

Glycated Hemoglobin As a Risk Factor

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Abstract: Due to high level of blood sugar, some glucose molecules are attached to the normal hemoglobin which is known as glycated hemoglobin (HbA1c). HbA1c indicates the average blood glucose levels over the past 6 to 8 weeks. Therefore, it has been recommended as a screening tool for the detection and monitoring of diabetes mellitus. HbA1c at high levels are associated with various metabolic disorder and other disease. In the present review, we summarized risk factors associated with increased level of HbA1c and its clinical significance.

Key words: Diabetes mellitus, HbA1c, Metabolic disorder, Obesity, Vascular disease

I. INTRODUCTION

Glycated hemoglobin is also referred as glycosylated or glucosylated hemoglobin. The fraction of glycated hemoglobin increases along with increase in plasma glucose level such as in the case of diabetes mellitus. HbA1c is a measure of the beta-N-1-deoxy fructosyl component of hemoglobin (Miedema, 2005; Peterson et al., 1998).

II. RISK ASSOCIATED WITH HIGHER HbA1c

Measurement of HbA1c is considered to be the gold standard test for the glycaemic control in diabetic patients. It is most extensively used test of glycaemia (Syed and Khan, 2011). Among known risk factors, higher levels of HbA1c were associated with metabolic syndrome, obesity, renal disease, coronary artery disease, CVD, stroke, cerebral white matter disease and peripheral arterial disease (Muntner et al., 2005; Ikeda et al., 2013; Selvin et al., 2010).

A. HbA1c and metabolic syndrome

Aggregated closely related cardiovascular risk factors is defined as metabolic syndrome (Grundy et al., 2005). HbA1c is considered as one of the best indicator of glycemic control in diabetic patients. However, there is correlation between glycated hemoglobin and accumulated cardiovascular risk factors (Giuffrida et al., 2010). The literature suggested effect of chronic hyperglycemia (HbA1c) on metabolic syndrome which is associated with both major types of diabetes (Giuffrida et al., 2010). HbA1c below the level for prediabetes might be a predictive measure of metabolic syndrome (Janghorbani and Amini, 2012). The study suggested that along with fasting plasma glucose, addition of new HbA1c criteria might be useful in identification of person with increased risk of diabetes (Kim et al., 2012). Measurement of HbA1c has facilitated as not

only diagnostic tool for diabetes development but also an important substitute for cardiovascular disease (Rohlfing et al., 2000; Inoue et al., 2008; Park et al., 2012).

B. HbA1c and diabetes

Diabetes is reaching pandemic proportions across the world (Shimodaira et al., 2015). As per International Diabetes Federation, 387 million people have diabetes worldwide upto 2014 (IDF, 2014). The number of people with diabetes is expected to rise to 592 million by 2035 (IDF, 2014). Prediabetes usually precedes diabetes and is more prevalent than diabetes (Wild et al., 2004). Therefore, identification of person with diabetes and prediabetes is key factor to prevent complications or delay disease progression from prediabetes to diabetes (Shimodaira et al., 2015).

The use of HbA1c measurements to screen patients for diabetes and prediabetes will likely be popular with clinicians and has recently been recommended for the diagnosis of diabetes on the basis of a detailed analysis of IEC (IEC, 2009) and ADA recommendations (ADA, 2009). The optimal HbA1c value for diagnosis of diabetes varied in different population such as in Australian, American Chinese and Japanese populations it ranged from 5.3% to 6.1% (Ko, et al., 1998; Rohlfing et al., 2000, Colagiuri, et al., 2004; Shimodaira et al., 2015).

