ABSTRACT

Today, obesity is one of the crucial public health concerns of the 21st century. Once, known as a condition of high-income countries, obesity rates are exploding worldwide. Unfortunately, over the past 3 decades prevalence of obesity has doubled and is the 5th leading cause of death worldwide. Data on global estimates for prevalence of overweight and obesity as given by WHO (2018), depicts that up to 2016, 1.9 billion adults (>18 years or older) were overweight (39%) and 650 million adults were obese (11%). Obesity is not just limited to adults but has also affected 41 million children under age of five. Globally, in 2015 increased BMI has contributed to 4 million deaths

Adiposity – Based Chronic Disease (ABCD) is a new diagnostic term for obesity. American Medical Association and Canadian Medical Association had started officially recognizing it as a disease. This terminology will help to diagnose amount, distribution and health impact of fat which BMI fails to do. This could also be one of the major factors contributing to the epidemic of obesity as there are many people who look thin and fall in a normal range of BMI but have high adiposity leading to a risk of co-morbidities and triggering the development of low-grade inflammation. Looking into the exploding prevalence of obesity even after what we have known so far, being reasonably dissatisfied there is a strong need to reevaluate strategies and focus on underlying mechanisms that control body weight, specifically hormones that resist weight-loss and mechanisms that we do not know.

In less than one decade there have been several studies on different kind of prebiotics and three of them namely Fructooligosaccharide (FOS) and Galactooligosaccharide (GOS) and Inulin-type fructan have gained a lot of limelight. Looking into the potential of FOS in modulating various health parameters like lowering cholesterol and insulin response, gut microflora, gut hormones, reducing appetite and inducing satiety, reducing adiposity and low-grade inflammation, studies are now diverting toward various food resources wherein they can extract FOS and reduce the cost. There are also several studies on

technological functionalities, sensory attributes, and rheological properties of FOS. Several products have been developed using FOS and trials are still going on around the world. FOS is also being added to the infant formulas and nutritional supplements. However, not all health regulatory bodies have approved FOS addition to infant formula.

The present study focuses on unraveling the potential mechanisms that can form a new line of treatment and help understand the newer aspects of body physiology responsible for the obesity epidemic. The present study aimed to prove four broad objectives (1) Snap-shoting the presence of obesity in young bank employees or urban Vadodara.(2) Comparison between baseline parameters of non-obese and obese bank employees with regards to Socioeconomic status (SES), anthropometric measurements, family medical history, personal medical history, defecation profile, personal habits, addiction profile, physical activity pattern, hunger and satiety scale, depression scores and dietary intakes, gut hormones (GLP-1, GIP, PYY, Leptin, Ghrelin and Insulin) and gut microflora (*Bifidobacterium, Lactobacillus, Clostridium* and *Bacteriodes*). (3) To study how efficiently FOS supplementation in obese subjects for a period of 90 days can change or modulate parameters in terms of anthropometric, biophysical measurements, dietary parameters, hunger -satiety scores, depression profile, defecation profile, fasting plasma levels of gut-hormones and gut flora. (4) Analyzing physical and organoleptic evaluation of FOS addition at varying levels in four popular Indian snacks having different cooking methods and comparing with their standard products (*Dudhi Muthiya, Vegetable Chilla, Handwa, Vegetable Mini Samosas*).

Cross-sectional study design for phase-I was used for screening 650 bank employees irrespective of age and gender for their anthropometric and biophysical measurements. Results revealed that 69% of bank employees were young and belonged to age group of 25 – 35 years. Overweight (20%), obese grade-I (34%) and obese grade-II (7%) all together accounted for 61% prevalence rate of BMI > 23 kg/ m^2. Mean values of BMI depicted all 650 bank employees to be overweight according to new Asia Pacific classification for Indians and 61% of them had increased risk of co-morbidities. Abdominal obesity, central obesity, and excess of body fat percentage were present in

44%, 56% and 58% of employees respectively. 68% of bank employees had elevated SBP and maximum were males (130.81 ± 13.59 mmHg). 42% had elevated DBP and 69% were hypertensive. On analyzing further, we found that hypertension and higher body fat % both coexisted in 42% of bank employees and their association was statistically significant ($\chi 2 - 11.11$, $p<0.001$). The odds' of developing hypertension by employees whose body fat % is also high was 1.74% and relative risk of 1.21%. The absolute risk reduction, the probability of not developing hypertension was 31% higher in employees who could manage to reduce their body fat%.

Convenient sampling design was used in Phase-II, for enrolling 150 non-obese and 150 obese grade-I bank employees for comparative analysis of their baseline parameters with respect to their anthropometry profile, biophysical profile, medical history, family history of diseases, defecation profile, hunger and satiety, depression status –BDI scale, habituation profile, dietary intakes – 24 hr, 3 days recall, gut satietogenic hormones (GLP-1, GIP, PYY, Leptin, Ghrelin and Insulin) using Luminex–xMAP technology and gut microflora (*Lactobacillus, Bifidobacterium, Bacteroides and Clostridium*) and understand the correlations amongst these parameters.

