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The Role of HbA1c as a Screening and Diagnostic Test for Diabetes Mellitus in Benghazi City

Noor-Alhooda Milood Al-Awkally[1], Ibrahim Mohamed Ghriba[2], Salwa Muftah Eljamay[3], Rana Mohammed Alabeedi[4], Maree Dokally Ali[5], Alreda Miloud Al-Awkally[6], Suhaylah Meeloud Awad[7], Wisam Omar Mousaay[8], Nesrine Miloud Al-Awkally[9], Khaled S. Ghareeb[10]

[1,5] Medical laboratory Department, Higher Institute of Science and Technology, suluq, Libya
[2] Medical laboratory Department, Higher Institute of Science and Technology, Mizda, Libya
[3] Health Department, College of Medical Technology, Derna, Libya
[4] English Department, Faculty of Education, University of Benghazi, Libya
[6] Central Pharmacy, Ministry of health, Darna, Libya
[7,8] Omar Almukhtar General Hospital, Al Baida, Libya
[9] Sergery Department, Alhaowari hospital, Benghazi, Libya
[10] Chemistry Department, Faculty of art and science, University of Omar Al Mukhtar, Libya

*Corresponding author: Noornooor1973@gmail.com

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Abstract: Bacterial meningitis is a medical emergency associated with high mortality rates. Cerebrospinal fluid (CSF) culture is the gold standard for diagnosis of meningitis and it is important to establish the susceptibility of the causative microorganism to rationalize treatment. Objective of this study was to assess the seasonality of the bacterial meningitis and the antibiotic resistance of incriminated bacteria through the year in Tobruk city. This Laboratory-based retrospective analysis of 367 CSF cultures was conducted in Tobruk Medical Centre, Tobruk, from January 2020 - December 2020. Of whom 367, 188 (59%) were male, while 179 (49%) were female. Of 367. Three isolated pathogen was *Klebseilla* spp 2(1%), followed by *streptococcus pyogen* and *Staph aureus* 1 (0%) equally. While 363 (99%) was no growth. The majority of cases 110 (30 %) were cultured in autumn 110 (30%) followed by winter 95 (26%) and spring 88 (24%). in our study the decreasing of bacterial isolation from CSF samples, is maybe due to several reasons such as administration of antibiotics to the patients before CSF sample culturing or the patients were infected with viral infections or the patients were not infected at all. Additional study should focus on avoidable features of vaccines, to reduce the disease problem.

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Introduction

More than 220 million people worldwide have been diagnosed with diabetes. [15] Glycated hemoglobin (hemoglobin A1c, HbA1c, A1C, or Hb1c; is also known as HbA1c or HGBA1c) is a form of hemoglobin which

is measured principally to detect the average plasma glucose concentration over prolonged periods. The HbA1c/Total Hemoglobin ratio is expressed as percentage HbA1c (%HbA1c). [24] The accurate measurement of glycated hemoglobin (HbA1c) is of essential importance for checking diabetic patients. [22, 23] It is being observed that it is formed in a non-enzymatic glycation pathway by hemoglobin's exposure to plasma glucose. HbA1c is a measure of the beta-N1-deoxy fructuously component of hemoglobin.[7,8] HbA1c is defined as hemoglobin which is permanently glycated at one or both N-terminal valines of the beta chains. [9] The HbA1c is currently suggested as a standard of care for testing and checking diabetes, specially the type 2 diabetes. [1] Analysis of glycated hemoglobin (HbA1c) in blood provides evidence about an individual's average blood glucose levels during the previous two to three months, which is the establish half-life of red blood cells (RBCs). [2] Haemoglobin A1 and haemoglobin A1c Chromatography of normal adult blood divides in two parts: HbA (HbA0) 92-94%. HbA1 (6-8%) in which the B chain has an extra glucose group. HbA1 contains of three dissimilar glycations, the HbA1c typically measured by isoelectric focusing or electrophoresis.[11] The glycation of haemoglobin occurs at a inconstant (non-linear rate) over time, during the lifespan of the red blood cell (RBC), which is of 120 days. Laboratory normal range is different depending on whether HbA1 or HbA1c is measured and on the method used. [12] HbA1c is a reliable indicator of diabetic control except in the following situations: Situations where the average RBC lifespan is significantly >120 days will usually give increase to decrease HbA1c grades because 50% of glycation occurs in 90-120 days. Common causes include an increase in red cell income: a- haemolysis, myelodysplastic disease, blood loss, haemoglobinopathies and red cell disorders. B- Interference with the test (this depends on the method used: persistent fetal haemoglobin and haemoglobin variants, carbamylated haemoglobin). C- In patients who vary between very high and very low levels- glycated haemoglobin in that case readings can be misleading (the clinician should compare with extra information obtained from home capillary blood glucose tests). D- HbA1c can be useful in recognizing patients who may be giving an idealistically good report of their home glucose tests**.[**14] Nathan *et al*. used continuous glucose checking, which measures interstitial glucose levels every 5 minutes, for 3 months in both -diabetics and non-diabetics with relatively constant glycaemia. They reported accurate relationship between HbA1c and mean blood glucose, meaning HbA1c could be conveyed in an equivalent mean glucose. [16] Chemical charge is existing on the molecule of HbA1c, and the amount of the charge varies from the charges on the diverse components of hemoglobin. The molecule of HbA1c has variance in size from the other components. HbA1c may be separated by charge and size from the other hemoglobin. A component in blood by a procedure known as in elevation pressure liquid chromatography (HPLC) [19, 20].