C. HbA1c and obesity

Obesity is the most common metabolic disorder which leads to diabetes mellitus, cardiovascular diseases and metabolic syndrome. The incidence of obesity is increasing globally day by day specially in urban population (Singh et al., 2011). According to Global Health Observatory, more than 600 million people worldwide are obese (WHO, 2015) and have serious impact on various health outcomes (Lewis et al., 2009). World Health Organization (WHO) recognizes

obesity and its complications amongst the top 10 global risk factors leading to ~40 % global deaths (Sabale and Barhate, 2014). Early detection of obesity will be useful to restrict the ever increasing incidence of diabetes and other metabolic syndrome caused by obesity. The literature suggested that the obesity is significantly related with poorly controlled hemoglobin glycation in diabetic and non-diabetic subjects (Sheth et al., 2015). Therefore, targeting to decrease the obesity is likely to reduce HbA1c not only in diabetic subjects but also in non-diabetic subjects.

D. HbA1c and heart failure

HbA1c influences heart disease also. Elevated levels of HbA1c not only increases incidence of CHD but also responsible for successive complications of CHD such as congestive heart failure. The literature suggested that each 1% rise in HbA1c results in more coronary problems and more hospitalizations due to heart diseases (Gerstein et al., 2008). Glycated hemoglobin is an independent predictor of heart failure in diabetic persons also. When incidence of heart failure was compared between diabetic and non-diabetic populations, the incidence was 2.5 times higher among diabetic patients with elevated HbA1c (Nicholas et al., 2004).

E. HbA1c and peripheral vascular disease

The menace of peripheral vascular disease increases by more than two folds due to diabetes, and is reason of 70% non-traumatic amputations. It is an indication of cardio vascular disease which is not extremely fatal but associated with serious risk of stroke and CHD. Selvin and coworkers concluded that HbA1c is positively associated with low ankle-brachial index and symptomatic peripheral vascular disease, although it is not only due to macrovascular disease but a great element of microvascular disease (Selvin et al., 2006; Syed and Khan, 2011).

F. HbA1c and cancer

The literature suggested that there may be an increased risk of cancer associated with increased level of HbA1c ($\geq 6\%$), predominantly in those persons with moderately elevated HbA1c levels (6%–6.9%), that is at HbA1c levels below the accepted threshold indicative of diabetes (Travier et al., 2007). It is noted that most consistent increase was found for all types of cancers. Even though persons with highly elevated HbA1c levels are also exposed to increased cancer risks, increased risks were usually highest among the persons having moderately elevated HbA1c level (Travier et al., 2007). Increased risk of cancer, particularly respiratory and endometrial cancers, due to elevated level of HbA1c is also consistent with other findings (Travier et al., 2007).

G. HbA1c and end stage renal disease

It is well known that glycated hemoglobin has association with diabetes mellitus which is the most common cause of end stage renal disease (ESRD). The literature suggested that HbA1c lower than 6.5% was associated with a reduced incidence of ESRD and at increased level of HbA1c above 6.5% has increased risk of ESRD (Oh et al., 2011). One of the recent study shows that the higher level of HbA1c is related with higher risks for clinical outcomes in diabetic patients with stage 3–4 CKD but not in stage 5 CKD (Kuo et al., 2016). Furthermore, some more research on patients with type 2 diabetes mellitus and preserved kidney function have revealed that tight glycemic control targeting a HbA1c level of <6%–6.5% reduced the development of albuminuria, but the effect on ESRD, was inconclusive (Patel et al., 2008; Duckworth et al., 2009; Ismail-Beigi et al., 2010; Kuo et al., 2016).

In the diabetes management, monitoring of blood sugar plays a vital role. Most of the physicians and patients trust on glycated hemoglobin test to measure average blood sugar level of an individual. This test is extensively reliable in the medical community and normally used for long-term blood sugar test. According to Inaba et al., (2007) “glycemic control is best assessed by a combination of blood glucose monitoring and quarterly measurement of glycosylated hemoglobin. The degree of glycosylation of hemoglobin depends not only on the level of glycemic control but also on the half-life of red blood cells. American Diabetes Association, International Diabetes Federation and American College of Endocrinology recommended HbA1c as an alternative criterion for the diagnosis of diabetes and as a screening test for persons at high risk of diabetes (IEC, 2009; WHO, 2011).

III. REFERENCES

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