Phase-II results depicted obese employees having significant higher body fat % (27.85%) and higher BMR (28.35%), though it was not too high to induce weight loss. Probably it can be stated from this finding that with an increase in 1% of body-fat, BMR gets elevated by 1%. A higher percentage of obese employees (48%) had an excess of body fat along with 8% of non-obese employees with odds of 88.25%, RR-6.31 and RD – 79.03%. No statistical difference was observed in physical activity level of both the groups. Data on habituation profile revealed highest consumption of aerated drinks, tea and alcohol by 28% of obese employees. Also, 16% of non-obese employees were also habituated to the above beverages and this association was statistically significant (χ^2 - 17.53, $p<0.001$). On analyzing effect of habituation in non-obese group, data revealed that as degree of habituation increased, derangement in anthropometric and biophysical parameters was observed. It could be interpreted that development of obesity is directly proportional to degree of habituation. Clinical depression was more prominent in non-

obese (10%) and mild mood disturbance in obese (14%). Strong association (χ^2 – 10.5, $p<0.001$) was observed in the reported constipation by 11.67% obese (mildly constipated) and 6% non-obese (severely constipated) employees. Dietary data revealed significantly higher intakes of all macronutrients except fiber intake and delayed satiety during lunch, evening and dinner by obese employees as compared to non-obese bank employees. Fat intake was exceptionally high by 96.40% and 38.38% from RDA in obese and non-obese group. Colonization of obese gut was dominated by pathogenic bacteria *Clostridium* (4.32%) and non-obese by *Bifidobacterium* (4.27%) and *Bacteroides* (8.17%). Most of the gut hormones secretion was attenuated in obese employees (GLP-1 – 63.04%, GIP – 58.42%, PYY – 41.16% and Ghrelin – 56.14%). Leptin being directly proportional to fat, it was almost +200% higher in obese employees as compared to non-obese. Weight positively correlated with hypertension, defecation frequency, alcohol, tea, Leptin and Insulin. Weight also negatively correlated with depression, soluble dietary fiber, *Bacteroides*, GLP-1, GIP, PYY and Ghrelin. The strongest predictor of obesity to the accuracy of 58% in young bank employees was hormone PYY followed by soluble fiber, alcohol, tea, fat intake, *Bacteroides* count, Ghrelin and *Clostridium* counts.

For phase-III, double-blind, placebo-controlled randomized trial design was selected to assess the impact of 20g FOS intervention for 90 days on obese bank employees. Parameters similar to phase-II forming pre-intervention data were used for collecting post intervention data. Weight loss was the primary parameter. Obese employees (150) from phase-II were rolled over in phase –III and were divided in experimental group (N=75) receiving 20g FOS and placebo group (N=75) receiving 10g equicaloric maltodextrin.

Results revealed that FOS intervention for 90 days proved to be an effective supplement for achieving weight loss. Reduction in weight was observed to be 3.25% along with reduction in BMI (3.25%), WC (2.31%), WHR (1.07%), body-fat % (3.39%), SBP (1.51%). FOS also helped reducing hunger pangs and achieved early satiety during lunch and dinner. This was reflected in their reduced dietary intakes of total energy (8.84% - 247 kcal/day), CHO (8.67%), total Fat (10.78%). No significant difference was observed in protein intake. Weight loss brought positive impact on depression scores and reduction

by 26.77% was observed. FOS also normalized defecation profile and reduced flatulence. FOS intervention proved effective in sensitizing secretion of gut hormones and increase in plasma levels of GLP-1 (3.34%), GIP (0.77%), PYY (3.11%) and Ghrelin (14.77%). As hormone Leptin is directly proportion to body fat, reduction in plasma levels by 5.87% was observed along with optimum uptake of Insulin (6.23%). FOS modulated the obese gut by colonizing it with *Lactobacillus* (22.64%), *Bifidobacterium* (7.99%) and reducing *Clostridium* by 4.49%. No significant change was observed in counts of *Bacteroides*. *Bifidobacterium* positively correlated with GLP-1, PYY and negatively with Leptin. Ghrelin negatively correlated with soluble dietary fiber. Leptin positively correlated with BMR and negatively with PYY. Stepwise regression model summary revealed BMR as strongest predictor of obesity in Obese Population to the accuracy of 87%, followed by GLP-1 to the accuracy of 88%. Obesity can be predicted to the accuracy of 90% when all factors like BMR, GLP-1, satiety scores for dinner, total fiber intake and depression scores are considered

For Phase IV of study, FOS was added at varying levels of 5g, 10g, 15g, and 20g in selected four food products namely steamed *Dudhi Muthiya*, shallow fried *Vegetable Cheela*, baked *Handwa* and deep fried *Veg. Mini Samosa*. They were assessed for their physical and organoleptic properties. At 20g addition of FOS, results revealed reduction in WAP % by 25 – 50 % in all 3 products except *Veg. Mini Samosa.* Moisture loss was observed in *Handwa* (8.95%) and *Dudhi Muthiya* (15.67%). Moisture retention was highest in *Veg. Mini Samosa* (21.03%). Increase in percent yield and bulk density was also observed in all four products. Organoleptic evaluation revealed enhanced sensory attributes in three products up to 20g FOS addition except *Veg. Mini Samosa* which was acceptable up to 10g FOS addition.

Hence, obese phenotype definitely differs from non-obese phenotype with respect to significant statistical differences observed in baseline comparable parameters selected for the study. FOS is a promising supplement in achieving or maintaining a healthy body weight, improving defecation profile, healthy gut flora, modulating gut satietogenic hormones. This study also proves the existence of bidirectional mechanism and relationship between gut flora and gut hormones.