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Biomarkers for Nutritional Assessment

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Abstract
Assessing the food intake and its effect in our body has become a major concern as food and our dietary habits can tell us a lot about our health and nutritional status. An individual's nutritional status tells us how effectively their physiological nutrient demands are being satisfied at a specific stage of life. Biomarkers are more accurate and provide accurate nutritional assessment. Assessment can be done with the help of questionnaires and as well as biomarkers that are present in food or formed inside are body. Biomarkers play a major role for assessing the nutritional status of an individual. These can be overcome by using biomarkers which can assess the food consumption without any dietary assessment. Biomarkers can be affected by the state of health so, it's important to identify the biological effect of food and their impact on our health. Biomarkers can be analyzed by two methods that is static and functional analysis. Static analysis measures the concentration of a nutrient or a bioactive compound or a biomarker whereas functional analysis looks upon the response or function. Sources of biomarkers can be many ranging from the urine to hair, nails or the sample collection from hard tissues. These biomarkers can be used to measure intake, analyze the physiological or pathological responses to certain food components or diets, identify any dietary deficiency, to provide individual recommendations. Different approaches such as "omics" can help to determine new biomarkers and to improve our knowledge of biomarkers in relation to nutrition and health and that are genetic biomarkers, transcriptase biomarkers, epigenetic biomarkers, proteomic biomarkers and many more.

Keywords: Nutritional Assessment, Biomarkers, Bioactive Compounds, Functional Analysis

1. Introduction

Biomarkers, also known as biological markers, are quantifiable traits or signs that can be used to assess pathological alterations, normal biological processes, or reactions to treatments or exposures. Numerous biological samples, including DNA, tissue samples, blood, and even urine, may include these markers. The physiological condition of an individual, including their general health, the presence of illnesses, or the response to therapies, may be understood through the use of biomarkers. They are used in medical practice and research for diagnostic, prognostic, and predictive reasons. Because they can offer precise assessments of nutrient intake, absorption, utilization, or status, biomarkers are useful tools for evaluating nutritional status. These biomarkers can be used to gauge a person's nutritional status in a number of different ways. Biomarkers are essential for giving objective data that represent many facets of a person's state in the field of nutritional evaluation. These indicators can reveal nutritional status generally or reveal nutrient intake, absorption, or utilization. These biomarkers can be examined to learn important information about a person's nutritional health and sufficiency of nutrient intake. An individual's nutritional status tells us how effectively their physiological nutrient demands are being satisfied at a specific period of life. An appropriate nutritional status promotes growth, development, correct cell and tissue turnover, and general health when nutrients are ingested in a balanced way, neither in inadequate nor excessive quantities. Dietary evaluation and nutritional status have generally been evaluated using methods that depend on information about dietary consumption, including food diaries, meal frequency questionnaires, or 24-hour dietary recalls. The technical aspect of data collecting techniques remains, nevertheless. It's possible for people to have trouble precisely estimating

portion sizes, remembering every detail of their meals, or recalling certain foods or meal components. Measurement errors in nutritional assessment are influenced by these elements [1].

Furthermore, people frequently underreport their nutritional consumption, particularly when it concerns items that are considered socially acceptable, when they have a history of dieting, or when they are overweight, which may indicate higher eating control. The inadequate categorization of some nutrients, especially trace components, in food composition tables is another drawback. It is challenging to determine nutritional status effectively based on food alone because of this deficiency. Similar to how food composition databases could not accurately reflect the current properties of commercially available items, the nutritional value of food might fluctuate significantly. These databases frequently fall behind in documenting changes in dietary habits, such as rising whole grain product use. Factors related to nutrient absorption also influence nutritional status. The efficiency with which nutrients are absorbed may be modified through feedback control systems in response to a person's nutritional state. A person with a poor calcium status, for instance, will be able to absorb calcium more effectively. Absorption may also be affected by the mix of foods consumed. While iron absorption is improved when ingested with vitamin C, dietary fibre may reduce the availability of food carotenoids [2]. Furthermore, the composition, quantity, and absorption of nutrients may be affected by the extent to which food is cooked and processed. other nutrients, like heme-iron, are more bioavailable in their original state, while other micronutrients, like calcium and zinc, may be linked with proteins that improve their bioavailability.

