CHAPTER 1
INTRODUCTION

Earlier in India where under-nutrition was a biggest challenge today it is facing a dual burden of Malnutrition on extreme edges. Where undernutrion is on one edge, Obesity is the other extreme edge impacting drastically the "Weight of Nation", associated co-morbidities and the healthcare cost !!! (WHO, 2017; Kalra & Unnikrishnan, 2012). At simplest level we all know that, obesity is a mismatch between the energy intake and expenditure but it's not as simple as it seems. Unfortunately, if we look at the data over last 3 decades we have seen increase in obesity prevalence and current scenario has forced healthcare professionals to declare obesity as a "Disease". In last two decades there have been various terminologies coined for the word "Obesity" based on its exploding prevalence rates and associated co-morbidities. To name a few, it has been termed as "New World Syndrome" (Mohan et al., 2012), "Globesity" (WHO, 2001), and "Diabesity" (Ethan, 1973). Now it's time to consider newer approaches to evaluate, diagnose and to combat this epidemic of obesity.

Recently, in 2017 according to a new position statement released by the American Association of Clinical Endocrinologists (AACE, 2017) and the American College of Endocrinology (ACE, 2017) Obesity has bagged one more diagnostic term named "ABCD – Adiposity – Based Chronic Disease"**.** Since BMI being a one dimensional approach and unable to differentiate between fat and muscles, authors find BMI a bit vague as a sole diagnostic tool and have emphasized more on "complications-centric" three pronged approach that considers assessment of excess body fat in terms of amount, distribution and its physiologic impact on health (Kedist, 2017). In 2004, Portugal was the only country in entire Europe that officially recognized Obesity as "Disease" (The Lancet Editorial, 2017). Later it was followed by Scottish Intercollegiate guidelines network in 2010. Moving forward, American Medical Association (AMA, 2013) and Canadian Medical Association (CMA, 2015) official recognized Obesity as a Disease.

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 (WHO, 2018). Globally, in 2015 increased BMI has contributed to 4 million deaths (The GBD, 2015). Obesity and overweight is a primary initiator of developing chronic diseases, including type-2 diabetes, cardiovascular disease, hypertension, and stroke. The key causes are an increased consumption of energy-dense foods high in saturated fats and sugars (Karla & Unnikrishnan, 2012).

Obesity is not just aggrandizing alone but is also augmenting the prevalence of NCD's. Most of the literature had mentioned obesity as the gateway to all co-morbidities like cardiovascular diseases, diabetes, hypertension, stroke etc and is the single prime key modifiable risk factor for curtailing and /or ameliorating NCD's (WHO, 2018; EASO, 2017; Laura et al., 2012).

According to obesity update given by organization for economic cooperation and development (OECD, 2017), The self reported data for survey year 2015 India depicts 5% of total population aged 15 years and over as obese i.e. 65 million out of 1320 million total Indians were obese (Figure 2.3). Obesity rates in India have doubled in last 10 years. According to survey conducted by ministry of health and family welfare (MOHFW, 2016) and data recorded by national family and health survey (NFHS - 4, 2015-2016) for BMI >25 for 15 – 49 years population, 19% – 21% of population was found to be obese. Obesity was more prevalent in urban India (26% -31%) as compared to rural India Prevalence varies within the country because of differences in the lifestyle, mainly in the dietary patterns, and physical activity. In addition to this urbanization and industrialization are the main culprits for the increase in the prevalence of obesity. Unhealthy processed foods are now easily accessible due to India's integration in global food market (Gulati & Misra, 2017). Obese individuals exhibit unique features like excess body fat, abdominal adiposity, increased subcutaneous and intra-abdominal fat, and deposition of fat in ectopic sites (such as liver, muscle and others).

Apart from Dietary factors, consuming alcohol also affects components of energy-balance equation. Results of several review of literatures on alcohol and obesity demonstrates that heavy drinking is a major risk factor for obesity as compared with light to moderate intake.

Alcohol provides 7 kcal/g consumed and contributes to extra calorie intake, which is never compensated for (Traversy & Chaput, 2015; Yeomans, 2010). There are several health issues associated with alcohol intake, but relationship between alcohol intake and weight gain has been extensively explored in cross-sectional, longitudinal and experimental studies (Bendsen et al., 2013; Sayon-Orea et al., 2011; Yeomans, 2010).

Also, studies conducted by Röjdmark et al. (2008) and Raben et al. (2013) demonstrated that alcohol intake influences number of hormones linked to satiety. Alcohol may influence energy intake by inhibiting the effects of Leptin, or Glucagon-like peptide-1 (GLP-1). To date, the evidence suggests that alcohol does not appear to increase appetite through the action of Peptide YY (PYY), Ghrelin, Gastric inhibitory peptide (GIP), or Cholecystokinin (CCK) (Calissendorff et al., 2006; Manabe et al., 2013; Traversy & Chaput, 2015).

There are recent prospective studies that have demonstrated heavy drinking being strongly associated as a major risk factor for weight gain as compared to light-moderate drinking (MacInnis et al., 2014; Sayon-Orea et al., 2011; Schütze et al., 2009; Rissanen et al., 1991).

