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DIABETES MELLITUS: A REVIEW OF SOME OF THE PROGNOSTIC MARKERS OF RESPONSE TO TREATMENT AND MANAGEMENT

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Abstract:
According to WHO, the inadequacy of insulin secretion or inaction can cause disturbances with protein metabolism, fat and carbohydrates along with chronic hyperglycemia overall disturbing the metabolism are known as "Diabetes Mellitus" (DM). Late diagnosis or uncontrolled conditions can lead to life-threatening conditions. The assessments' of biomarkers is done in order to identify it at an early stage leading to early treatments of this condition. The characteristics such as choice, sensitivity, types and descriptive information of the biomarkers play a vital role
The predictive biomarkers' includes elements related to blood such as platelets, glycated hemoglobin, and platelet-to-lymphocyte ratio. Moreover, white blood cells including its perspective ratios like neutrophil-to-lymphocyte ratio, neutrophils, and total leukocytes. Also, many proteins are involved such as C-reactive Lipoproteins, D-dimer, Very Low Lipoproteins, Low-Density Lipoproteins, High-Density Lipoproteins, and Fibrinogen.
The level of Diabetes and the biomarkers are usually working in an inverse proportion. This shows that the level of Diabetes increased shows a decrease in the partial thromboplastin time, prothrombin time, red blood cells, activated thromboplastin time and hemoglobin concentration. As a conclusion, the early diagnosis can lead to fewer complications and better treatment of the diagnosed problem according to the guidance.

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1.0. INTRODUCTION

A metabolic disorder marked by the abnormal metabolism of lipids, proteins, and carbohydrates is known as Diabetes Mellitus. This is of two types; In Type 1 Diabetes, the deficiency of insulin release is seen along with abnormal metabolism rate, however, in Type 2 Diabetes, the high level of blood insulin is examined due to chronic hyperglycemia which leads to complications related to cardiovascular and metabolic dysfunction (Agu, 2018).

The abnormality is usually due to the abnormal mechanism of T2DM2 which causes biochemical and pathophysiological effects. Furthermore, these mechanisms compromises of (1) Pancreatic βcells produce less insulin; (2) Glucose production is increased in the liver; (3) Pancreatic α-cells secrete a higher amount of glucagon; (4) High level of lipolysis; (5) Brain changes leading to Insulin resistance or abnormal neurotransmitters; (6) The small intestines reduces the incretin effect; (7) The peripheral tissues such as liver, adipose tissue or skeletal muscles fail to uptake glucose; or (8) absorption of renal glucose is increased (Banu, 2018).

Diabetes Mellitus (DM) can lead to many complications or disorders such as blood disturbances, metabolic disorders, cellular or organic disorders along with vascular disorders in extreme cases. In case the diabetes is not controlled or tracked, it can lead to complications such as cardiovascular diseases or atherosclerosis. Nevertheless, neuropathy, retinopathy, and nephropathy are also risked leading to glycated connective tissues, glycated hemoglobin (HbA1c) or glycated low-density lipoproteins (LDL) (Agu, 2018).

For the treatment of Diabetes, two main treatments are done. This includes a hormone therapy in form of injections or oral hypoglycemic therapy such as medications especially in Diabetes Type 1 which usually show many side effects like hypoglycemia, hypersensitivity reactions, gastrointestinal disturbances or weight gain. A great research is being carried out by the researchers, practitioners, and biochemists in order to overcome the side effects. This research is done by varying the biomarkers present and how the medications are being administrated or absorbed to change the levels leading to better results of the patients (Galstyan, 2014).

Markers of Anaemia

During the anemic considerations, the factors of hemoglobin synthesis, cellular morphology of red blood cells and the biochemical integrity of hemoglobin are mainly observed for the glucose levels. Changes in the level of coagulation references, WBCs and RBCs and platelet are mainly seen in people with Diabetes leading to the dysfunction and abnormalities. The reference ranges of hemoglobin in normal males are <13.5 g/dl and in females 12.0 g/dl (Gillespie, 2017).

