameters in bariatric group (BG)**

Parameters	No of patients	First follow up	Second follow up	Third follow up	P value
BMI (mean±SD)	150	38.30±7.9	35.05±6.83	32.26±4	<.001
Exces weight loss%	150	15.69±9.62	26.79±9	20.83±11	<0.001
Glycosylated hemoglobin	150	6.9±0.56	6.33±0.25	5.88±0.25	<.01
Insulin units	78	33±6.24	32 (N=10)	00 (N=0)	>0.001
OHA	72	1554+250	1255±365	500±25	>0.001
			N=40	N=15	

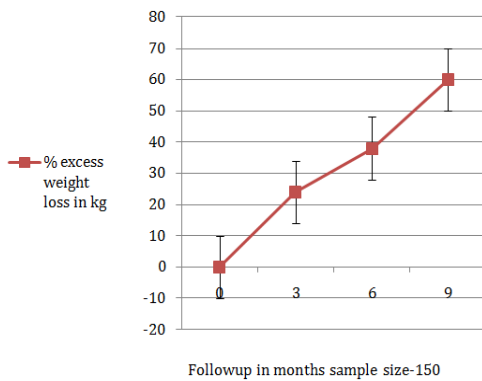
\*p value<.05 (significant) p \*\*<.01 (more significant) \*\*\*p value.001 (highly significant), CG (Conventional group), BG (Surgical Group)

### Diabetes remission and use of anti diabetic medication

At base line, 86% of conventional group was receiving insulin at an average of 44±6.24 units. This was increased to 87% and dose also increased to 45±26 units at the end of the study. Remaining 13% were on oral hypoglycaemic drug metformin alone or in

combination at an average dose of 1533.33±561.74. In bariatric group 52% were using insulin at an average 49.5±7.71 U and 48% were on OHA in double and triple drug combinations at an average dose of 1071.43±305.12 mg/day. Months after surgery, the insulin intake was drastically reduced and became zero at the end of the study period. Only 15% patients were taking anti diabetic

medication at an average of 500 mg/day in the bariatric group at one year post surgically. D. E Mumme *et al.* reported that after surgery only 20% patients need antidiabetic medications [6, 11]. In our study similar result was observed.



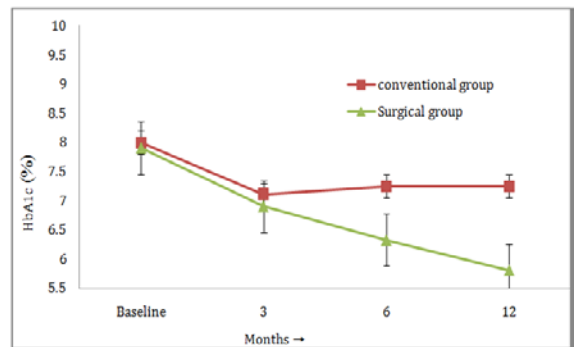
**Fig. 1: changes in excess body weight loss after surgery**

Here the average weight loss >20% at each follow up showed in the Y axis. The X axis showing follows up in months.

**HbA1c value**

The remission of diabetes, (HbA1c less than 6% without active pharmacological therapy) was achieved in more than 85% patients of bariatric group at the end of study. In the conventional group only

5% achieved 6.5% HbA1c level with antidiabetic medication. Two multi-centre study conducted by Daniel E, Mumme, Michal Mathiason [6] reported 89% remission of diabetes after bariatric metabolic surgery. In our study also more than 80% bariatric patients achieved remission at one year. The result of our study is comparable with above study. Complete remission means discontinuation of all diabetes related medication and HbA1c less than 6%. Elevated HbA1c is an indicator, widely accepted for diabetes measurement, every 1 % decrease in HbA1c the risk of diabetic complication decreases by 37% [9]. Bariatric surgery can result in diabetes remission. Buchwald *et al.* conducted a study for obesity and related complications reported that after bariatric surgery significant and consistent reduction HbA1c value was observed relative to the baseline value [7]. Fig. 2 shows the comparison of HbA1c at base line and after intervention in both groups. In conventional group mean HbA1c is 7.5% where as in bariatric group it is less than 6%.