The World Health Organization statistics (2013) has described depression as “The number one cause of disability in the United States and the third largest, behind heart disease and stroke, in Europe” (World Health Statistics, 2013). Dr. Michael Craig Miller, an assistant professor of psychiatry at Harvard Medical School explains that depression and obesity feed each other. "Obesity affects parts of the brain that regulate your mood. When you're depressed, low energy and motivation can translate into less activity and exercise, this may result in weight gain” (Havard Health Letter, 2013).

Hunger and satiety regulation and body weight is a homeostatic process. This homeostasis is maintained by Long-term hormonal signals and short-term neural signals. Long–term hormonal signals communicate information regarding general health and short-term signals regulate meal initiation and termination by neural signals from brain and hormonal signals from the gut (Perry & Wang, 2012; Wilding, 2002).

Gut hormones like Ghrelin, Glucagon –like peptide (GLP-1), Peptide YY (PYY), Pancreatic polypeptide (PP) and Cholecystokinin (CCK) are known to induce satiety and meal termination leading to dramatic impact on energy balance homeostasis (Mishra, 2016). Leptin and Ghrelin hormones regulating energy homeostasis through neuroendocrine control develop resistance. The development of resistance of both hormones is a hallmark of obesity (Figure 2.13). However, strategies that were developed till date to slow down the current epidemic of obesity have been hampered. This is attributed largely to lacking knowledge owing to the underlying mechanisms and their resistance to the action of hormones (Cui, Lopez & Rahmouni, 2017).

There are several tenable factors that play role in development of obesity but role of gut microflora plays a very important role. People these days can now be identified based on the structure of individuals gut microbiota using microbiota "fingerprints" with help of metagenomics approach (Dahiya & Puniya, 2017; Franzosa et al., 2015).

Disequillibrium in energy homeostasis being the prime reason of obesity could be induced by dysbiosis in gut microbiota. In experimental model there are numerous mechanisms by which gut microflora induces obesity. However, specific microbial community that is directly linked to obesity is unknown due to its complex nature (Dahiya & Puniya, 2017). Recent studies provide evidence for the paramount role of gut microflora present in the human GI tract in the onset and establishment of obesity. The nutrient acquisition and energy homeostasis gets affected by the adhered gut microflora and influences the number of effectors' molecules that decide fat storage in adipocytes (Dahiya & Puniya, 2017; Rosenbaum, Leibel, 2015).

Since, microbiota has a crucial role in obesity then probably the phenotype of obese individuals should have a distinct microbial composition than lean individuals (Ley et al., 2005). During the study conducted on ob/ob mice, lean ob/C and wild-type counterparts analyzing differences in their gut microflora Ley et al. (2005) found that genetically obese mice had less of *Bacteroidetes* and more of *Firmicutes* as compared to lean mice. The concept of prebiotic came into existence before 2 decades. The original definition of prebiotic was given by Gibson and Roberfroid (1995).

Since it's well known that all prebiotics are dietary fibers, but not all fibers can be classified as prebiotics. For any food ingredient to qualify as a prebiotic, the scientific prerequisites for that ingredient as specified by Gibson and Roberfroid (1995) are:

- Food ingredient should resist gastric acidity, hydrolysis by mammalian enzymes and absorption in the upper gastrointestinal tract;
- Is fermented by the intestinal microflora;
- Selectively stimulates the growth and or activity of intestinal bacteria potentially associated with health and well-being.

(Slavin, 2013; Gibson & Roberfroid, 1995)

Oligofructose is a potential prebiotic candidate that enhances satiety and has positive organoleptic properties that would foster incorporation into a variety of foods (Boulangé et al., 2016; Van Hoffen et al., 2009; Cani et al., 2006; Daddaoua et al., 2006; Delzenne et al., 2001). The mechanisms by which oligofructose enhances satiety may involve fermentation by select bacterial strains and increased production of short-chain fatty acids in the gut lumen (Boulangé et al., 2016; Parnell & Reimer, 2013; Pylkas, Juneja & Slavin, 2005). The effectiveness and mechanisms by which oligofructose may act to promote weight loss in humans warrant further investigation.

Gut satietogenic hormones like glucagon like peptide-1 (GLP-1), gulucose-dependent insulinotropic hormone (GIP), and Peptide YY (PYY) are secreted in response to meal and they are regulated by the communication between gut and hypothalamus in brain that

control energy balance (Mekkes et al., 2014). There are very few human studies on gut hormones and their role in obesity. Results of these studies have indicated diminished plasma concentrations of GLP-1, GIP and PYY in obesity (Lean & Malkova, 2016). When these secretions of gut hormones are impaired they may induce development of obesity or also may hinder weight loss or both together. There are ample evidences based on human trial on FOS as a prebiotic. There are several studies on infants, as well as in animal and in vitro studies depicting that, prebiotics even at a very low dose of 5-8 g/day significantly amplifies fecal *Bifidobacteria* and sometimes *Lactobacillus* (ILSI Europe, 2011), however its potential to enhance satiety has to be further validated.