Due to abnormal blood ranges, the level of urinary albumin excretion, HbA1c, glomerular filtration rate are also examined. Also, due to the lack of production of erythropoietin in kidneys, the Anaemia results broke into the factors, edema, dyslipidemia, urine protein-to-creatinine ratio, and hypoalbuminemia are ≥3 and also in the Red Blood Cells membrane proteins the non-enzymatic glycosylation is increased. Many types of research have therefore approved the abnormal levels of RBCs, packed cell volume and abnormal hemoglobin in a diabetic rat proving the stance of the anemia (Kaku, 2016).

The kidney related diseases which are already affected by diabetes can result in anemia. This is because of the abnormal signaling of erythropoietin in kidneys which is mainly under the concept of nephropathy particularly known as autonomic neuropathy or nerve damage in neuropathy deducing it to anemia (Gillespie, 2017).

One of the authorized treatments being used by people with T2DM is Metformin. This drug is usually being used for long terms up to 15 years consecutive affecting the metabolism system by malabsorption of Vitamin B12 as reported to cause a deficiency in around 30% of the population. As a conclusion, it is reported that Peripheral Neuropathy in which nerve damage of arms, hand, feet, and legs is seen and also anemia is perceived due to deficiency of Vitamin B12 (Kilpatrick, 2015).

Immune components

An immune suppression is evaluated during the experimentation on the diabetic rats due to the abnormal levels of lymphocytes, WBCs, and platelets. This is because of pathogens being killed after attacking by larger pathogens or due to phagocytosis. Due to low immunity level, many mild to severe complications can result. However, in Diabetes Type 1, there is an increased WBC count, neutrophils, total leukocytes but low levels of eosinophils by reason of non-infectious systematic inflammations causing diabetes ketoacidosis which usually causes high expressed cytokines of the pro-inflammation (Kilpatrick, 2015).

For this, it is investigated that the presence of acute infection or hyperglycaemic crisis could be administered by checking the leukocyte counts which usually serves as a prognostic biomarker of a diabetic patient. It is significant to advice that biochemical and physiological event's array, which are basically initiated in the time period of atheroma formation in the blood vessels endothelium by the influence of HbA1c and some other advanced (AGEs) glycation end products, comprising glycated LDL and species of reactive oxidative, which appeal macrophages which eventually shape foam cells with a resultant inflammatory pharmacological chemical's release, may also boost the elevated mobilization and these immune factors' recruitment (Robertson, 2014).

Markers of Dyslipidaemia

T2DM is a component of the MS (metabolic syndrome) which includes dyslipidemia, impaired hematological indices, and hypertension. Lipid metabolism irregularities, specifically hypertriglyceridemia and HDL of low level, are the most perpetually originated in patients with (hyperglycemia) impaired glucose homeostasis. Hypertriglyceridemia may further triglyceride-rich VLDL which potentiates the activity of platelet an impact which mediated partially through apolipoprotein E and an interface with the platelet-LDL receptor (Siddiqui et al., 2018).

The dispensation of HDL reconstituted' HDL the patients of DM has been stated to endorse cholesterol efflux from platelet membranes, it overwhelms aggregation. Additionally, the lipids and glucose interaction which results in the glycated LDL formation has been said to indicate to impaired (NO) nitric oxide fabrication and elevated intra-platelet calcium absorption, further supplying to hyper-reactivity of platelet, which additionally obscures the DM condition. However, plasma laboratory assessments, HDL, LDL, and VLDL may be considered positive predictive markers in the DM monitoring (Siddiqui et al., 2018).

Advanced Glycation End Products

The result of hyperglycemia in disturbances in cellular metabolism due to the increased generation of reactive oxygen species and many macromolecules' non-enzymatic glycation, it further leads to an alteration in the structure of cellular and formation and function of AGEs. Hyperglycaemia's recurrent episodes lead to an interaction of non-enzymatic between the group of carbonyl and of declining sugar and the basic amino protein group, leading to reactions of the cascade; the final output of which a group of heterogeneous of compounds recognized as AGEs (Starup-Linde and Vestergaard, 2016).