2. Biomarkers for Nutritional Assessment

Shortcomings of nutritional status estimation techniques highlight the need for accurate and objective measurements. Compared to assessment of food intake, biomarkers provide a more accurate and immediate indicator of nutritional status. Biological samples can be used to quantify objective traits known as nutritional biomarkers. It serves as a indicator of nutrition related to food consumption and metabolic activity [3]. Biochemical examination of reference metabolites indicating nutrient bioavailability offers an objective technique for evaluating nutritional status in comparison to nutritional evaluation. Improved ability to identify missing conditions and reduced incidence of methodological mistakes. Folate, iron, vitamin B12, copper, and zinc are all biomarkers that may be used to investigate dietary contributions to diseases like anaemia [4]. These biomarkers are particularly useful in the medical field.

Clinical biomarkers are primarily used to diagnose medical conditions and may not be directly related to diet. However, metabolic disorders may overlap if there are certain indicators such as: B. Circulating lipid profiles or urea levels can be altered by both dietary factors and disease. The purpose of nutritional biology is to examine whether a person's nutritional status promotes overall well-being. "It includes assessment of mild subclinical symptoms and moderate exertion. In such situations, a combination of nutritional assessment techniques, such as food testing and biochemical measurements, can help estimate nutrient intake and assess health risks. This combined approach alleviates some of the shortcomings of different techniques for assessing nutritional status [3].

Table 1: Provides examples of potential nutritional biomarkers connected with exposure to and/or effects of foods, dietary patterns, or macronutrients. Samples may be collected using non-invasive or minimally invasive techniques [5].

Proposed Biomarker	Sample Type	Intended use as a nutritional biomarker
Alkylresorcinols	Plasma	Whole grain food components
Allyl methyl sulfoxide	Urine	Intake of garlic
Alllyl methyl sulphide [AMS]	Urine/breath	Intake of garlic
Arbutin	Plasma	Pear intake
Carotenoids	Plasma	Fruit and vegetable intake
Carotenoids with Vitamin C	Plasma/serum	Consuming fruit and vegetables combining biomarkers is advised since they are more accurate than using carotenoids or vitamin C alone.
Creatine	Serum	Intake of meat and fish
Creatinine	Urine	Intake of meat and fish
Daidzein	Urine/plasma	Intake of soy and items made from it
Dyhydrocaffeic acid derivatives	Urine	Acute and ongoing coffee exposure
Genistein	Urine/plasma	Intake of soy and soy-based products
Homocysteine	Plasma	One carbon metabolism and folate status
n-3 fatty acids: docosahexaenoic acid	Urine	Intake of tomato juice
EPA as phospholipid	Plasma	EPA status
Nitrogen	Urine [24 hours]	Protein intake
Phloretin	Urine	Apple intake
Phloretin glucuronide	Urine	Apple intake
Proline betaine	Urine	Acute and habitual citrus exposure
S-allylcysteine [SAC]	Plasma	Intake of garlic
Urolithin B	Urine	Eating apples, including strawberries, raspberries, and walnuts, which contain ellagitinins
S-allylmercapturic acid [ALMA]	Urine	Intake of garlic

Researchers utilize a wide range of indicators in nutritional studies to completely grasp the complex link between diet and health. These biomarkers may be divided into three primary groups: those that indicate exposure, those that indicate effects, and those that indicate the presence or absence of health and illness.