According to the 2014 estimation, the occurrence of diabetes in the world was 9%, between adults aged 18 years or older. It is estimated that by the year 2035, those affected by diabetes will be about 592 million. Every seven seconds, diabetes causes the death of people globally, and in 2014 only, 4.9 million deaths were documented to diabetes with 80% of deaths linked to diabetes reported from low- and middle-income countries. In 2013, type 1 diabetes was reported in more than 79,000 children. Gestational diabetes was responsible for more than 21 million live births, affecting both the mother and the neonatal, in one way or the other, in 2013. [21] Objective this study was studied the value of HbA1c as a screening and diagnostic test for diabetes mellitus in Libyan individuals. Historically, HbA1c was first isolated by Huisman *et al.* [3] in 1958 and characterized by Bookchin and Gallop, [10] in 1968, as a glycoprotein. The raised levels of HbA1c in diabetic patients were described by Rahbar *et al*. in 1969. Bunn *et al*. recognized the pathway principal to the formation of HbA1c in 1975. Via the HbA1c as a biomarker for checking the levels of glucose between diabetic patients was first planned by Koenig et al. in 1976. [3,4,5,6] In 1976, HbA1c was described as a useful mean for monitoring the glycaemic control in diabetic patients, [16] in 1995 the International Federation of Clinical Chemistry (IFCC) procured the lead in developed an identical international standardization of HbA1c because the absence of standardization resulted in wide variability within results (4.0% to 8.1%) on the same sample making it problematic to compare patients results between laboratories. This disparity has always been a source of anxiety among health care providers. It becomes even more vital in this age of heavy economical migration, when people travel long distances and take their native record with them. Therefore, having same method and unit to measure HbA1c is need of the day. [17, 18]

Material and methods

This study was undertaken in Private laboratory. A total of 5747 participants were successfully screened from January 2021 to July 2021. Blood (2cc) specimens were obtained from the antecubital vein in a sitting position and specimen collection and preparation of K2-EDTA or NH4-heparinized whole blood for the determination of HbA1c. Inset 50 Micro into G8 Variant Elution Buffer His R1, R2 and R3 (Tosoh Automatic Glycochemoglobin Analyzer HLC-723^{8} G8) and incubate 8 min.

3.1 Normal range

Normal range of HbA1c is 4 % to 6 % in people without diabetes.

3.2 System Information

TOSOH G8 HBA1C Variantion analyzer

3.3 Statistical analysis: - Analysis was done by Excel method.

Results and discussion

Some problems are accompanying blood glucose measurements, such as pre analytical variables like sampling method (e.g., glucose levels decrease by 3–8 mg/dL per hour at room temperature) and fasting status previous to blood sampling and inter individual biological variations. HbA1c does not require fasting and has an analytical variation of less than 2%. Purpose of HbA1c has currently become more useful than plasma glucose measurements, meanwhile HbA1c is biologically more established and remains mostly unaffected in the short time via nutritious status, stress, or other disorders [25].

4.1 Distribution of the patient according to age.

5747 patients, the most age group enrolled in the study was 20-40 (28%) followed by 40-60 (25%) and 10-20 (21%) respectively. While the lowest age group recorded was 1-5 (3%) followed by 5-10 (7%).

Table 1 Distribution of the patient according to age.