In human interventional studies prebiotic fiber have been reported to be involved in appetite regulation by modulating gut peptides, induce satiety and increase breath-hydrogen excretion. It also prompted the growth of *Bifidobacteria* and *Lactobacilli.* However, it was unknown whether these prebiotic fibers stimulated growth of whole *Bifidobacteria* genus or a particular species (Dahiya & Puniya, 2017; Parnell & Reimer, 2009; Cani et al., 2009b, Cani et al, 2006; Gibson et al., 2004).

In a randomized clinical trial on FOS supplementation in healthy obese adults of 21g/d for 3 months in experimental group demonstrated decreased food intake, body weight gain (1.03 ±0.43 kg, $p<0.01$) and fat mass development in obese subjects of experimental group, making evident weight reduction properties of prebiotics. The investigators also found higher plasma PYY levels following a meal, along with drop in Ghrelin over a 6 – hour meal tolerance test (Parekh et al., 2012; Parnell & Reimer, 2009).

Vandeputte et al. (2016) initiated a randomized, double-blind, placebo-controlled, cross-over trial. Chicory-derived Orafti inulin was supplemented to healthy adults with mild constipation with dose of 12 g/day of for a 4-week treatment period. Study results established significant increase in stool frequency resulting from inulin consumption (Micka et al., 2017) leading to a first positive opinion by the European Food Safety Authority on chicory inulin and 'maintenance of normal defecation' (EFSA Panel, 2015)

Obesity primarily being a state of energy imbalance, it becomes sort of mandatory to develop "designer novel foods" that can dilute the energy density of foods without compromising on the sensory and organoleptic attributes and in addition promotes satiety. Eventually, these "designer foods" would provide first line of defense in maintaining energy homeostasis (Valéria Maria et al., 2011; Amar et al., 2008).

Hence, the present study entitled "Acceptability Trials of Fructooligosaccharide (FOS) Added Popular Indian Recipes and Impact Evaluation of FOS Intervention in Modulating Gut Microflora, Gut Satietogenic Hormones and Anthropometric Indices of Young Obese Bank Employees of Urban Vadodara: A FAT – FIT Study" was undertaken in 4 phases with following objectives:

OBJECTIVES

PHASE I – SNAP-SHOTING THE PRESENCE OF OBESITY IN YOUNG BANKS EMPLOYEES OF URBAN VADODARA

- Screening the subjects from various banks of Vadodara city for their anthropometric measurements, body composition analysis, random blood sugar and blood pressure.

- To classify screened bank employees in various categories of BMI
- Determining presence of obesity according to WC, WSR, WHR and Body- fat percentage in screened bank employees
- Determining the presence of hypertension in screened bank employees
- Associations and correlation amongst anthropometric and biophysical parameters of screened bank employees

PHASE II–COMPARISON BETWEEN BASELINE PARAMETERS OF NON-OBESE AND OBESE BANK EMPLOYEES WITH REGARDS TO:

- Socio economic 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 of non obese and obese subjects

- To study Gut-microflora of non-obese and obese subjects with regards to
  - *Bifidobacterium*, *Lactobacillus*, *Clostridium* and *Bacteriodes*

- To determine the baseline levels of six Gut-hormones

  - Glucagon-like Peptide -1 (GLP-1) - Gut Incretin

- Gastric Inhibitor Polypeptide (GIP) - Gut Incretin
- Peptide YY (PYY) - Anorexogenic hormone
- Ghrelin (Hunger hormone) - Orexogenic hormone
- Leptin (Energy Expenditure hormone) - Anorexogenic hormone
- Insulin - Anorexogenic hormone

- Correlation of weight with various parameters of non-obese and obese bank employees and regression analysis to identify strongest predictor of obesity

PHASE III – TO STUDY IMPACT OF FOS INTERVENTION FOR 90 DAYS IN OBESE SUBJECTS: A RANDOMIZED CONTROL TRIAL

To study how efficiently FOS supplementation in obese subjects for period of 90 days can change or modulate parameters in terms of:

- Anthropometric and biophysical measurements
- Dietary parameters, hunger and satiety scores
- Depression and Defecation profile
- Fasting plasma levels of gut-hormones : GLP-1, GIP, PYY, Ghrelin, Leptin and Insulin post intervention
- Gut-microflora: *Bifidobacteria, Lactobacillus, Clostridium, Bacteriodes* post intervention
- Correlation of gut-hormones and gut-microflora with various parameters
- Regression analysis for identifying strongest predictor or obesity in obese bank employees
- Follow up data for time-point interval analysis

PHASE IV– ACCEPTABILITY TRIALS OF FOS ADDED POPULAR INDIAN RECIPES

- Analyzing physical properties of FOS addition at varying levels in four popular Indian snacks having different cooking methods and comparing with their standard products namely:

    - *Dudhi Muthiya* - Steamed
    - *Vegetable Chilla* - Shallow fried
    - *Handwa* - Baked
    - *Veg. Mini Samosas* - Deep Fried

- Conducting the organoleptic evaluation of the developed products using 9 point Hedonic scale.