2.1 Biomarkers of Exposure

Exposure biomarkers are a broad category that includes several different kinds of indicators used to evaluate dietary nutritional, nonnutrient, and behavioural consumption. A biomarker of protein consumption might be nitrogen in the urine. Because they allow for improved participant classification in relation to exposure to certain nutrients, these sorts of biomarkers are highly intriguing. Furthermore, it serves as a quantifiable indicator of how well participants are adhering to the study's recommended diet in intervention studies looking at the health effects of dietary change. These biomarkers could not only be a reflection of individual nutrients, but of overall dietary patterns and food groupings as well. Sucrose, fructose, and erythronic acid in the urine are indicators of sugar consumption, whereas plasma concentrations of alkylresorcinols are considered biomarkers of whole grain intake [6]. Genistein and daidzein are two biomarkers of soy or soy-based product intake that may be found in the urine and plasma, respectively. Additionally, genistein and daidzein levels in the blood and urine serve as markers for soy or soy-based food consumption [7]. The availability of trustworthy data on additional legume markers is currently limited. This allows for marker combinations to more accurately portray different types of food. Vitamin C and carotenoids, for instance, may be more reliable as a pair of biomarkers than any one of them alone, when applied to fruit and vegetables [8].

2.2 Biomarkers of Effects

According to Thompson *et al*. (2010) [2], these are biomarkers that are connected to a target's function or biological response. Not only do these biomarkers mirror dietary habits, but they also provide light on how certain nutrients may affect metabolic rate and other bodily functions. The effects of many nutrients and their interactions may be reflected in biomarkers, not only those of individual nutrients. Some metabolic biomarkers of carbon compounds, like homocysteine, provide insight into not just dietary habits but also pathological and physiological processes [8,9].

2.3 Biomarkers of Function

Functional biomarkers aim to assess the functional impact of deficiency or excess of a particular nutrient, making them more biologically meaningful than static biomarkers. Research into the relationship between diet and chronic disease increasingly uses functional biomarkers as a surrogate for actual disease outcomes. When used in this way, they are called 'surrogate biomarkers' [10] (Yetley *et al*., 2017). Functional biomarkers it can be classified into two groups. Functional biochemical biomarkers serve as early indicators of subclinical deficiency by measuring changes associated with the initially affected biochemical system, with consequent impacts on health and well-being. This may include measuring abnormal metabolites in urine or blood, or assessing the activity of nutrient-dependent enzymes. Promising functional biochemical biomarkers include alterations in DNA damage, gene expression and immune function, some of which may be recognized as surrogate biomarkers for chronic disease [10].

2.4 Biomarkers of Health/Disease and Physiological Status

These are the destination points that provide insights on how well someone is and their potential for illness. These biomarkers are often utilised in clinical practise because they indicate intermediate illness and phenotypes or particular disease severity. High levels of fasting plasma glucose are associated with insulin sensitivity and may be a sign of diabetes, while high levels of plasma cholesterol and triglycerides are connected to cardiovascular disease. While precise illness detection and treatment prediction are essential, nutritional biomarker research focuses on biomarkers linked with health and disease. The latter area is currently undergoing intensive development and research [11].

2.5 Factors Affecting the Choice of Nutritional Biomarkers

Biomarker selection should be made carefully considering limitations in various health conditions, inflammation, genetic factors and disease states. Several biological aspects are outlined in the following section that may affect the use of nutritional indicators for evaluating nutritional status. These biomarkers may be impacted by non-biological factors such as the methods used to collect and store the samples, the season, the time of day, contamination, stability, and laboratory quality assurance. Both biological and non-biological factors contribute to variability and can affect the efficacy, accuracy, precision, specificity, sensitivity and predictive value of biomarkers. Measurement errors can occur randomly or systematically in almost any technique, so use calibrated equipment and ensure personnel are trained in standardized and validated techniques is important. Continuous monitoring with appropriate quality control procedures should also be implemented [12].

3. Selection of Biomarkers

3.1 Population Setting

It is crucial to take into account elements like ethnicity and life stage group while selecting biomarkers. These factors may influence biomarker selection to ensure biomarker relevance and accuracy within a given population. Hormonal changes and the increased volume of plasma present in the body during the second and third trimesters of pregnancy, for instance, may cause vitamin B12 and serum zinc levels to change. Therefore, it is very important to identify pregnant women in order to be able to accurately interpret the biomarker values in this particular population [1,4].

