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REVIEW-INVITED ARTICLE

Nutrigenomics research: a review

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Abstract The excitement about nutrigenomics comes from a growing awareness of the potential for modifications of food or diet to support health and reduce the risk of diet-related diseases. It is an emerging field that tends to unfold the role of nutrition on gene expression which brings together the science of bioinformatics, nutrition, molecular biology, genomics, epidemiology, and molecular medicine. The present review focuses on nutrigenomics research and to find out India's status with respect to other countries. It covers the general overview of nutrigenomics, its associated diseases, and the role of SNP in gene alteration, diet supplementation and public awareness. It is understood that with the increasing changes in the food habits and life styles, people are becoming more prone to diet related disorders. Therefore there is an urgent need to boost more research in this field to help people in understanding the relationship between diet and health, and to ensure that everyone benefits from the genomic revolution.

Keywords Nutrigenomics · Diet-gene interaction · Nutrition · Food supplement · Diabetes · Obesity

Introduction

"The new science of nutrigenomics teaches us what specific foods tell your genes. What you eat directly determines the genetic messages your body receives. These messages, in turn, control all the molecules that constitute your metabolism: the molecules that tell your body to burn calories or store them. If you can learn the language of your genes and control the messages and instructions they give your body and your metabolism, you can radically alter how food interacts with your body, lose weight, and optimize your health." (Mark Hyman 2006)

Origin of nutrigenomics The concept that diet influences health is an ancient one. Nutrigenomics includes known interactions between food and inherited genes, called 'inborn errors of metabolism,' that have long been treated by manipulating the diet. One such example is Phenylketonuria (PKU); it is caused by a change (mutation) in a single gene. Affected individuals must avoid food containing the amino acid phenylalanine. Another example is lactose intolerance, majority of adults in the world are lactose intolerant, meaning that they cannot digest milk products, because the gene encoding lactase, the enzyme that breaks down lactose, is normally 'turned off after weaning. However some 10,000–12,000 years ago a polymorphism in a single DNA nucleotide appeared among northern Europeans. This single nucleotide polymorphism—a SNP—resulted in the continued expression of the lactase gene into adulthood. This was advantageous because people with this SNP could utilize nutritionally-rich dairy products in regions with short growing seasons and with the revolution in molecular genetics in the late twentieth century, scientists set out to identify other genes that interact with dietary components. By the 1980s companies were commercializing nutrigenomics. The Human Genome Project of the 1990s, which sequenced the entire DNA in the human genome, jump-started the science of nutrigenomics. By 2007 scientists were discovering numerous interrelationships between genes, nutrition, and disease.

Nutrigenomics brings along new terminology, novel experimental techniques and a fundamentally new approach to nutrition research, such as high-throughput technologies that enables the global study of gene expression in a cell or organism.

Nutrigenomics would require a collaborative effort from people in genetics and the industries of public health, food

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science and culinary. It's very easy to make good-tasting food. Put some lard or butter in it, and it's going to taste good. The challenge is how to take the fat out and create healthful but also good-tasting food." Therefore a shift in public health is greatly needed, and with an increasing incidence of obesity and chronic diseases such as type-2 diabetes, nutrigenomics might prove to be the panacea in the future.

Increasing rates of chronic disease

World health scenario Despite the worldwide increasing rates, chronic diseases remain surprisingly neglected in the global health agenda. Because of changes in dietary and lifestyle habits—a phenomenon that can be linked to the whole globalization process—developing countries now face a fast "epidemiological accumulation" of non-communicable and infectious diseases and must cope with urgent and competing health priorities. Non-communicable diseases (NCDs)—especially cardiovascular diseases, cancers, chronic respiratory diseases and diabetes—caused 60 % deaths globally in 2005 (approximately 35 million deaths). Total deaths from NCDs are projected to increase by a further 17 % over the next 10 years. By 2020, it is predicted that NCDs will account for 80 % of the global burden of disease, causing seven out of every 10 deaths in developing countries. This places a considerable (double) burden on limited health budgets, particularly in emerging economies. Thus the promises of nutrigenomics must be addressed with respect to this current growing epidemic, both in developed and developing countries (Gobard and Hurlimann 2009).

India's health scenario In India, the rates of fatal diseases are lower than those seen in Western countries. However, this rate is rising with increasing migration of rural population to cities and changes in lifestyles (Rao 2001; Shetty 2002; Sharma and Majumdar 2009). In recent decades, consumption of food grains also has shifted from coarse grains to refined rice and wheat (Sinha et al. 2003) (Table 1).

India has some of the highest Coronary Heart Disease (CHD) rates in the world, with urban rates being three times higher than rural rates. In addition, rates for obesity (Fig. 3a and b) and diabetes are increasing dramatically in urban areas and in high-income rural residences (Sinha et al. 2003) (Fig. 1). Obesity is related to several chronic diseases, including type-2 diabetes, hypertension, cardiovascular diseases, various types of cancers and psychosocial problems. The major reasons for its development are changing lifestyles and food habits. Diet appears to be related to the high rates of CHD, obesity, and diabetes (Hossain et al. 2007; Kaput et al. 2007); although a genetic component may exist in some cases (Fig. 2). Therefore, a general awareness of diet and diet related problems leading to gene alteration has to be known and for this nutrigenomics should be studied extensively (Fig. 3).

Table 1 Change in dietary pattern

Nutrients	Paleolithic diet	Modern Diet
Protein ~	30–40 %	10–20 %
Carbohydrates ~	35 %	60–70 %
Sugars ~	2–3 %	15 %
Fats ~	30–35 %	30–35 %
Saturated fats ~	7.5 %	15–30 %
Trans-fat	< 1 %	5–10 % of fats
Omega-6/omega-3 ~	2:1	10–20:1

Source: Melvyn A Sydney-Smith

Global status of nutrigenomics research (as per Scopus database)

Country-wise and subject-wise analysis To unravel the mystery of these chronic diseases, nutrigenomics work is booming in many parts of the world. According to Scopus database, US and UK have the highest contribution, while India is in 16th position, suggesting that nutrigenomics research in India is still in the infancy. This data was obtained by giving the following search terms: "Nutrigenomics", "Nutrigenetics", and "Diet-gene interaction" in Scopus database. A total of 1072 records were obtained which were refined on the basis of document type. The 769 records obtained after refining were then analysed. The contribution of top 20 countries shows that India has only 14 papers while US and UK have 210 and 97 papers respectively as per the Scopus results (Fig. 4). Subject-wise analysis shows that nutrigenomics work is mainly done in the fields of Medicine; Biochemistry, Genetics and Molecular Biology; Agricultural and Biological Sciences and Nursing (Fig. 5).