Age	1_5	5_10	10_20	20_40	40_60	60_75
Patient's number	169 (3%)	428 (7%)	1180 (21%)	1590 (28%)	1442 (25%)	941 (16%)

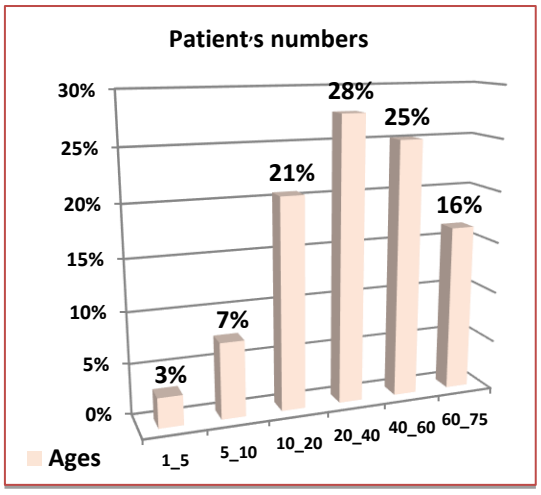

Figure 1 Distribution of the patient according to ages**.**

4.2 Comparison between high HBA1C Level and ages.

The highest detectable HBA1C level represents the highest measurable level of HbA1c was 1590 (29%) in ages between 20-40 followed by 1442 (26%) in ages between 40-60 and 1047 (19%) in ages between 10-20. Helminen *et al*.52 measured the value of HbA1c levels in expecting the clinical disease in genetically predisposed children with multiple autoantibodies. They observed that a 10% increase in HbA1c levels in samples obtained 3–12 months separately anticipated the diagnosis of clinical disease, suggesting the effectiveness of HbA1c as a marker for forecasting the time to diagnosis of type 1 diabetes in children with multiple autoantibodies. [26]

Table 2 Comparison between high HBA1C Level and ages.

Age	1_5	5_10	10_20	20_40	40_60	60_75
Patient with high HBA1C level	118 (2%)	324 (6%)	1047 (19%)	1590 (29%)	1442 (26%)	941 (17%)

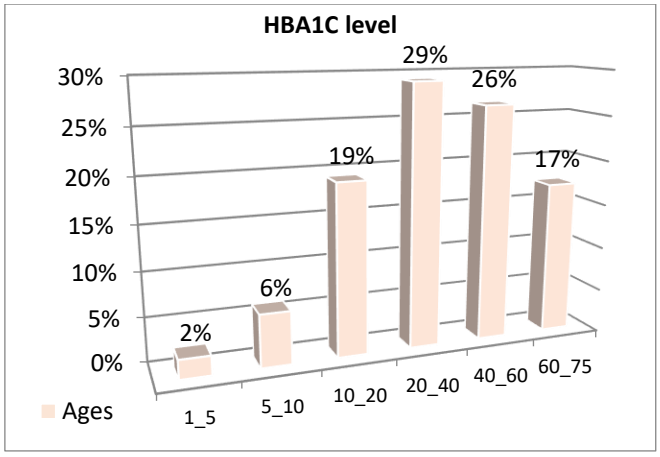

Figure 2 Distribution of the patient according to ages**.**

4.3 Distribution of patients with high HBA1C level according to seasons.

The majority of cases were 2251 (41 %) in spring followed by summer 1677 (31%) and winter 1535 (28%).

Table 3 Distribution of patients with high HBA1C levels according to seasons.

Season	Winter	Spring	Summer	Autumn
Patient with high HBA1C level	1535 (28%)	2251 (41%)	1677 (31%)	0 (0%)

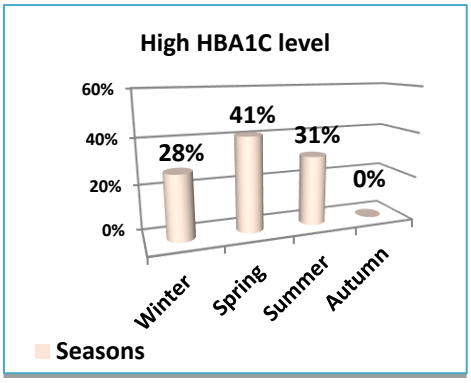

Figure 3 Distribution of the patient with high HBA1C level according to seasons.

4.4 Comparison between patients according to high HBA1C and normal HBA1C levels.

Total of 7547, 5492 (95%) samples recorded high HBA1C level, while 307 (5%) with normal HBA1C level. The prediabetes usually has the HbA1c levels as 5.7%–6.4%, while those with 6.4% or higher HbA1c levels have diabetes. [27,28] Excessive usage of vitamin C, B, and E complements and enlarged levels of Liver, cholesterol, and kidney diseases can also present abnormally high levels of HbA1c. [29,30] Glycosylation of hemoglobin may also affect membrane lipid protein interactions in RBCs, altering their internal viscosity, modifying viscoelastic properties of erythrocyte membranes, and impairing RBC deformability. [31] Also lowers oxygen-carrying capacity, thereby promoting hypoxia and its related systemic vascular vasodilatory adaptations and responses. [6]

Table 4 Comparison between patients according to high HBA1C and normal HBA1C levels.