A number of challenges can arise with proper collection, transport, centrifugation and storage of biomarkers in rural settings. For example, ensuring a temperature-controlled supply or cold chain for sample collection can be challenging [1].

3.2 Validity

Validity refers to how accurately a biomarker describes a nutritional parameter of interest. If the study's aim is to assess total nutrient reserves in the body, but the biomarker of choice reflects recent food consumption instead, the biomarker is considered invalid. Valid biomarkers are sensitive and specific, ideally free of random or systematic errors. Unfortunately, inflammation, stress, or the effects of certain agents on enzyme activity and nutrient metabolism can alter nutritional status and affect the efficacy of nutritional biomarkers. For example, acute-phase reactions observed during infections can cause changes in certain nutrient levels

in the blood (e.g. plasma ferritin increases while plasma zinc and retinol-binding protein levels decrease) [1,2]. Some biochemical measurements (such as serum iron) have very high intra-subject biological variability, with coefficients of variation exceeding 30%, which can be greater than any analytical variability [13].

3.3 Sensitivity and Specificity

Sensitivity refers to how well a biomarker can identify people who actually have the condition under study, such as a nutritional deficiency. Sensitive biomarkers show large changes even with small fluctuations in nutritional status. A biomarker with 100% sensitivity will accurately identify all individuals who actually have the deficiency without classifying those with the deficiency as "good" (no false negative results). Sensitivity is the fraction of those who really have the disease who test positive (true positives) relative to the total number of people who either do or do not have the condition .Biomarker sensitivity depends on disease prevalence and chosen cut-off point [14].

4. Criteria for Selecting Biomarkers

There are many specific criteria for selecting appropriate biomarkers in nutritional research [15]. These criteria are enumerated below:

4.1 Criteria for Biomarker Selection

4.1.1 Methodological Aspects Except Study Design

- Methods should be validated according to recognized guidelines.
- Good sensitivity
- Appropriate specificity
- Reproducibility, precision, standardization, stability (sample quality) and technical variability
- Biological variation

4.1.2 Reflect/Mark the Biological Purpose of the Biomarker

- Changes in biomarkers are associated with changes in endpoints in one or more target populations.

4.1.3 Relevance to Nutritional Research

- What is the considered normal range in healthy people?
- What is a significant change (both biological and statistical)?
- Is there evidence that diet affects markers? If so, what effects have been reported?
- What other factors might affect the biomarkers?
- Are there experimental data where dietary interventions did not produce the expected change?

5. Current Challenges in the Development of Health Biomarkers

Health and disease biomarker research and development is motivated by clinical demands, and its primary focus is on detecting and quantifying disease states and processes as opposed to measuring and quantifying individuals' health. Was hired to do. Diet and nutrition science, however, has as its principal objective the achievement and upkeep of health in its many forms. Finding biomarkers for the very early stages of modifications that may eventually result in a disease is essential in preventing the onset of a disease. These biomarkers may be seen more as indicators of health and/or ability to avoid illness than as indicators of disease itself. Homeostatic responses to certain environmental or dietary stressors may be used to detect alterations in homeostatic balance that occurred prior to the onset of sickness [16]. Nutrigome techniques, which analyse functional genomic responses on a genome-wide scale when applied to the nutritional sector, have been and will continue to be of significant help in these fields due to the complexity of homeostasis. biomarkers for health. Signalling routes, processes, and molecular interactions involving mechanisms in many cells, tissues, and organs are the foundation of human health. The maintenance of health is a complex process involving a wide range of biochemical and physiological systems in the face of ever-evolving environmental factors including nutrition, infectious illnesses, temperature, exercise, and stress. Many of the issues people confront may be successfully resolved when they are in excellent health by the systems that maintain homeostasis. Phenotypic plasticity is a function of adaptive reactions [16].