Objective

The present review aims at giving an insight on the nutrigenomics research (focusing on India) so as to bring

- public awareness about the changing lifestyle and food habits,
- how nutrigenomics can contribute in making life longer, healthier and better,
- encourage more research in this field.

Methodology

A literature search on nutrigenomics focusing on India was conducted by using various databases: Web of Science, Bio

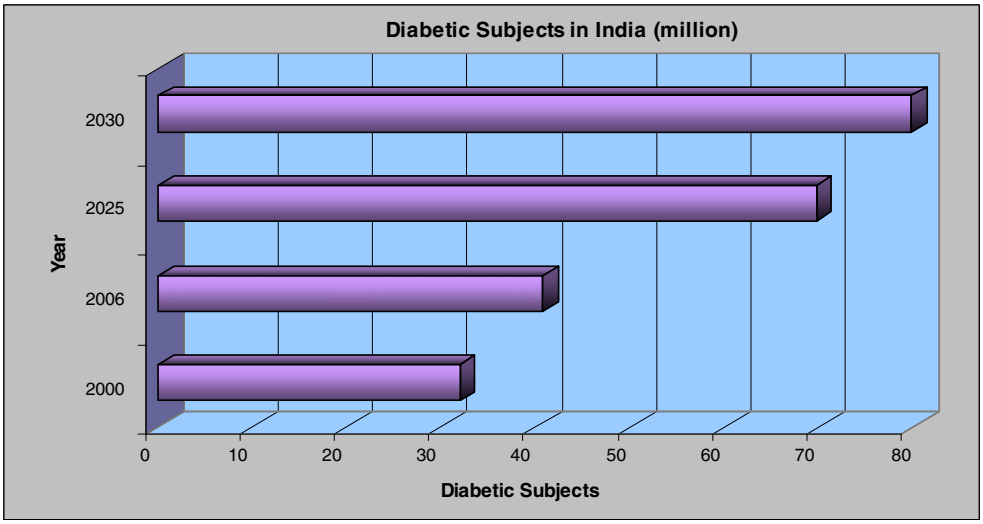

Fig. 1 Estimated number of Diabetic subjects in India. Source: Mohan et al. 2007a, b

Med Central, Taylor & Francis, PubMed, Science Direct, Springer and National Center for Biotechnology Information (NCBI) and Scopus Database to find out the global status of nutrigenomics research. The study used the following search terms: Nutrigenomics India, Nutrigenetics, Diet-gene Interaction, Gene-Environment Interaction, and Nutraceutical etc. We also examined bibliographies of all studies for other potential citations. Although these databases covered many papers on Diet-gene interaction but few papers were found on nutrigenomics work in India. Other than nutrigenomics we have also reviewed some of the works done in the areas of diet supplementation, deficiency diseases, diet-gene interaction, dietary guidelines etc.

Nutrigenomics overview

Throughout the 20th century, Nutritional Science focused on finding vitamins (Ghoshal et al. 2003) and minerals (Menon et al. 2010), defining their use and preventing the deficiency diseases (Gopalan 1992; Godbole et al. 2009; Rao 2001; Naushad et al. 2010) that they caused. As nutrition related health problems of the developed world shifted to overnutrition, obesity (Raj et al. 2007) and type-2 diabetes (Mohan et al. 2007a, b), the focus of modern medicine and of Nutritional Science changed. To prevent the development of these types of disease, nutrition research is investigating on how nutrition can optimize and maintain cellular, tissue, organ and whole body homeostasis. This requires understanding how nutrients act at the molecular level which in turn involves a multitude of nutrient-related interactions at the gene, protein and metabolic levels. As a result, nutrition research shifted from Epidemiology and Physiology to Molecular Biology and Genetics and nutrigenomics was born.

Nutrigenomics involves the characterisation of gene products, their physiological function and their interactions. It focuses on the effect of nutrients on genome, proteome,