HBA1C level >6%	HBA1C level =6%
5492 (95%)	307 (5%)

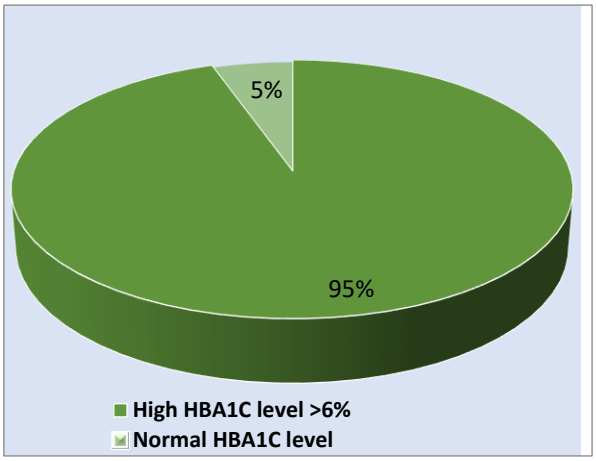

Figure 4 Comparison between patients according to high HBA1C and normal HBA1C levels.

Conclusion

The present study results suggest that HbA1c could be used to make a diagnosis of diabetes mellitus in Libya. As the endemic of diabetes uninterrupted to rise worldwide, HbA1c test may remain to be applied as part of the diagnostic and prognostic tool, leading to better patient care and successful clinical outcomes. HbA1c is made by the non-enzymatic glycation of free amino groups at the N-terminus of the β-chain of hemoglobin A0. The level of HbA1c is relational to the level of glucose in the blood. As the glucose leftovers bound to the red cell during its life cycle, measurement of HbA1c offers a suggestion of the mean everyday blood glucose concentration over the previous two months. Measurement of HbA1c is, consequently, considered a significant diagnostic method in the checking of nutritional regulators and healing systems through the management of diabetes. Effective regulator of blood glucose levels is essential in the inhibition of ketosis and hyperglycemia, and may decrease the occurrence and severity of late diabetic disorders such as neuropathy, retinopathy, nephropathy, and cardiac disease. As the prevalent of diabetes persists to rise worldwide, HbA1c test may remain to be useful as part of the diagnostic and analytical tool, principal to improved patient care and effective clinical outcomes.

References

[1] World Health Organization (WHO). Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus. Abbreviated Report of a WHO Consultation. Geneva: WHO; 2011.

[2] Khan MI, Weinstock RS. Chapter 16: Carbohydrates. In: McPherson RA, Pincus MR, eds. Henry's Clinical Diagnosis and Management by Laboratory Methods. 22nd ed. Philadelphia, PA: Saunders Elsevier; 2011:210–25.

[3] Bookchin RM, Gallop PM. Structure of haemoglobin A1c: nature of the N-terminal beta chain-blocking group. Biochem Biophys Res Commun. 1968; 32:86–93.

[4] Rahbar S, Blumenfeld O, Ranney HM. Studies of an unusual hemoglobin in patients with diabetes mellitus. Biochem Biophys Res Commun. 1969; 36:838–43.

[5] Bunn HF, Haney DN, Gabbay KH, Gallop PM. Further identification of the nature and linkage of the carbohydrate in haemoglobin A1c. Biochem Biophys Res Commun. 1975;67:103–9.

[6] Paffett ML, Walker BR. Vascular adaptations to hypoxia: molecular and cellular mechanisms regulating vascular tone. Essays Biochem. 2007; 43:105–20.

[7] Miedema K (2005) Standardization of HbA1c and Optimal Range of Monitoring. Scand J Clin Lab Invest 240: 61-72.

[8] Peterson KP, Pavlovich JG, Goldstein D, Little R, England J, et al. (1998) What is hemoglobin A1c? An analysis of glycated hemoglobins by electrospray ionization mass spectrometry. Clin Chem 44(9): 1951- 1958.

[9] Kobold U, Jeppsson JO, Dulffer T, Finke A, Hoetzel W, et al. (1997) Candidate reference methods for hemoglobin A1c based on peptide mapping. Clin Chem 43: 1944-1951.