6. Sources of Biomarkers

Excreta (urine, faeces), blood (plasma, serum, and red blood cells), and easily accessible samples are the most frequent biological samples utilised in nutritional epidemiology (nails, saliva, hair). In some cases, biopsies and hard tissue samples such as muscle, fat, and skin may also be of value. When processing blood samples, the choice of sample type is an important factor. They can be removed without removing anticoagulant blood components. Serum can be obtained by clotting the blood, centrifuging it to remove clots and cells, and collecting the supernatant. Plasma is an aqueous fraction containing metabolites such as blood proteins, electrolytes, etc. It is also useful to focus on specific fractions such as erythrocytes and leukocytes to assess biomarkers in blood cells. For instance, the Omega-3 Index, which determines the percentage of total erythrocyte membrane fatty acids that are eicosapentaenoic acid (EPA) and docosahexaenoic acid, may be used as a viable biomarker for evaluating omega-3 fatty acids (DHA) [7]. The process of obtaining transcriptome-based biomarkers from peripheral blood cells (PBC) via noninvasive techniques has generated a great deal of attention. Due to its dependability as a homogeneous sample for transcriptome analysis, the peripheral blood mononuclear cells (PBMCs) within PBCs that comprise lymphocytes and monocytes have been the subject of much investigation. The positive benefits of hyaluronic acid-containing extracts on human joint health are reflected in PBMC transcriptomes, it has been revealed. Furthermore, PBMC have been proven in preclinical models to precisely represent the effects of dietary and environmental treatments on the liver and hypothalamus, two organs that are notoriously challenging to analyse in healthy humans [18]. Avoiding *in vitro* gene expression alterations necessitates stringent methods for isolating PBMCs promptly after blood collection. In the case of multicenter investigations, this might provide logistical and technological difficulties. In addition, the PAXgene blood RNA system may be used. This makes it possible to isolate and stabilise RNA from blood cells without resorting to any further processing. This approach not only offers advantages in terms of sample collection, storage and transport, but also reduces sample handling time, thereby improving standardization and reproducibility. Therefore, it is an attractive method for obtaining biomarkers in human nutrition research [19]. A limitation of using whole blood cells, however, is the inability to classify specific cell populations. Background noise is higher and stimulus response is lower than in PBMC, according to many studies. However, PBMCs and whole blood (measured using PAXgene tubes) share a

great deal of gene expression patterns, indicating that PBMC-identified indicators may be applicable to whole blood. indicates, which is useful for investigations involving huge numbers of humans [20]. When a little amount of blood, usually from a finger or heel prick, is needed for a diagnostic purpose, the dry blood spot method may be performed. Some hormones and metabolites, such fatty acids, ma9(y be analysed with this method, and it is also employed in the newborn screening for the hereditary disorder phenylketonuria. In order to measure food intake, identify nutrient-related risk indicators, quantify markers of dietary metabolic status, and even quantify markers of disease risk, dried blood stain methods are being developed thanks to the rapid development of technology [21].

Since urine is a concentrated source of ejected metabolites, it has historically been used for the examination of metabolites or cellular material connected with renal and metabolic issues. Glycosuria is one of the signs of diabetes and inappropriate carbohydrate intake. Thanks to the development of metabolomics techniques, urine samples and blood fractions are currently the most relevant physiological fluids for determining nutritional markers. Blood samples are commonly used for nutritional research and long-term monitoring because they reveal changes in the endogenous metabolome, which in turn reflect the impact of the food we eat on the body. The microbiota's metabolic processes are also reflected in a person's urine. Intestinal bacteria may be stimulated to produce hydroxyhippuric acid and other byproducts when a diet high in polyphenols is consumed [7].

Faeces are a valuable biological resource for studying the composition of the gastrointestinal microbiota and its byproducts and determining the relative abundance of nutrients that are not absorbed or metabolized [8].

Nails and hair are readily accessible tissues that have been demonstrated to assist measure mineral status in relation to chronic excessive alcohol intake, exposure to toxic metals, and illness [11,12]. However, the nutritional concentrations in the bodies of healthy people are not always accurately reflected in these samples. When other markers of functional condition are lacking, hair analysis may be used to determine zinc, copper, chromium, and manganese levels. It is also useful for monitoring cadmium and lead, two metals with the potential to cause serious health problems [12].