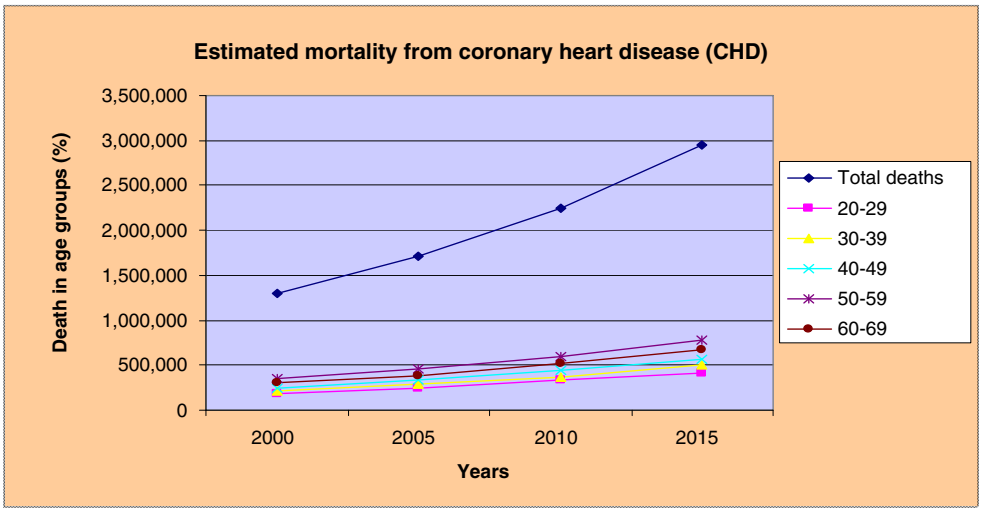

Fig. 2 Estimated mortality from coronary heart disease. Source: Trehan 2006

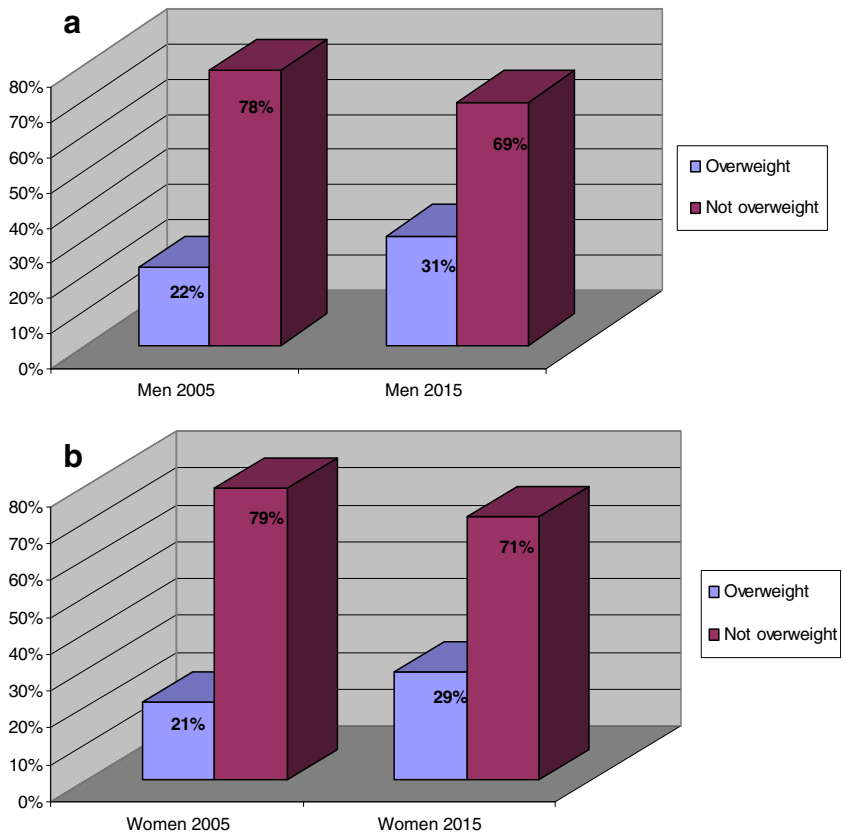

Fig. 3 **a** Projected prevalence of overweight males in India aged 30 years or more, 2005 and 2015. Source: WHO Report **b** Projected prevalence of overweight females in India aged 30 years or more, 2005 and 2015. Source: WHO Report

metabolome (Fig. 6) and explains the relationship between these specific nutrients and nutrient-regimes on human health.

Overall, a Nutrigenomic approach provides:

- a snapshot showing genes that are switched on/off (the genetic potential) at any given moment;
- a view of how gene/protein networks may collaborate to produce the observed response; and
- the method to determine the influence of nutrients on gene/protein expression.

It is hoped that by building up knowledge in this area, it will promote an increased understanding of how nutrition influences metabolic pathways and homeostatic control, which will then be used to prevent the development of chronic diet related diseases such as obesity and type-2 diabetes (Ramachandran 2006; Kandaswamy 2011; Pathak et al. 2000).

Nutrigenomics research tools

The new tools now available in the post-genomic era opens a new future for nutritionists to screen the genetic background, to monitor the transcriptome, proteome and metabolome and to ultimately develop dietary strategies which are

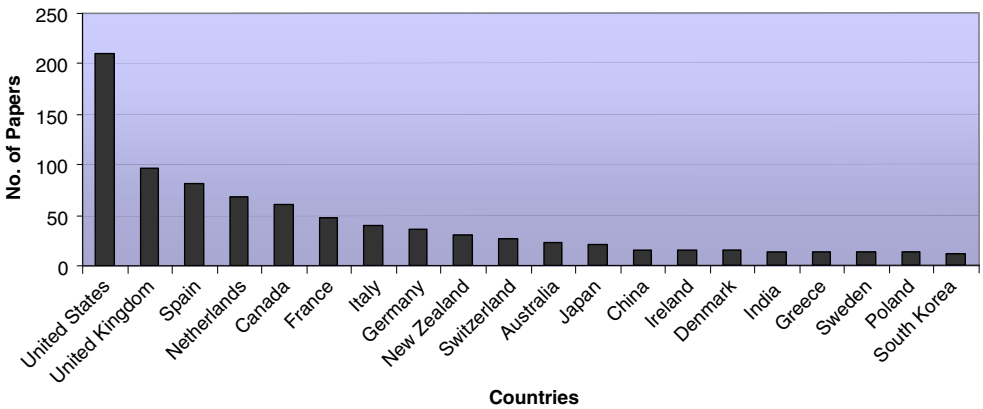

Fig. 4 Country-wise contribution to nutrigenomics research. Source: Scopus Database

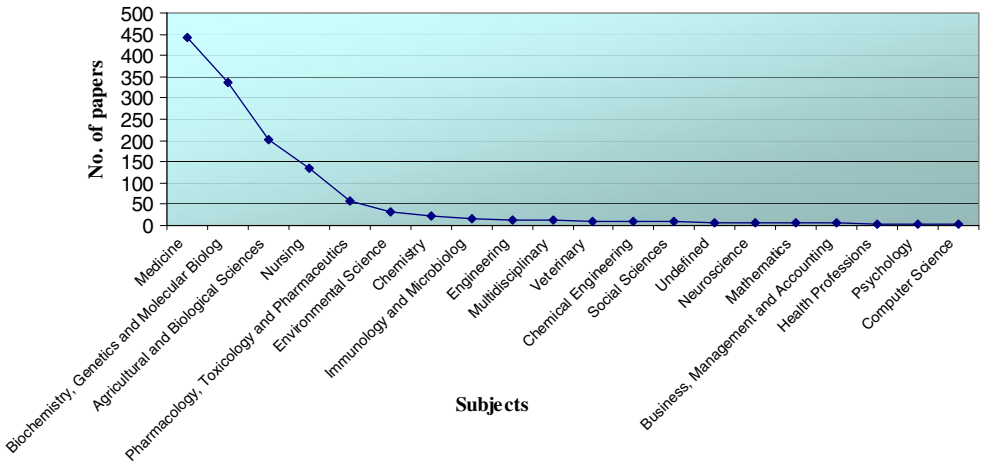

Fig. 5 Subject-wise contribution to nutrigenomics research. Source: Scopus Database

targeted to supply the optimum nutrition for single individuals. These tools are the focus of the emerging field of nutrigenomics.

The use of microarray technologies—the main tools of transcriptomics, has allowed new information concerning the physiological effect of different dietary proteins, of omega-3 polyunsaturated fatty acids and dietary conditioning of colon cancer. DNA microarray technology and quantitative real time Polymerase Chain Reaction (PCR) have successfully evaluated the interactions between diet and genes measured as changes in genetic expression. The use of proteomics tools (mainly two-dimensional electrophoresis) revealed new information concerning the protein composition of egg and poultry meat proteins, the effect of dietary methionine on breast-meat accretion, the toxicity of dioxin and the safe use of transgenic crops in animal nutrition. Metabolomic analysis allowed the detection of changes in the biochemical profiles of plasma and urine from pigs fed different diets and the determination of metabolite profiles in the liver of rats used as an animal model to characterize the toxicity of triazol fungicides. In livestock species, the microarray technology was discussed and reviewed as potential nutrigenomics tools, in context to its economic benefits and improvement of the food quality and safety in dairy and meat industries. This widely utilized microarray or DNA chip technology in nutrigenomics research enables not only the simultaneous screening of large number of genes, giving a comprehensive picture of the variation of gene expression patterns, but will also provide explanations for complex regulatory interactions, such as those between diet-nutrients and genes (Zduńczyk and Pareek 2009).