AGEs formation improves metabolic disturbances and also enhances the production of reactive oxygen species through the interaction with the appropriate receptor for AGE (RAGE). HbA1c is one part of the AGEs which comprises the complicated glycosylation of hemoglobin. HbA1c elevates the highly reactive formation of free radicals inward the RBCs, however changing its properties of the cell membrane, leading to aggregation of blood cell and elevated viscosity of blood, with the connected impaired flow of blood in severe DM like cases. Additional these events are the base of changes in biochemical information and biophysical properties of membrane basement; with additional causes the alteration in permeability and vasodilation of vessels of blood (Starup-Linde and Vestergaard, 2016).

In the procedure to accurately diagnose DM and in the frank hyperglycaemias lack (plasma glucose > 200 mg/dL) or in the crises of hyperglycemia it is beneficial to recurrence the identical diagnostic examination for confirmation. In conditions where there are two non-identical examinations with opposing results, the examination which is positive must be repeated and a DM diagnosis should be made after a confirmatory examination has been done. For those individuals whose examination results became negative for diabetes, need to repeat the examination at three-year intervals (Siddiqui et al., 2018).

Markers of Blood Coagulation

a) Plasma Platelets

It is not fully understandable and clear that what roleplay is there in hyperglycemia in platelet hyperactivity in DM. the overall congealing cascade is dysfunctional in DM; elevated fibrinogen and plasminogen level activator inhibitor support both defective and thrombosis of clots once shaped. T2DM platelets individual observe to vascular endothelium and collective more promptly as compared with physiologic situations. Sensitivity loss to the general inhibitory signal practiced by (PGI-2) prostacyclin and NO produced by the vascular endothelium gives as the high defect in the function of the platelet (Starup-Linde and Vestergaard, 2016).

In this case, insulin is the general antagonist course of hyperactivity of platelet as it sensitizes the PGI-2 platelet and improves the generation of endothelial of PGI-2 and NO. However, the declined or insulin sensitivity lack action in DM generates a complicated model of disordered platelet activity encouraging to the events of micro-vascular and macro-vascular.

Activation of platelet plays important role in athero-thrombosis specifically in T2DM and elevated in vivo activation of platelet with elevated thromboxane biosynthesis has been stated in those patients with damage of glucose metabolism, even in initial stages of the disease, and in the phases of practices (Siddiqui et al., 2018).

b) D-dimer

It is basically a fibrin squalor product, a fraction of protein present in the blood and in a clot of blood is degraded further by fibrinolysis. D-dimer also named this just due to it contains "D" fibrin fragments joined through a cross-link. Its concentration may further be determined by a blood examination to support diagnose thrombosis. Since 1990, it has generated a strong position to perform in the suspected thrombotic disordered patients (Starup-Linde and Vestergaard, 2016).

c) Plasma Fibrinogen

Multiple studies have represented that the occlusive thrombus formation, on an atherosclerotic lesion damage, it is highly general practice to participate the component of severe myocardial infarction. Fibrinogen itself basically determined through multiple non-modifiable and modifiable determinants such as sex, age, BMI (body mass index), hypertension, smoking, glycaemic control, alcoholism, urine albumin excretion rate and lipid profile (Kilpatrick, 2015).

d) C-Creative Proteins

Latest studies found that glycaemic poor control is particularly linked with the macrovascular DM complication development and they further have recognized the CRP is a significant cardiovascular disease risk factor as one of the severe phase markers of inflammatory response, like atherosclerosis. Thus, it was determined that CP is bluntly linked to glycemia and HbA1c in DM patients. CRP is an inflammation marker which concerned with many chronic diseases such as stroke, heart disease, and DM. The researcher has shown that not only the elevated level of CRP is a specific risk factor for stroke and heart diseases but also that declining CRP levels may considerably lesser an individual's risk of heart diseases (Kaku, 2016).

CONCLUSION:

It is significant to note that different events leading to DM may further be linked with dyslipidemia, obesity, cardiovascular diseases, and hypertension; however, changes in lifestyle like proper but healthy dietary plan, personal activities, cessation of smoking and pharmacological introduction in the shape of drugs are believed highly significant to stop or delay in the developmental timeline of DM. While investigating these events and in DM progression situation need highly advanced stage into stages presenting with other linked complexes, the parameters and markers may offer a high offer of information guidance, particularly in the treatment progression time. The obtained information may further guide the medical adviser of such patients on the choice of drug, the appropriate level of doses and administration period which best suit their situations.

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