

## Editorial

### **RICH WITH RUPEES OR RICH IN GOOD GUT MICROBIOTA: WHAT IS MORE IMPORTANT FOR OUR METABOLIC HEALTH?**

Metabolic good health signifies normal blood pressure, good glycemic control, normalcy in lipid profile, normal BMI and waist circumference. Good metabolic health signifies good cardiovascular health. To be healthy we should have good metabolic parameters.

Metabolic syndrome defined as central obesity (waist circumference more than cut off as per ethnicity) plus any two of the following entity like

1. Increased triglycerides  $\geq 150$  mg/dL (1.7 mmol/L) or specific treatment for this abnormal lipid.
2. Decreased HDL cholesterol  $< 40$  mg/dL (1.03 mmol/L) in males  $< 50$  mg/dL (1.29 mmol/L) in females or specific treatment for this abnormal lipid.
3. Increased blood pressure systolic BP  $\geq 130$  or diastolic BP  $\geq 85$  mm Hg or treatment of previously diagnosed hypertension.
4. Increased fasting plasma glucose (FPG)  $\geq 100$  mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes If more than 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

If BMI is  $>30$ kg/m<sup>2</sup>, no need to measure waist circumference, central obesity can be assumed (IDF Communications 2006). In South Asian population central obesity is defined as waist circumference more than 90 cm in male and more than 80 cm in female (Tan *et al.* 2004).

Metabolic good health means absence of metabolic syndrome. It is now important to see the role of good gut microbiome in maintaining metabolic good health. Financial wellness is generally directly proportional to non-communicable especially metabolic disease related illness. In a recently published article, it was mentioned that rising trend in diabetes is much higher in urban population than rural population in India (Gupta and Misra 2007). Inactivity, bizarre food habits, stressful lifestyle and inadequate sleep generally disturb the healthy milieu of metabolic system in financially healthy person. Let us review some evidences to see the effect of good gut microbiota in maintaining good metabolic health. It is not our bank balance which is necessary to have good metabolic health; it is our good gut microbiotas which determine good metabolic health.

It may sound surprising that are we really human or something else. Human body is comprised of 100 trillion bacterial cells (Reid and Greene 2014). Previously it was estimated that human cells are 1/10<sup>th</sup> of bacterial cells but newer researches suggest that we are 1/3<sup>rd</sup> to equal number of bacterial cells (Sender *et al.* 2016). In a lighter note with each act of defecation our human cells may have experience majority in the bacteria cell, dominant parliament. Human body can be considered as a house of good gut microbiota. If residents are good, they will make or maintain house healthy. If they are bad, they will surely destroy house. So, it is our responsibility to allow good residents to remain inside us. Gut microbiota helps host in energy metabolism, immune responses, vitamin synthesis, epithelial development and nutrient digestion and synthesis (Tappenden and Deutsch 2007, Flint *et al.* 2007). Generally human gut has the “big four”, firmicutes, bacteroidetes, actinobacteria, and proteobacteria (Dethlefsen *et al.* 2007). Among them firmicutes and bacteroidetes phyla are the major contributors.

First interaction with human and gut microbiota happens during child birth. Vaginal and C- section delivery lead to two different gut microbe environments. Researcher showed C- section delivery destroys mother-to-neonate transmission of specific microbial strains, associated coordinated microbial functions and immune-stimulatory potential during a critical window for neonatal immune system priming (Wampach *et al.* 2018). Neonatal stool (days after birth) were found with similar cluster when matched with stool, vaginal swabs, or breast milk of the mother. But this pattern quickly changes over the next days. Newborn gut is colonized with bacteria from mothers but within a few days it changes and gets his new gut microbiota profile. It is found that environment actually plays the greater role than genetic relationship behind the specific nature of gut microbiota colonization (Palmer *et al.* 2007).