Single nucleotide polymorphism How nutrients influence the consequence of gene expression i.e. synthesis of mRNA (transcriptomics), protein synthesis (Proteomics) and metabolite production (metabolomics) was explained by Munshi and Duvvuri (2008) by giving the example of Genetic Polymorphism (SNPs) which may be partially responsible for variations in individual's response to bioactive food components. The role of various nutrients on gene expression occurring normally in body and its application to various aspects was also studied by Siddique et al. (2009). Through molecular biology and the tools of genomics, scientists have identified genes responsible for production of nutritionally important proteins such as digestive enzymes, transport molecules responsible for carrying nutrients and cofactors at their site of use. A number of relatively common SNPs are known to influence nutrient requirements. An example comes from work on SNPs that modified the risk of developing organ dysfunction when humans were fed diets low in choline. Premenopausal women [carriers of a very common SNP (Methylenetetrahydrofolate dehydrogenate MTHFD1-G1958A)] were 15 times as likely as non-carriers to develop signs of choline deficiency on a low-

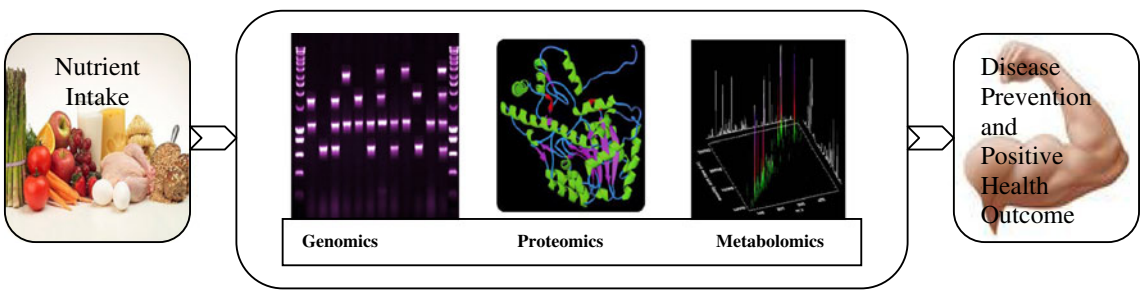

Fig. 6 Nutrigenomics approach in disease prevention

choline diet. The risk of having a child with a neural tube defect increased 4 times in mothers with this SNP, compared with women eating diets in the highest quartile for choline intake (Table 2). Zeisel (2011) also suggested that maternal dietary choline modulates fetal brain development in rodent models.

A growing interest in preventive medicine among people led to scientific research on alternative therapies, with particular emphasis on nutritional approaches to health and wellness. One such newly developed technology is the development of SNP array which helps to identify unique haplotypes. Majeed and Prakash (2006) discussed the role of nutraceuticals in health and diseases. Nutrigenomics, which investigates the interaction between diet and development of diseases based on an individual's genetic profile, would provide scientific validity to such approaches.

Mitra et al. (2005) focused on single nucleotide polymorphisms (SNPs) and its associated diseases (Cancer, Obesity, Diabetes, Cardio Vascular Diseases (CVD), Neural Tube Defect (NTD), Leukemia, Down syndrome, Spina bifida) (Table 2) and have also emphasized the interaction between folate nutrition and folate-dependent enzyme polymorphism (folate nutrigenomics). Ghodke et al. (2011) also profiled SNPs across intracellular folate metabolic

Table 2 Nutrient deficiency diseases and preventive food sources

Nutrients	Gene Alteration	Deficient Diet-Disease Potential	Food Intake
Folic acid (Vitamin B9)	Chromosome break and hampers DNA repair/ methylation	Cancer, heart disease, brain dysfunction, male infertility, leukemia	Liver, kidney, egg yolk, asparagus pea, cowpeas, lentils, peanuts, spinach, beetroot, broccoli, orange
Vitamin B12 (Cobalamin)	Chromosome break and hampers DNA repair/ methylation	Same as folic acid, memory loss	Liver, sardines, salmon, clam, beef, milk, cheese, yoghurt
Vitamin B6 (Pyridoxine)		Same as folic acid	Spinach, potato, bell peppers, turnip, mushroom, garlic, cauliflower, banana, chicken, pork, beef, salmon, tuna, turkey
Niacin (Vitamin B3)	Hampers DNA repair	Nerve problem, memory loss	Pork, tuna, prawns, kidney, liver, poultry, carrots, turnips and celery, mushrooms, beans, almonds, wheat products, rice bran, as well as milk and other dairy products
Vitamin E (Tocopherols)	Mimics radiation damage	Colon cancer, heart disease, immune dysfunction	Tomato, spinach, broccoli, blueberries, mangoes, kiwi, papaya, almonds, hazelnuts, peanuts, wholegrain cereals and vegetable oils
Vitamin D (Calciferol)	Prevent gene variation	Colon, breast, prostate cancer	Beef liver, cod liver oils, salmon, mackerel, tuna, egg orange juice, cow milk, yogurt, cheese
Zinc	Chromosome breaks	Brain and immune dysfunction	Oysters, beef, crab, pork, lobster, chicken, spinach, broccoli, cashew nuts, almond, milk, cheese, yogurt
Fatty acids	Alters gene expression	Obesity, CVD, Diabetes	Salmon, sardines, herring, mackerel, soyoil, sunflower oil, palm oil, flaxseeds, rapeseeds, peanuts, walnuts, almonds, mustard seeds, cloves, oregano, cauliflower, broccoli
Flavonoids	Alters gene expression	Cancer	Onion, green bean, broccoli, curly kale, endive, celery, cranberry, orange juice, grape fruits, lemons, red, blue and purple berries, peppers, tomatoes and eggplants
Vitamin A(Retinol)	Repression of PEPCK gene	Termination of pregnancy and fetal death	Carrots, spinach, turnip, kale, apricots, Cantaloupe, bell pepper, Papaya, mango, peach, beef liver, chicken liver
Protein	Alters gene expression	Kwashiorkor, marasmus	Egg, milk, soya milk, tofu, yoghurt, cheese, broccoli, almonds, peanuts, cashew, poultry

*Food sources abundant in respective nutrients are only mentioned

CVD Cardio Vascular Diseases; *PEPCK* phosphoenolpyruvate carboxykinase

pathway in healthy Indians (Fig. 7). The role of folate, vitamin B12 and homocysteine levels in acute lymphoblastic leukemia, suggest that gene-environment interaction may be an important factor in the development of acute lymphoblastic leukemia (Adiga et al. 2008).

