GENETICS OF OBESITY: THE RISE OF NEUTROGENETICS, ASIAN ADIPOCYTES AND STRATEGY TOWARDS PREVENTING OBESITY

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ABSTRACT

Obesity has recently reported to be a pandemic. Multiple factors such as individual’s genetic susceptibility, increased availability of high caloric and energy-dense food and sedentary lifestyle are involved that contribute to the development of obesity. Although much research on obesity has been conducted for the past few decades, yet the clear understanding regarding the causes and treatment of obesity remains unclear since a comprehensive study on the field of obesity still has not been explored extensively. The emergence of nutritional genomics which combines multiple elements such as health, diet, and genomics should be the driving force of future nutritional research to provide clear understanding on how obesity develops from the perspective of molecular nutrition to the prevention of disease. However, challenges are still there to identify the real potential cause of obesity and its associated disease and the adoption of current knowledge for more applicable and personalized dietary intervention strategies to combat diet-related disease still requires a lot of effort to break the molds of traditional nutrition research concentrated on nutrient deficiencies and deterioration of health.

KEY WORDS: Obesity, Genetics, Westernization, Single nucleotide polymorphisms (SNPs), Genes, Nutrigenomics.
INTRODUCTION
The prevalence of obesity has increased significantly throughout the world but the distribution differs across the region. Obesity is perhaps the most prevalent form of malnutrition, as a chronic diseases prevalent in both developed and developing countries, and affecting children as well as adults. From 1988 to 1994, the third National Health and Nutrition Examination Survey in the United States revealed that approximately 20% and 25% of US men and women were obese[1]. The increasing prevalence of obesity also has been reported in the United Kingdom from 7% to 16% from the year of 1980 until 1995[2]. Asian countries are not spared of this scourge when the prevalence of obesity has increased dramatically over the period of time. A pronounce increase has been reported in China when the proportion of Chinese men with a body mass index (BMI) >25kg/m2 almost tripled from 5% to 14.1% of the population and in women has doubled from 10.4% to 20.8% [3]. A study on the epidemic of obesity which covers several developing countries indicate the prevalence of overweight (body mass index >25kg/m2) for men and women ranged from 13.4% in Indonesia to 32.5% in Singapore[4]. In Malaysia, a rapid increase in the prevalence of obesity has been under the spotlight when the second and third National Health and Morbidity Surveys in 1996 and 2006 respectively, reported a three times increase of obesity cases among adults, escalating from 4.4% to 14% over the 10-year period[5]. The escalating population prevalence of obesity have been reported in the Pacific region as the proportion of men and women with a BMI of >30kg/m2, in Nauru was 77% in 1994[6], whereas; the prevalence rates for Pacific populations living in New Zealand in the early 1990s were about 65-70% [7]. The high prevalence rates of obesity also have been reported in urban Samoa where the percentage for adult women and men were 75% and 60% respectively[8]. Obesity is regarded as a major threat to the public health in the United Arab Emirates that might play important roles in the emergence of other chronic diseases[9]. The obesity epidemic is generally regarded as a villain of the piece with its associate disease and co-morbidities that threatens the global well-being. Obesity has been reported as a major risk factor for cardiovascular diseases, metabolic diseases (such as type 2 diabetes and dyslipidemia), osteoarticular diseases and several forms of cancer [10]. Obesity ranked the 6th most important risk factor contributing to the overall burden of disease throughout the world[11]. From an economic standpoint, overweight and obesity pose both substantial direct costs in which various intervention strategy have to be taken to combat obesity epidemic, to perform diagnosis and treatment services, whereas; indirect costs is explained as productivity decline in terms of national source of revenue.
as well as future earnings lost due to premature death for the health care system\textsuperscript{[12,13]}. Obesity (defined as a BMI above 30kg/m2) is associated with increased body fat and its physiological to pathophysiological effects at individual's level is not very well understood. There is a call for collaborative works among scientists from various disciplines such as nutrition, molecular biology, medicine, genomics and bioinformatics\textsuperscript{[14]} to perform an in-depth study on obesity as per our understanding on how obesity epidemic emerge at an alarming rate through a population remains a challenge, since the pattern is somewhat consistent over time and vary between low and high income countries\textsuperscript{[15]}. In low income countries, obesity is prominent among middle-aged women whose living in urban communities with a background of higher economic status. Otherwise, obesity in affluent countries is apparent among women, with lower socio-economic status and rural communities\textsuperscript{[16,17]}.