Sample collection from hard tissues like the liver for nutritional assessment often involves an intrusive biopsy, which is not always possible in people. Some few dietary intervention studies have looked at biopsies of adipose tissue, skeletal muscle, intestinal, and skin tissue. Peripheral blood mononuclear cells (PBMCs) and extracellular vesicles (EVs) have lately attracted interest as a possible alternative approach, particularly for application in epidemiological studies of large populations [17].

7. Types of Analysis

Laboratory analysis in nutritional studies can be categorized into two basic types: static and functional tests [18].

7.1 Static Analysis

Current nutrient, bioactive chemical, or biomarker concentrations may be determined by static testing. Serum iron, glucose, and cholesterol levels are all examples of static analysis. However, the quantity of a chemical in the bloodstream does not necessarily correspond to the amount stored in the body or its bioavailability. The amount of a nutrient or biomarker in the blood or other body fluids may be affected by how recently the person ingested it. Taking samples when the subject is fasting may help alleviate this problem to some degree [28].

7.2 Functional Analysis

Functional analysis measures biological responses or functions. This enables a dynamic evaluation with regard to biomarkers [28]. Functional tests quantify phenotypic flexibility and reflect the degree of stability of an individual's homeostasis. Oral glucose tolerance testing evaluates prediabetes and insulin sensitivity, as well as dynamic hyperlipidemia and the early diagnosis of metabolic syndrome as a biomarker of cardiovascular risk; both of these tests are examples of functional tests [28].

Triglyceride levels following lipid loading are one example of such a test. In order to measure how different metabolic variables in people react, a standardised mixed liquid diet combining carbs, lipids, and proteins has recently been developed [23]. Metabolic alterations in obesity may be better characterised with the use of other kinds of functional tests, such as those that measure responses to ambient hypoxia and oxygen restriction. This includes examining changes in biomarkers in response to fasting in humans [23].

In summary, static analyzes measure current concentrations of nutrients or biomarkers, while functional analyzes assess dynamic responses or functions associated with biomarkers. Both types of analysis are valuable in nutritional research for understanding the relationship between nutrient intake, biomarkers and physiological outcomes [23].

8. Approaches in the Identification of Biomarkers

"Omics" or global assessment methodologies have facilitated new research directions in the field of nutrients. Recent developments in DNA sequencing [3,4], microarray technology [7] mass spectrometry [7], and nuclear magnetic resonance [8], among others, have allowed for the simultaneous evaluation of multiple parameters, yielding remarkable insights into transcriptome, proteome, and metabolome responses. Technological developments have been made, most notably in the fields of DNA and RNA sequencing**,** mass spectrometry, single-molicular omics, and bioinformatics. Systems techniques provide a more thorough and in-depth comprehension of a character's physiology/pathology and offer a window into the complex relationships between food and health, enabling researchers to examine the function of dietary supplements in illness prevention and development. Therefore, it seems that omics systems are the best bet for discovering and characterising new dietary indicators to define people's dietary repute and to understand dietary bioactive components responsible for beneficial health effects [20]**.**

8.1 Genetic Biomarkers

In the field of nutrition research, single nucleotide polymorphisms (SNPs) are the kind of genetic variation that genetic biomarkers are most often used to detect. Since these biomarkers are determined by DNA analysis, they are readily detectable in nucleated cells isolated from almost any kind of biological material. In contrast to other types of biomarkers, the definition of genetic biomarkers does not evolve with time. DNA samples are also convenient since they can be stored, transferred, and analysed rapidly and inexpensively [8,9]. Genetic biomarkers must be included in order to completely understand the relationship between intermediate biomarkers (such as plasma lipids, fasting glucose, oxidative

indicators, and inflammatory markers) and the incidence of nutrition-related disorders. Different phenotypes of illnesses connected to poor nutrition have been linked to a large number of SNPs. Particularly when inter-individual variance is controlled by specific gene variations, it is necessary to demonstrate strong connections between food and illness by identifying the relevant genetic polymorphisms linked with phenotypes of interest [15].