Biomarkers Nutrigenomics is a revolutionary way of viewing the food, just for not sustenance, but as a pharmaceutical capable of reversing disease and stalling the rigors of ageing (Bhatt and Sharma 2011). A part of the approach, nutrigenomics involves finding markers of the early phase of diet related diseases; this is the phase at which intervention with nutrition can return the patient to health (Ramesha et al. 2010; Lau et al. 2008; Kore et al. 2008; Murray et al. 2010).

Markers can manipulate gene expression through use of nutrients or their combinations so as to improve productive as well as overall animal performance. The discoveries of these markers related to economically important traits like milk, meat, wool production etc., whose expression can be improved by dietary regimes, are needed today in nutrigenomic research. This will help in sustainable livestock production. By targeting specific genes through nutritional manipulation, it may be possible to get the desired livestock performance in terms of health as well as production (Kore et al. 2008). Coudron et al. (2006) illustrated the potential discovery of molecular markers using *Perillus bioculatus* (F.) (Heteroptera: Pentatomidae), when reared on an optimal vs. suboptimal diet, and analyzed the presence of differentially expressed genes resulting from the treatment. Biomarkers identified from this research could lead to development of a simple and rapid method for evaluating the quality and fitness of insect populations in the laboratory and in the field, leading to more efficient methods for rearing insects, as well as the production of high quality insects. In the broadest perspective, these developments will likely lead to more effective use of biological control methods and improvements in agricultural sustainability. Ramesha et al. (2010) utilized ten PCR-SSR (Polymerase Chain Reaction - Simple Sequence Repeats) microsatellite markers to gain better understanding on genotyping of certain nutrigenomic gene loci in nutritionally efficient silkworm breeds/hybrids. They used nutritionally efficient silkworm strains as a marker assisted selection or gene transmission in silkworm breeding programs and found that this developed molecular analysis in silkworm could be utilized for the benefit of farmers in Sericulture industry and also emphasized the future prospects of silkworm functional mechanism in nutrigenomics studies.

Nutrigenomics is surely expected to be the next wave for food industry, even though only a few practical ideas have emerged. One business model is the development of customized nutraceuticals based on specific genetic profiles. Another model may be foods for specified health use, which are already on the Japanese market. In Japan, about 350 items have been approved as food for specified health use by the Japanese Ministry of Health, Labor and Welfare. Each item has a specific health claim, such as food for hypertension, high cholesterol, diabetes, etc. based on clinical studies. All products have been developed based on scientific analysis and data, even though not on the genetic level yet. The food industry recognizes the need for nutrigenomics research as a basis for developing the concept of "personalized diets," for identifying molecular biomarkers

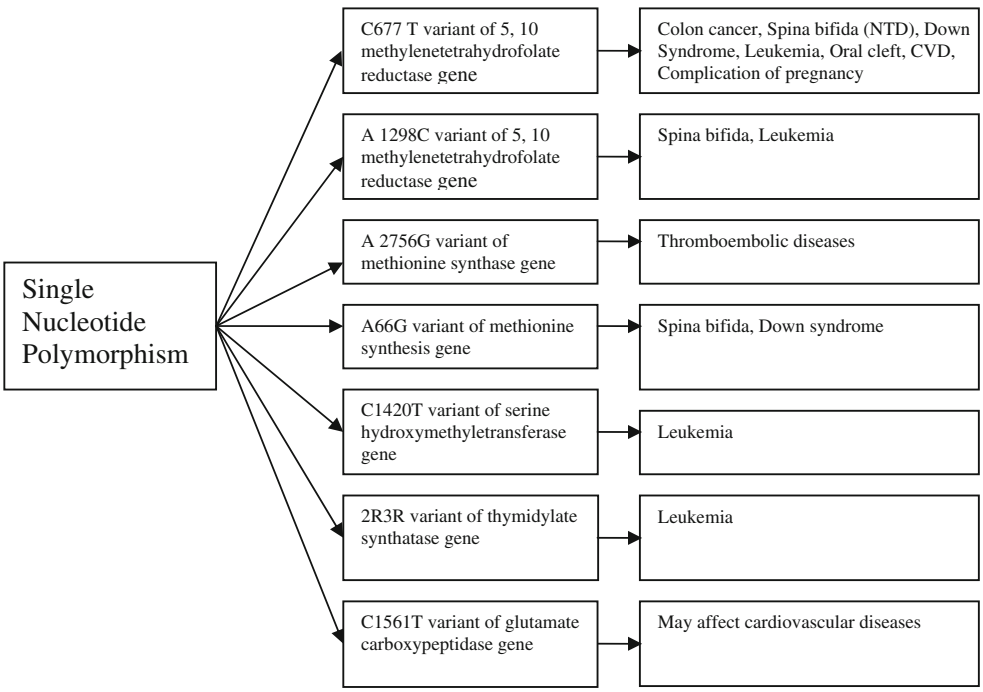

Fig. 7 Single Nucleotide Polymorphism, its associated gene alteration and diseases. Source: Modified from Mitra et al. (2005)

or new bioactive food ingredients, and for validating the effectiveness of these bioactive ingredients as functional food components or nutraceuticals. An important aim of nutrigenomics research is to study genome-wide influences of nutrition, with specific focus on the role of metabolic stress in the genesis of the metabolic syndrome, the collection of phenotypes combining inflammation, metabolic stress, insulin resistance, and diabetes. This goal is rather ambitious, but is based on the idea that nutrition should focus primarily on health and disease prevention and be complementary to pharmacological therapy, which targets the pathophysiological aspects of disease. To realize this goal, new genomics-based phenotypical biomarkers are needed that allow early detection of the onset of disease or, ideally, the predisease state of the metabolic syndrome, a condition referred to as metabolic stress. To approach this complex condition, molecular nutrition research on organ-specific dietary response patterns using transgenic and knock-out mouse models is combined with genomic technologies (Afman and Muller 2006).

Nutrigenomics & diseases

Nutrigenomics is widely used for studying heart-related disorders (Singh et al. 2002; Sivasankaran 2010; Rastogi et al. 2004) as well as diet-related disorders. The higher-income group who consumed excess fat and calorie-rich food had an increased prevalence of diabetes compared to the lower income group. In addition, visible fat consumption and physical inactivity showed a cumulative effect on increasing the prevalence of diabetes. Gene-diet interaction studies revealed that the adiponectin gene polymorphism contributed to insulin resistance and diabetes and this was exaggerated in those consuming diets with higher glycemic loads (Mohan et al. 2007a, b).