The Nutrition Shifting

The rapid phase of westernization, modernization and mechanization in most countries throughout the world is associated with shifts in dietary patterns towards the consumption of high fat and energy-dense food as well as the critical reductions in physical activity\textsuperscript{[15,18,19]}. In many low to-middle-income countries, the levels of overweight and obesity increased at a very significant level, surpassing those in the USA, and this burden is commonly associated with poverty and under-nutrition \textsuperscript{[19]}. A marked decrease in cost of vegetable oils and sugar outcompetes with cereals as the inexpensive food ingredients in the world, thus influence the rate of food intake derived from grain and grain products and has increased global average energy consumption despite the increase is unevenly distributed throughout the world’s population\textsuperscript{[20,19]}. Paradoxically, rapid urbanization and the growing incomes has the profound impact on the diet patterns as the traditional diets, rich in fibers and grains were replaced with diets high in sugar, fat and animal products\textsuperscript{[19,20]}. The westernization of global eating habits provide evidence on how fast foods, soft drinks and increased meat consumption has replaced the ethnic cuisine and unique traditional food habits\textsuperscript{[20,15]}. Thus, increased energy density due to the homogeneity and westernization of the global diet has become a problem among the poors in the countries, which are highly susceptible to both obesity and micronutrient deficiencies\textsuperscript{[15,20,21]}.

Factors Influencing Obesity

Obesity cannot be regarded as a single disorder. Rather, obesity develops by a heterogenous
group of conditions with multiple causes[22]. Human body weight is determined by an excellent combination between genetic, environmental and psychosocial factors that acts through the physiological mediators of energy intake and expenditure[22]. Although the marked increase in the prevalence of obesity would be best explained by behavioral and environmental changes due to technological advances[22], we would like to focus on the role played by the genetic factors in this review. An excellent review by Ordovas regarded obesity as the modulator effects of genotype-phenotype associations for multiple candidate genes on the phenotypic expression associated with the metabolic syndrome[23]. A known gene variants at several reported candidate genes such as adiponectin[24], Angiotensin 1-converting enzyme[25], Apolipoprotein A5[26], Cholesteryl ester-transfer protein[27], linkage signal on chromosome 1[28], Selectin-E[29], G-protein beta-3[30-32], interleukin-6[33], hepatic lipase[34], and Peroxisome proliferator-activated receptor-gamma[35] have shown similar modulating effect of obesity or BMI on genotype-phenotype associations related with cardiovascular disease (CVD) risk or metabolic syndrome[23]. Observable features in common by which SNPs in those genes have been associated with increased risk phenotype, where obesity act as an effect modifier[23] for inter-individual responses in the above mentioned genes.

CONCLUSIONS

It is of paramount importance to realize that nutrition is the most important environmental factor that regulates the gene expressions and its observable attributes[21]. Thus, the close interrelationships between genes and nutrition is undeniable and this paradigm contributes to the basis of the development of nutritional genomics, a highly potential new developing research area that could provide better results by which in the future could change the dietary disease prevention and therapy to break the molds of traditional nutrition research based solely on nutrient deficiencies and health deterioration[2,3,14]. Nutritional genomics (nutrigenomics) is a result of a combination of multiple areas between health, diet and genomics could provide the basis for individualized dietary recommendations based on individual’s genetic make-up besides other factors such as gender and obesity provided by both complete sequencing of individual’s genome as well as ascertainment of all informative SNPs[14,23]. This new area of research would create remarkable opportunities for us to seek knowledge and information regarding the gene-nutrient interactions as well as protein expression while influencing cellular and organismal metabolism[14]. Thus, nutrigenomics is of equal importance with other health-based research area which helps to promote an
increased understanding of how nutrition acts as a modulator to regulate metabolic pathways and homeostatic control, how the regulation is disrupted in the initial phases of diet-related disease, and to what extent a genetically susceptible individual would contribute to such diseases\textsuperscript{[14]}. In Malaysia, little is known about nutritional genomics and even the diet practitioners are keen to learn and increase their knowledge on human genetics and nutrigenomics\textsuperscript{[36]}, much remains to be done to ensure the right accomplishment of this goal including the combination of several research areas and coordinating work in the laboratory\textsuperscript{[23]} in order to help in developing a much better and personalized dietary intervention strategies for the sake of successful and healthy aging of our generations in the future.

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