**Fig. 2: Changes in mean value of glycosylated haemoglobin.**

**Table 4: Anova for conventional group**

Source	ss	df	ms	f	p
Total	5184557.93	15			
Follow ups	36086.47	3	18043.24	1.095	>0.05
Error	197794.02	12	16482.84		

ss-sum squares, df-degrees of freedom, ms-mean square\*p value<.05 (significant).

Table 4 shows the two factor anova for parameters and follow ups of conventional group. There is no significant difference between three follow ups because p value is more than (0.05). The parameters tested are BMI, excess weight loss and Glycosylated haemoglobin and medication use.

Table 5 shows the two factor anova for parameters and follow ups under the surgery group. There is significant difference between baseline and follow ups (P<0.05). The three followed parameters BMI, Excess weight loss and Glycosylated haemoglobin were found to be statistically significant for surgical group.

**Table 5: Anova for bariatric group**

Source	ss	df	ms	f	p
Total	3126088.73	24			
Parameters	3000438.82	3	500073.14	89.533	<0.001
Follow ups	25113.76	3	8371.25	1.499	<0.05
Error	100536.15	18	5585.34		

ss-sumsquares of mean, df-degrees of freedom, ms-mean square\*p value<.05 (significant).

**CONCLUSION**

Compared to conventional therapy bariatric surgery markedly improves diabetes and results in discontinuation or marked reduction of anti-diabetic medications in majority of patients treated, so bariatric surgery seems to be a better option for the obese diabetic patients.

**ACKNOWLEDGEMENT**

Authors are thankful to ethical committee of Moulana Hospital, Madavana, Pathaikara p. o Perinthalmanna, Malappuram, Kerala, pin 679322 for granting the approval for the study.

**CONFLICT OF INTERESTS**

Conflict of interest declared none.

**REFERENCES**

- Nocca D, Krawczykowsky D. A prospective multicenter study of 163 sleevegastrectomies. *Obesity Surgery* 2008;18:560-5.
- Pi-Sunyer X, Blackburn. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes. *Diabetes Care* 2007;30:1374-83.
- Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R. Medical management of hyperglycemia in type 2 diabetes. *Diabetes Care* 2009;32:193-203.

4. Garber A, Henry R, Ratner R, Garcia-Hernandez PA, Rodriguez-Pattzi H, Olvera Alvarez I, *et al.* Liraglutide versus glimepiride monotherapy for type 2 diabetes. *Lancet* 2009;373:473-81.
5. Raz I, Hanefeld M, Xu L, Caria C, Williams Herman D, Khatami H, *et al.* Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin as monotherapy in patients with type 2 diabetes mellitus. *Diabetologia* 2006;49:2564-71.
6. DE Mumme, Michal Mathiason, Kara J Kallies, B Shanu N Kothari. Effect of bypass surgery on HbA1c. *Surgery Obesity Related Disease* 2009;5:4-10.
7. Buchwald H, Estok R, Fahrbach K, Banel D, Jensen MD, Pories WJ, *et al.* Weight and type 2 diabetes after bariatric surgery. Systematic review and metaanalysis. *Am J Med* 2009;122:248-56.
8. D'Hondt M, Vanneste S. Laproscopic sleeve gastrectomy as a procedure for morbid obesity and resolution of comorbidities. *Surg Endosc* 2011;25:2498-504.
9. Dixon JB, Zimmet P, Alberti KG, Rubino F. Bariatric surgery: an IDF statement for obese Type 2 diabetes. *Diabetic Med* 2011;28:628-42.
10. Kalra S, Unnikrishnan AG. Obesity in India: The weight of the nation. *J Med Nutr Nutraceuticals* 2012;1:37-41.
11. Inghai A, Sharma P, Jha RK. Effect of sleeve gastrectomy and gastric bypass on diabetic Control in India. *Saudi J Obesity* 2014;2:59-62.