Gomase et al. (2009) explained genomics and its new aspects in cancer research. This study gave a broader idea of its history, strategies, technology, applications and current research. SNP array has significant impact on the genetic analysis of human disorders. It can be used to measure both DNA polymorphism and dosage recommendations. SNP arrays are an ideal platform for identifying both somatic and germline genetic variants that lead to cancer. Nair and Pillai's (2005) review article on Human papillomavirus (HPV) and disease mechanisms provided a number of critical observations associated with the role of HPV in cervical and oral cancer. Diet–gene interactions are also likely to contribute considerably to the observed inter-individual variations in cancer risk. This is in response to exposures to the nutritional factors that have the potential to promote or protect against cancer.

An investigation was carried out to know the role of parental folate pathway SNPs in altering the susceptibility to neural tube defects in 50 couples with NTDs offspring and 80 couples with normal pregnancy outcome. Naushad et al. (2010) observed high incidence of NTDs in South India where consanguinity is common and vitamin deficiencies were reported, which indicate the role of genetic and nutritional factors as the possible etiological factors specifically pointing towards folate metabolism. This study indicates significant gene-gene interactions between different loci and thus, highlights the importance of multiple loci in folate pathway for predicting the risk of NTD. They also emphasized the need to investigate gene-nutrient interactions for more precise risk prediction. A review of Indian literature on NTDs focusing on the role of folate and vitamin B12 nutrition and common genetic polymorphisms in 1-carbon metabolism was also conducted by Godbole et al. (2009). This study highlighted the importance of folic acid and vitamin B12 and the need for large studies in the area of gene-nutrient interaction in association with NTD in India.

The effects of chronic feeding of different diets containing vanaspati (trans fatty acid (TFA) rich), palm oil (saturated fatty acid (SFA) rich) and sunflower oil (polyunsaturated fatty acid (PUFA) rich) at 10 % level on 11b-HSD1 gene expression in rat retroperitoneal adipose tissue was reported. The diets rich in trans fatty acids and saturated fatty acids increased 11b-HSD1 gene expression in Retroperitoneal White Adipose Tissue (RPWAT) of rats as compared PUFA enriched diet. This increased the local amplification of glucocorticoids than PUFA-rich diets. Thus, the increased local conversion of inactive to active glucocorticoids in adipose tissue increased the risk of developing obesity and insulin resistance (Prasad et al. 2010). Diacylglycerol (DAG) rich mustard oil is capable of reducing arteriosclerotic factors like total cholesterol and non-LDL (low-density lipoprotein) cholesterol and increase anti-atherosclerotic factor such as high-density lipoprotein (HDL) cholesterol (Dhara et al. 2011). Another study addressed the hypothesis that some dietary fatty acids may attenuate the proinflammatory insulin resistant state in obese adipose tissue. The potential antidiabetic effect of a c9, t11-CLA–enriched diet (*cis*-9, *trans*-11–conjugated linoleic acid) was determined, focusing on the molecular markers of insulin sensitivity and inflammation in adipose tissue of *ob/ob* C57BL-6 mice, a well-characterized model of obesity and insulin resistance. Feeding the c9, t11-CLA– enriched diet improved glucose and insulin metabolism compared with the control linoleic acid–rich diet. This evidence suggests that it may be possible to reduce the impact of obesity-induced insulin resistance with nutrient-based anti-inflammatory strategies (Moloney et al. 2007). An 8-week study on mice demonstrated that HFD (High Fat Diet) induces obesity, reduces whole-body insulin sensitivity and

decreases insulin sensitivity of heart, muscle and visceral fat deposits (Wilde et al. 2009). The dietary combination of fish protein and fish oil decreased the contents of serum triacylglycerol, serum cholesterol, liver triacylglycerol and liver cholesterol in addition to altering liver lipid fatty acid composition. These effects are partly due to the increase in fecal cholesterol, bile acid excretion, and increased enzyme activities of fatty acid β-oxidation in the liver. These data suggest that combined intake of fish protein and fish oil lead to both hypocholesterolemic and hypotriglyceridemic effects in serum and the liver, while sole intake of fish protein or fish oil decrease only cholesterol and triglyceride levels, respectively and it may play a beneficial role in the prevention of lifestyle-related diseases (Hosomi 2011). Dhaka et al. (2011) have also proved the direct connection of trans fatty acids with cardiovascular diseases, breast cancer, shortening of pregnancy period, risks of preeclampsia, disorders of nervous system and vision in infants, colon cancer, diabetes, obesity and allergy. Kaur et al. (2012) found that essential fatty acids (like α-Linolenic acid, eicosapentaenoic acid and docosahexaenoic acid) reduced the risk of these diseases.

Pro-resolving and anti-inflammatory mediator products of murine 12/15-lipoxygenase (LOX) (lipid-oxidising enzymes) exhibit potent actions on vascular inflammation and protect against the progression of atherosclerosis (uncontrolled inflammation). Merched et al. (2011) determined whether augmenting dietary lipids modulates the body's endogenous anti-inflammatory pro-resolving mechanisms and promotes atherosclerosis. Conditions of aggressive accelerated atherosclerosis induced by a Western diet usurp the protective function of 12/15-LOX expression and bioactive mediator production, lead to a heightened pro-inflammatory burden. These studies demonstrated that 12/15-LOXs provide endogenous anti-inflammatory signals and protection during normal progression of atherogenesis mediated by downstream products, such as LXs (lipoxins), protectins, and D-series resolvins, effects that seem to be totally annulled in the presence of Western-diet-induced hyperlipidemia.

Nutrigenomics & diet supplementation

Today we live in a nutritional environment that is very different from the environments to which we had genetically adapted. Major changes in our food supply accompanied the domestication of animals and the agricultural revolution about 10,000 years ago. Later, the Industrial Revolution and developments in food technology brought about further major changes in the composition of foods, one of the most important of which was a change in the quantity and quality of the various fatty acids. Srinivasarao et al. (1997) study was primarily aimed at determining the magnitude of changes in long chain fatty acids, polyunsaturated fatty acids, and molar ratios of cholesterol to phospholipids in synaptosomal membranes, in response to feeding of different dietary fats (safflower, mustard, peanut, and coconut Oil) by using discontinuous sucrose density gradient ultracentrifugation.

Diet is an important factor in cancer etiology and prevention. Ayurveda medicine prescribes many plant-based medicines for the treatment of cancer. Sinha et al. (2003) conducted a symposium on cancer risk and diet in India and explained the possible dietary and other factors associated with cancer. Turmeric has shown to be a potent antioxidant and anti-inflammatory agent with additional promise as a chemo-preventive agent.