Moreover, when there is a limited safe range between safe and hazardous levels, or when it changes bioavailability, genetic diversity within the genome may alter the accuracy of the evaluation of micronutrient status. Thus, genetic biomarkers based on genetic polymorphisms provide valuable information about the relationship between diet, disease risk and nutrient status in nutritional research.

8.2 Epigenetic Markers

Epigenetics refers to changes to the genome that do not modify the DNA sequence but instead include chemical alterations that may impact gene expression. Depending on the demands of the organism, these variations may be either generationally stable or quickly adaptable. The main methods of epigenetic regulation include DNA methylation and histone changes, such as site-specific methylations and acylation [11]

Children's metabolisms are programmed by perinatal epigenetic changes, such as those brought on by alteration in DNA methylation status. For instance, the expression of the Pdx1 gene, which controls insulin gene transcription in response to glucose, was suppressed in the offspring of rats with intrauterine growth retardation. Other epigenetic marks were discovered to be reversible, but this one seemed to be persistent in the first generation [15]. The maternal diet in mice impacted the DNA methylation of the Nr4a1 gene in skeletal muscle, which is associated to insulin sensitivity, and was afterwards modulated in the offspring by voluntary exercise. According to animal studies, maternal nutrition during pregnancy may modify the epigenetic patterns of certain genomic regions (metastable epi-alleles) in the early embryo, leading to stable phenotypic alterations in the posterity. Evidence is mounting that prenatal nutrition may elicit long-lasting alterations in DNA methylation in humans, despite the paucity of studies on this topic. It has been shown, for instance, that the methylation patterns of metastable epialleles in children are linked to changes in maternal methyl donor consumption that are impacted by seasonal variances in food. In order to anticipate DNA methylation alterations in newborns postnatally, researchers have found many biomarkers linked to essential micronutrients involved in one-carbon metabolism in maternal plasma. Prenatal starvation, such that which occurred in the Netherlands during the Hunger Winter after World War II, has also been linked to changes in DNA methylation. Years later, it was discovered that their DNA methylation levels at different loci were different from those of their unaffected same-sex siblings. These differences were primarily attributed to periconceptional famine exposure, suggesting that the methylome is particularly susceptible to changes during the early stages of development .Complex interactions between different nutrients are probably involved in the control of epigenetic processes [20].

8.3 Transcriptome Markers

The transcriptome, which includes all of the genes expressed in a particular tissue at a given time, may be studied thanks to advances in the field of transcriptomics [17] .Methods such as real-time RT-PCR may be used for investigating single genes, whereas DNA microarrays and RNA sequencing (RNA seq) can be used for examining large numbers of genes concurrently. Although DNA microarrays have been widely used for transcriptome studies, RNA seq is quickly becoming a competitive method. More RNAs can be analysed by RNA seq, which might lead to more in-depth functional insights. However, at the moment, researchers are concentrating mostly on annotated transcripts, which are abundant on DNA microarrays. There is a need for more advanced bioinformatics analysis and more technological advancements in RNA seq, especially for small samples. Nonetheless, as sequencing technologies continue to improve and costs decrease, RNA sequence is expected to become the standard approach [24].

8.4 Proteomic Markers

The whole range of proteins that may be generated by a certain cell, tissue, or organ at any given time is referred to as its "proteome." Similar to the transcriptome, the proteome is dynamic and changes depending on the kind of cell and its functional state. Although the impacts of bioactive dietary components on the genome tend to be modest, they may have significant effects on the transcriptome and proteome [23].

Traditionally, proteomic techniques, such as two-dimensional electrophoresis, have limitations due to biases towards highly abundant proteins, difficulty in detecting proteins with extreme properties, and challenges in protein identification. Prior to recent developments in mass spectrometry, it was difficult to detect, identify, and quantify proteins in blood and other biological fluids. However, these developments have substantially improved sensitivity, specificity, and resolution. The use of mass spectrometry and isobaric tagging in larger population studies has yielded robust and consistent results for biomarker discovery. Additionally, factors like gender, age, and fat mass can influence proteomic profiles and need to be considered for diagnostic applications [22,24].