If we lack our good old friend and allow enemies to grow up in gut, it will produce serious threat to our metabolic health. Decrease in short chain fatty acids (SCFAs) producing beneficial bacteria and increase in opportunistic pathogens produces ‘Gut Dysbiosis’ which leads to increase in insulin resistance, increased gut

permeability, endotoxemia, raised pro inflammatory cytokines, increase calorie intake. These all factors are responsible for metabolic syndrome (Boulangé *et al.* 2016). Anti-inflammatory species like bifidobacteria, lactobacilli, *Faecalibacterium prausnitzii* (*Clostridiaceae* phyla), *Bacteroides thetaiotamicron* (*Bacteroidetes* phyla) can be destroyed by high fat and high sugar diet, stress and antibiotics and produce proinflammatory species like *Bacteroides* spp. (*Bacteroidetes* phyla), *Clostridium difficile* (*Firmicutes* phyla). Healthy diet and lifestyle, prebiotics, probiotics, fecal transplantation can convert pathobiont predominated gut to symbiont predominated one. It is extreme important to maintain gut microbial ecology to prevent metabolic diseases (Zhang *et al.* 2017). Obesity and related metabolic bad outcomes are related to complex multidirectional interaction between host genetics, environment, diet and the gut microbiota. It was found that in metagenome wide association study, type 2 diabetes patients have a moderate degree of gut microbial dysbiosis, decrease in the abundance of some universal butyrate-producing bacteria and increase in various opportunistic pathogens (Qin *et al.* 2012). TMAO and choline level increased in western diet fed mice which is associated with cardiac fibrosis. Those mice showed increased expression of TNF alpha and interleukin 1 beta- two pro inflammatory markers (Chen *et al.* 2017). Production of TMAO is associated with gut microbial dysbiosis. To treat gut microbial dysbiosis we have options like:

**Eating right:** Recent evidences suggest vegan diet has beneficial metabolic effects compare to non-vegan diet. Stress should be given in terms of more fruits, vegetables, whole grains. “Eating a plant-based diet with ample fibre changes the gut microbiome composition for the better by feeding the right kind of bacteria notably short-chain fatty acid producing *Faecalibacterium prausnitzii*, which deliver many metabolic benefits including weight loss, increased insulin sensitivity, and fat loss, including visceral fat loss” noted by Dr. Hana Kahleova, Director of clinical research at the Physicians Committee for Responsible Medicine (PCRM), Washington DC.

**Using probiotic and prebiotic:** Prebiotic is defined by product which promotes growth of microorganisms which are beneficial to human. They are type of fibre that the human body cannot digest. They serve as food for microorganism. Probiotic is live beneficial microorganism which is usually present in yogurt and different fermented products. It is available as capsules also.

**Restricting antibiotics:** Antibiotics kill good gut microbiota. Unnecessary usage of antibiotics may lead

to gut dysbiosis. Antibiotic and one health approach is a common area of concern now in view of antibiotic resistance. Gut microbial disturbance can also occur by consumption of animal meat that is exposed with antibiotics. Antibiotics treated children during the first 3 years of life have different gut microbiome compositions (Yassour *et al.* 2016). A course of macrolide antibiotics leads to a long-lasting change in the gut microbiota in children which may be associated with obesity and asthma in later life (Korpela *et al.* 2016).

**Use of proper anti-diabetic drugs:** In diabetes patients two anti-diabetes drugs metformin and acarbose have favourable effects on gut microorganisms. Metformin increases the abundance of *Akkermansia* spp., a mucus-degrading Gram-negative bacterium, in the gut. It restores reduced regulatory T (Treg) cells and ameliorates low-grade tissue inflammation in the adipose tissue of obese animals. Metformin increases life span of *Caenorhabditis elegans* which is also a symbiont (Hur and Lee 2015). Among alpha glucosidase inhibitors acarbose increases production of short chain fatty acids and hydrogen gas by fermentation of polysaccharides which reduce pro-inflammatory cytokines, like IL-1 $\beta$ , TNF- $\alpha$  and IL-6 in inflammatory tissues (Joshi *et al.* 2015). This feature of acarbose may be causing cardiovascular benefit. Indirectly acarbose acts as a prebiotic and helps to fight for the host against dysbiotic gut.

**Faecal microbiota transplantation (FMT):** Faecal transplant is a futuristic option to treat metabolic syndrome. FMT has shown great success in managing recurrent *Clostridium difficile* infection. But though evidences are less but theoretically it has a great probability to have grand success in preventing and treating metabolic diseases. So, time will say whether financially rich but metabolically poor individual who have more bad gut microbiota will seek help from financially poor but metabolically and good gut microbiota wise rich fellow to borrow their gut microbiome in terms of faecal microbiota transplantation.

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