The contribution of various factors including macronutrients and recommendations for obesity management has been studied (Kumar and Singh 2009). Jeyakumar et al. (2005) reported Vitamin A as a known regulator of adipose tissue growth. The chronic dietary vitamin A supplementation at a high dose effectively regulates adipose tissue mass both in lean and obese phenotypes of the WNIN/Ob strain. Vitamin A is also required for normal embryonic and fetal development, as well as maintenance of the fully differentiated state in the adult. Ghoshal et al. (2003) investigated the effect of vitamin A depletion on the developing liver (mouse) by examining the phosphoenolpyruvate carboxykinase (PEPCK) gene as a prototype retinoid-responsive gene (Table 2). Singh et al. (1994) reported the effect of low energy, fruit and vegetable enriched diet on central obesity and other disturbances associated with glucose intolerance in patients after acute myocardial infarctions in the randomized trial.

HCA-SX or Super Citrimax, a novel derivative of HCA (dried fruit rind of *Garcinia cambogia*, also known as Malabar tamarind), is a unique source of (−)-hydroxycitric acid (HCA). It is safe when taken orally and is bioavailable in the human plasma. Under the experimental conditions, Roy et al. (2004) demonstrated that HCA-SX supplement has been observed to be conditionally effective in weight management and lowered abdominal fat leptin expression in experimental animals as well as in humans. In 2008, Lau and his co-workers also showed that supplementation of HCA and niacin-bound chromium (III) (NBC) is safe and efficacious for weight loss.

The use of new bioactive foods and nutraceuticals in cardio-protection and management is growing (Sharma and Singh 2010). Thompkinson et al. (2012) indicated that foods rich in omega-3 fatty acids, antioxidant vitamins and fibres may be beneficial for cardio-vascular health. Kamra et al. (2005) conducted an experiment for studying bioactive dietary components and their physiological activity in the intact organisms and the role of diet in cancer prevention. He

found out that fish oils, nutraceuticals in vegetable fat-free diets and restricted life style enhances cardio-protection and plays a major role in positive gene regulation.

Genomics and proteomics offer new tools for better understanding the genetics of male infertility. The review by Singh and Jaiswal (2011) provides insights into the plausible chromosomal, genetic and epigenetic alterations, which may result into infertile phenotype. In this paper they have revealed the application of nutrigenomics in Male Infertility. SNP arrays will be useful in getting a more general overview of changes in whole genome of infertile men and especially in the X chromosome. Folate, Vitamin B12 and Zinc supplementation was found to have a positive effect on spermatozoa number and motility. This was also observed by Dhillon et al. (2007) by conducting a case–control study, in which they included 179 oligoasthenoteratozoospermia patients and 200 fertile men.

A dialyzed aqueous extract of fenugreek seeds was investigated in vivo for hypoglycaemic potential and its effects on insulin signalling pathways in the primary targets of insulin, adipocytes and liver cells, were examined in vitro, by the use of mechanism-based innovative contemporary strategies. Vijayakumar et al. (2005) experimentally demonstrated that a dialyzed aqueous extract of fenugreek seeds possesses hypoglycaemic properties and that it stimulates insulin signalling pathways in adipocytes and liver cells. The hypolipidemic effect of a novel thermostable extract of fenugreek seeds (TEFS) has been studied in vitro by employing differentiating and differentiated 3T3-L1 cells, and HepG2 cells cultured in normal or sterol-enriched conditions and suggested that the TEFS may have potential application in the management of dyslipidemia and its associated metabolic disorders (Vijayakumar et al. 2010).

The isolation of microsomal ω-6-desaturated gene (fad2-1) from soybean was carried out (Kishore et al. 2006) for improving soybean seed oil profile, making it nutritionally more beneficial and stable for human consumption. P-soyatose supplementation results in an increased transcription of fibroin mRNA leading to an increased silk production of *Bombyx mori L*. Raman et al. (2007) demonstrated that soyprotein extract supplementation is of importance in regulating the fibroin gene expression at transcriptional level. Nutrigenomic analysis of intestinal response to partial soybean meal (SBM) replacement in juvenile Atlantic halibut (Hippoglossus hippoglossus L.) showed that there is no significant difference between fish fed with the fish meal (FM) and SBM diets (Murray et al. 2010).

A successful attempt of fortifying human diets with natural α - tocopherol by taking recourse to genetic engineering of an important oilseed crop, *Brassica juncea* was described by Yusuf and Sarin (2006). α -Tocopherol intakes in excess of the recommended daily allowance (RDA) are associated with decreased risk of cardiovascular diseases, improved immune function, slowing of the progression of a number of degenerative human.

Curcumin and its dietary source turmeric are important for the prevention and/or treatment of diabetic retinopathy. The vascular-endothelial-growth-factor (VEGF) expression analyzed by both real time polymerase chain reaction (PCR) and immunoblotting showed that curcumin and its dietary source turmeric can inhibit VEGF expression in strepotzotocin (STZ)-induced diabetic rat retina (Mrudula et al. 2007). Kumar et al. (2009) also investigated the antiglycating potential of cumin in vitro and its ability to modulate the chaperone-like activity of α-crystallin vis-à-vis the progression of diabetic cataract in vivo. Through slit lamp examination, they revealed that cumin has antiglycating properties that may be attributed to the modulation of chaperone activity of α-crystallin, thus delaying cataract in STZ-induced diabetic rats.

AMP-activated protein kinase (AMPK) has become one of the most important key elements in energy control, appetite regulation, myogenesis, adipocyte differentiation, and cellular stress management. Metformin, an insulin sensitizing agent, is known to lower insulin resistance and enhance metabolic profile, with an additional weight reduction capacity, via activation of AMPK. A high-fat diet is correlated with a decreased expression of mRNA for the AMPK-α2 isoform as well as AMPK phosphorylation with consequent decreased activity of this enzyme in skeletal muscle, leading to decreased glucose uptake, meanwhile in adipose tissue it promotes preadipocyte differentiation, lipolysis and the secretion of adipokines (TNFα),perpetuating the process. Foods with low glycemic index may be beneficial in regulating body weight in two ways: first by promoting satiety and secondly by increasing fatty acid oxidation, both explained by the action of AMPK. A high-protein diet is capable of controlling food intake due to enhanced proopiomelanocortin (POMC) expression and repression of neuropeptide Y (NPY) in the hypothalamus, via activation of mTOR (mammalian target of rapamycin) and low phosphorylation rates of AMPK. Therefore dietary components can greatly affect the activity of AMPK (Rojas et al. 2011).

Nutrigenomics & public awareness

Addressing the genetics and nutritional genomics knowledge gap will help in eradicating the social issues, create more awareness, confidence and trust among the public. Public concerns over nutrigenomics are relevant to science and to the food industry. Past and present food scares, such as genetically modified, demonstrate the importance of addressing public concerns sooner rather than later, and of taking the social issues around science as seriously as technical ones. Regulation is necessary both to ensure responsible use of research and to assure the public that products can be trusted.