[10] Huisman TH, Martis EA, Dozy A. Chromatography of hemoglobin types on carboxymethylcellulose. J Lab Clin Med. 1958; 52:312–27.

[11] Koval D, Kašička V, Cottet H (2011) Analysis of glycated hemoglobin A1C by capillary electrophoresis and capillary isoelectric focusing. Anal Biochem 413(1): 8-15.

[12] Reynolds TM, Smellie WS, Twomey PJ (2006) Glycated haemoglobin (HbA1c) monitoring. BMJ 333(7568): 586-588.

[13] Koenig RJ, Peterson CM, Jones RL, Saudek C, Lehrman M, et al. (1976) Correlation of glucose regulation and hemoglobin AIc in diabetes mellitus. N Engl J Med 295(8): 417-420.

[14] Xanthis A, Hatzitolios A, Koliakos G, Tatola V (2007) Advanced glycosylation end products and nutrition--a possible relation with diabetic atherosclerosis and how to prevent it. J Food Sci 72(8): R125-R129.

[15] Grundy SM, Benjamin IJ, Burke GL, Chait A, Eckel RH, et al. (1999) Diabetes and cardiovascular disease: a statement for healthcare professionals from the American Heart. Association Circulation 100(10): 1134-1146.

[16] Nathan DM, Turgeon H, Regan S (2007) Relationship between glycated haemoglobin levels and mean glucose levels over time. Diabetologia 50(11): 2239-2244.

[17] Little RR, Wiedmeyer HM, JD England, AL Wilke, Rohlfing CL, et al. (1992) Interlaboratory standardization of measurements of glycohemoglobins. Clinical Chemistry 38(12): 2472-2478.

[18] Uwe Kobold, Jan Olof Jeppsson, Thomas Dülffer, Andreas Finke, Wieland Hoelzel, et al. (1997) Candidate reference methods for hemoglobin A1c based on peptide mapping. Clinical Chemistry 43(10): 1944-1951.

[19] Melissa Conrad Stöppler (2016) HbA1c Test (Hemoglobin A1c).

[20] Pohanka, Miroslav (2009) Monoclonal and polyclonal antibodies production - preparation of potent biorecognition element. Journal of Applied Biomedicine (De Gruyter Open) 7(3): 115-121.

[21] International Diabetes Federation (IDF). Available from: www.idf.org; 2015.

[22] D.B. Sacks, M. Arnold, G.L. Bakris, D.E. Bruns, A.R. Horvath, M.S. Kirkman, et al., Guidelines and recommendations for laboratory analysis and management of diabetes mellitus, Clin. Chem. 57 (2011) e1–e47.

[23] American Diabetes Association, Glycemic targets, Diabetes Care 38 (2015) S33–S40

[24] Niederau CM, Reinauer H Glycohemoglobins In: Thomas L, ed. Clinical Laboratory Diagnostics. Use and assessment of clinical laboratory results. Frankfurt/Main:TH-Books Verlagsgesellschaft mbH, 1998: 142-148.

[25] Diagnosis and classification of diabetes mellitus. Diabetes Care 2010; 33 Suppl 1: S62–9.

[26] Helminen O, Aspholm S, Pokka T, et al. HbA1c predicts time to diagnosis of type 1 diabetes in children at risk. Diabetes. 2015;64:1719–27.

[27] American Diabetes Association (ADA). Standards of medical care in diabetes. Diabetes Care. 2014;37:S14–80.

[28] American Diabetes Association (ADA). Diagnosis and classification of diabetes mellitus. Diabetes Care. 2011;34:S62–9.

[29] Luk AO, Ma RC, Lau ES, et al. Risk association of HbA1c variability with chronic kidney disease and cardiovascular disease in type 2 diabetes: prospective analysis of the Hong Kong Diabetes Registry. Diabetes Metab Res Rev. 2013;29:384–90.

[30] Xu R, Zhang S, Tao A, Chen G, Zhang M. Influence of vitamin E supplementation on glycaemic control: a meta-analysis of randomised controlled trials. PLoS One. 2014;9:e95008.

[31] Watala C, Witas H, Olszowska L, Piasecki W. The association between erythrocyte internal viscosity, protein non-enzymatic glycosylation and erythrocyte membrane dynamic properties in juvenile diabetes mellitus. Int J Exp Pathol. 1992;73:655–63

Author's short biography

Noor Alhooda M. Alawkaly, master microbiology and bachelor medical laboratory. Lecturer assistant in higher institute of Science and Technology, Suluq. Researcher in laboratory specialization for 25 years and academic lecturer for ten years.