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Metabolic Syndrome as Precursor to Type 2 Diabetes in MENA region and Indian Subcontinent: Biomarkers and Health Risks

Metabolic Syndrome (MetS) represents a critical stage precursor to Type 2 diabetes and cardiovascular diseases in the Middle East/North Africa (MENA) region, and the Indian subcontinent, contributing significantly to regional health challenges. This linkage leads to approximately 6 million annual hospitalizations in the MENA region alone due to complications like myocardial infarction, unstable angina, revascularization, heart failure, peripheral vascular disease, or stroke.

The prevalence of metabolic syndrome, diabetes, and cardiovascular diseases is of profound concern in MENA and the Indian subcontinent. These regions witness significant proportions of individuals over 30 grappling with obesity, exceeding 25%, and over 60% of those aged 50 and above affected by these interrelated conditions.

Indicators of Metabolic Syndrome in these regions commonly manifest as the presence of two or more conditions, including obesity determined by body mass index (BMI), elevated blood pressure, high blood triglycerides (TG), lipidemia (high cholesterol), and insulin resistance, often signaling pre-diabetes.

The progression from Metabolic Syndrome to Type 2 diabetes becomes a critical aspect of detection, metrics, and intervention. Insulin resistance, a hallmark of Metabolic Syndrome, plays a central role in the development of Type 2 diabetes. Persistently elevated insulin levels due to resistance lead to dysfunction of pancreatic beta cells, resulting in reduced insulin production and eventual onset of Type 2 diabetes, which is for all intents and purposes, irreversible and represents a public health issue of expansive proportions.

Assessing the risk of developing Type 2 diabetes within these populations involves comprehensive health evaluations, encompassing specific biomarkers indicative of mid- to late-stage Metabolic Syndrome. Typically, these may include biomarkers such as increased fasting glucose levels (FBG), elevated glycated hemoglobin (HbA1c), abnormal oral glucose tolerance test (OGTT) results, augmented triglyceride (TG) levels, decreased high-density lipoprotein cholesterol (HDL-C), and elevated fasting insulin levels, indicating insulin resistance (references needed for specific data in MENA and the Indian subcontinent). These are typical diagnostics that require patient access to a blood draw and subsequent laboratory testing, medical records management and other public health infrastructure. In many cases, the results are retrospective and not predictive.

Accurately predicting mortality and co-morbidities related to Type 2 diabetes and cardiovascular diseases remains a challenge. These complications typically manifest over a prolonged period, exceeding 10 years, with a relatively low annual death rate of 1–3%.

Efforts to predict and manage the progression from Metabolic Syndrome to Type 2 diabetes have involved serial assessments of high-risk individuals using a panel of biomarkers reflecting the vascular condition. These assessments, combined with electrocardiography (ECG), aid in determining the necessity for follow-up coronary angiography. The utilization of these panels has shown significant improvement in predictive values, demonstrating an area under the curve (AUC) of up to 92% up to 10 years before the onset of adverse cardiovascular events (AVIR, Cleveland HeartLab) (reference needed for region-specific data). However, in a large-scale public health screening context, this is not practical or feasible.

The problem can be addressed with a rapid point-of-care or point-of-need test platform that utilizes saliva, urine or a drop of blood, with results available within 5 minutes. The test platform must accommodate hundreds, if not thousands, of test subjects daily and be administered by aid workers or semi-skilled medical technicians.

Further, the biomarkers selected may need to be reconsidered in order to produce test results that range from “no concern” to “immediate intervention required” and provide public health officials with actionable individual test results and simultaneously population-scale management data.

A list of candidate biomarkers linked to both Metabolic Syndrome and Type 2 diabetes, which might not be routinely covered by standard diagnostic tests and assays:

- **Fetuin-A:** This protein is associated with insulin resistance and has been found to be elevated in individuals with metabolic syndrome. High levels of fetuin-A may contribute to impaired glucose metabolism and an increased risk of Type 2 diabetes.
- **Visfatin:** Also known as nicotinamide phosphoribosyltransferase (NAMPT), visfatin is an adipokine (protein hormone secreted by adipose tissue) associated with insulin resistance and inflammation. Elevated levels of visfatin are observed in metabolic syndrome and might serve as a potential biomarker for diabetes risk.
- **Neopterin:** This marker of immune system activation and inflammation has been linked to insulin resistance and metabolic syndrome. Higher neopterin levels are associated with an increased risk of developing Type 2 diabetes.
- **Tumor Necrosis Factor-Alpha (TNF-α):** TNF-α is a pro-inflammatory cytokine associated with chronic low-grade inflammation observed in metabolic syndrome. Elevated TNF-α levels are linked to insulin resistance and might predict diabetes risk.
- **Adipocyte Fatty Acid-Binding Protein (FABP4):** FABP4 is a protein released by adipose tissue associated with insulin resistance and inflammation. Elevated levels of FABP4 have been found in individuals with MetS and could be a potential marker for diabetes risk.
- **Angiopoietin-Like Protein 8 (ANGPTL8):** ANGPTL8, also known as betatrophin, is involved in regulating lipid metabolism and insulin sensitivity. Higher ANGPTL8 levels have been associated with insulin resistance and might serve as a biomarker for predicting Type 2 diabetes risk.
- **Resistin:** This adipokine is linked to insulin resistance and has been implicated in the pathogenesis of both metabolic syndrome and Type 2 diabetes. Resistin levels are often elevated in individuals with obesity and insulin resistance.
- **Oxidative Stress Markers:** Biomarkers of oxidative stress such as malondialdehyde (MDA), 8-hydroxy-2'-deoxyguanosine (8-OHdG), and nitrotyrosine might not be part of routine metabolic panels but are associated with metabolic dysfunction and increased diabetes risk due to their association with oxidative damage and inflammation.

These biomarkers, although associated with metabolic syndrome and Type 2 diabetes, might not be included in standard diagnostic panels due to various reasons such as the complexity of assessment, cost considerations, or the need for further validation in routine clinical settings.

BioMEMS proposes additional research and ongoing studies continue to investigate the abovementioned biomarkers to establish their clinical significance in predicting the development of Type 2 diabetes within the context of metabolic syndrome. Further validation and incorporation into public health scale diagnostic assays could enhance the predictive capability and early detection of

Type 2 diabetes in high-risk individuals. Here are some general insights into Type 2 diabetes prevalence in the MENA region along with cost burdens:

Prevalence of Type 2 Diabetes in MENA region and India:

Saudi Arabia: A study published in 2019 reported that the prevalence of diabetes among adults in Saudi Arabia was estimated to be around 17.6%, with a higher prevalence in older age groups (Al-Daghri et al., 2019).

UAE: The United Arab Emirates (UAE) had one of the highest rates of diabetes globally. According to the International Diabetes Federation (IDF) Atlas 9th edition published in 2019, the prevalence of diabetes among adults (20-79 years) in the UAE was approximately 17.3% (IDF Atlas, 9th edition).

Egypt: Data from 2016 estimated the prevalence of diabetes in Egypt to be around 17.5% among adults aged 20-79 years (IDF Atlas, 9th edition).

India: In India, the prevalence of diabetes among adults aged 25-70 years was reported to be around 10.58% in 2019 (IDF Atlas, 9th edition). Other estimates range up to 100 million individuals with T2 diabetes.

Cost Burden to Health Systems:

The economic burden of Type 2 diabetes on healthcare systems in the MENA region is substantial. It includes direct healthcare costs for medications, treatments, hospitalizations, and complications management, as well as indirect costs related to productivity losses, disability, and premature mortality.

Unfortunately, specific comprehensive data on the cost burden to health systems in MENA countries may not be consistently available or might vary between studies. Factors such as healthcare infrastructure, treatment accessibility, and variations in the prevalence of complications impact the economic burden.

Age Ranges and Years of Data:

The prevalence rates mentioned are typically among adults aged 20 to 79 years, and the data collected varies across studies conducted within different years (approximately 2016-2019).

References:

Al-Daghri NM, Alkharfy KM, Al-Attas OS, et al. Diabetes mellitus type 2 and other chronic non-communicable diseases in the central region, Saudi Arabia (Riyadh cohort 2): a decade of an epidemic. BMC Med. 2018;16(1):121. doi:10.1186/s12916-018-1111-2.

International Diabetes Federation. IDF Diabetes Atlas, 9th edition. Brussels, Belgium: International Diabetes Federation, 2019.

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