There has been some disappointment in the use of proteomics to studies of nutrition, although advancements are being made. Proteomics has been examined as a way to analyse the advantages of dietary regimens in cancer treatment, and it has been shown that purple vegetables, carrots, and potatoes all contribute to metabolic health. Serum/plasma potential biomarkers may be hypothesised as a result of data collection on the cellular localizations, functions, and expression patterns of proteins and peptides in different organs and cell types. These putative biomarkers may then be directly evaluated. It is anticipated that the creation of blood protein databases will help in the discovery of new biomarkers [24].

8.5 Metabolomic and Lipidomic Markers

Analysis and screening of tiny metabolites in biological samples constitutes metabolomics, also known as metabolite profiling. In the last two decades, the area of metabolomics has greatly evolved, in great part due to advancements in equipment technology, including mass spectrometry, gas and liquid chromatography, as well as bioinformatic tools and software [22].

Targeted and untargeted methods are both viable options for metabolomics research. Metabolites having comparable structures, such amino acids, fatty acids, acylcarnitines, and phytochemicals, are the primary focus of targeted metabolomics. This method is quantitative and is designed to answer certain biochemical questions or test specific hypotheses about one or more pathways. Targeted metabolomics, for example, led to the identification of a set of

five amino acids (leucine, isoleucine, valine, tyrosine, and phenylalanine) whose fasting levels significantly predict the development of diabetes. Targeted metabolomics has also shown a collection of metabolites (leucine/isoleucine and glycerol) whose response to an oral glucose may serve as a predictor of insulin sensitivity [25].

On the other hand, untargeted metabolomics is a thorough examination of metabolites with no specific aims in mind. In addition to allowing for the identification of new biomarkers or metabolic pathways, it offers a more comprehensive perspective of the metabolome. Untargeted metabolomics is particularly useful in exploring complex diseases or conditions where the underlying metabolic alterations are not well understood [24].

The ability to detect and measure metabolites has been greatly enhanced by developments in instrument technology and data processing, which have benefited both targeted and untargeted metabolomics. These methods offer the ability to analyse the impact of dietary changes on the metabolome, find biomarkers for different disorders, and provide light on metabolic pathways [24].

Conclusion

Biomarkers are also known as biological markers and are the quantifiable traits or signs that can be used to assess pathological alterations, normal biological processes, or reactions to treatments or exposures. These indicators can be found in a variety of biological samples, including genetic material, tissues, blood and urine. These biomarkers can be used to look on a person's nutritional status in a different ways. Biomarkers provide a more accurate and immediate indicator of nutritional status. Clinical biomarkers are mainly used to diagnose medical conditions and may not be directly related to diet. Biomarkers like folate, iron, vitamin B12, copper, and zinc help identify possible diet related causes of illnesses such as anemia. They are useful in the medical field. These biomarkers may be divided into four primary groups and they indicate effects, exposure, function, and the presence or absence of health and illness. Biomarkers of exposure are used to assess the dietary consumption of nutrients. They are quite intriguing since their use can enhance the classification of participants according to the exposure to certain nutrient. Biomarkers of effect are that related to target function or biological response. They also provide insight into the nutrient metabolism. Biomarkers of function aim to assess the functional consequences of specific nutrient deficiencies or excess making them more biologically meaningful than static biomarkers. Biomarkers of health/disease are indicative of a person's health or their risk of developing it. There are certain factors that affect the choice of nutritional biomarkers like objective of study, population setting, validity, sensitivity and specifity and many others. There are different criteria for selecting biomarkers like methodological aspect. Biomarkers can be provided by different sources are blood borne specimens like plasma, serum, blood cells, excretion products like urine, feces and easily obtainable samples like hair, nails, skin, etc. Biomarkers analysis in laboratory can be categorized into static and functional. Static analysis measures the concentration of a nutrient, bioactive compound, or biomarker in sample whereas functional analysis measure the response or function.

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