Manufacturers need regulation and public engagement both for the guidance they provide and to demonstrate a will to improve the safety, reliability and health benefits of their products Sherwood (2006).

Public awareness programmes The relationship between changing lifestyles, nutritional status of the Indian population and formulation of appropriate programmes and strategies for public awareness was explained by Rao (2001). A Genomics Policy Executive Course was conducted by Acharya et al. (2004) that provided a forum for stakeholders to discuss the relevance of genomics for health in India. The course goals were to familiarize participants with the implications of genomics for health in India; analyze and debate policy and ethical issues; and develop a multi-sectoral opinion leaders' network to share perspectives.

To overcome diet related diseases and promote health, Krishnaswamy (2008) found that it is essential to develop and implement Food Based Dietary Guidelines (FBDG). In this post genomic era, the genes we inherit cannot be altered, but certainly one can change its response to the environment (dietary) and obtain the desired results. A multidisciplinary group comprising nutritionists, agriculturists, technologists, home scientists, dieticians etc. was constituted to develop FBDG. Healthy food choices are central in the prevention of both under and over nutrition, and the ultimate objective of FBDGs is to grow what is needed and preserve what is required (Fig. 8).

The future perspectives of nutrigenomics foods; its benefits and risks were explained by Ghosh (2009). Nutrigenomics is an emerging science with high consumer expectations, but the major concerns are twofold. First, it is doubtful whether the goal of matching foods to individual genotypes to improve the health of those individuals can be attained or not. Secondly, the entry of personalized nutrigenomics foods in world's food markets depends on numerous hurdles being overcome: some scientific in nature, some technical and others related to consumer, market or ethical issues.

The emerging paradigms of nutritional genomics as they relate to the functional food market were discussed by Ghosh (2010). He emphasized on the consumer acceptance and market penetration of the product based on this concept to improve human nutrition and health and thereby deliver societal and economic benefits. Later Ghosh and Gorakshakar (2010) emphasized on the goal of integrating genetics into the public health in India and Aswini and Varun (2010) also gave a general awareness about the new gene-based technologies that can be easily utilized by the modern healthcare units.

Conclusion

Trends, based on current and projected data, indicate that India is facing considerable challenges as under-nutrition evolves

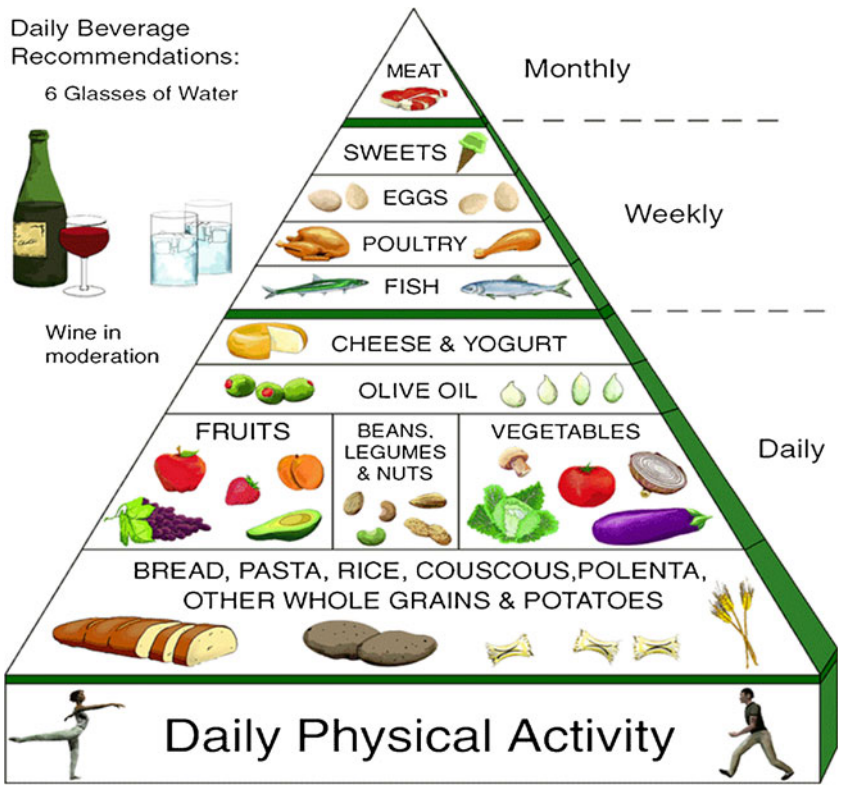

Fig. 8 Food dietary guidelines

into over-nutrition as the community becomes developed. India has some of the highest CHD rates in the world, with urban rates being three times higher than rural rates. In addition, rates for obesity and diabetes are increasing dramatically in urban areas and in high-income rural residents. This increasing number of diet related disorders in India (obesity, cardio-vascular diseases, diabetes, neural tube defects, etc.) has led us to investigate the nutrigenomics research in India.

The literature collected so far shows that, India has a keen interest in the field of nutrigenomics. In the year 2005, 2008 and 2009 Indian authors gave a broader description of nutrigenomics. They have well explained the mechanism, the basic concept of nutrigenomics and how nutrients influence the gene expression. In 2004, a course was conducted that provided a forum for stakeholders to discuss the relevance of genomics for health in India. But after that, no awareness programme was carried out. In 2008 and 2010 the authors described about the future perspectives of nutrigenomics and gave an insight on the role of genetics in public health. It has been noticed that from 2002 onwards various studies on diseases related to insufficient diet, lack of physical activity and changing lifestyles were conducted, but only few work were done in the area of nutrigenomics. Thus, more research work will enhance consumer confidence, awareness and a better future, which in turn will upgrade the country's status.

Convincing evidence about the interaction of nutrients, genetic variations and health implications is still uncertain. We see this as the future, nutrigenomics concept does make sense, but we are still far from personalised nutrition. The literature search on "nutrigenomics" using various databases concludes that there is a high hope and need of nutrigenomics in India. This study shows that more research work and increasing awareness can possibly help in the prevention of nutritional and other non communicable disorders. Hence, the early identification of at-risk individuals and appropriate intervention in the form of weight reduction, changes in dietary habits and increased physical activity could greatly help to prevent, or at least delay the onset of dietary disorders in India.

The ultimate aim of this emerging field of science is prevention than cure. This is very similar to the dictum of Hippocrates - Father of Medicine (460–360 BC), who said "Leave your drug in the chemist's pot if you can heal the patient with food".

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