

# Reference Range of Hemoglobin A1c in Khartoum State



**Ibrahim A Ai<sup>1\*</sup>, Hisham M Abdel Rahim<sup>1</sup>, Babiker Almobasher<sup>1</sup>, Rihab M Badi<sup>2</sup>, Abdarahiem Alborai<sup>3</sup>, Abdelmohisen Hussein<sup>4</sup>, Kamal M Awad<sup>4</sup>, Elmoataz H Taha<sup>5</sup>, Aamir A Elmagzoub<sup>1</sup> and Omer A Musa<sup>1</sup>**

<sup>1</sup>Department of Physiology, National Ribat University, Sudan

<sup>2</sup>Department of Physiology, University of Khartoum, Sudan

<sup>3</sup>Department of Physiology, Omdurman Islamic University, Sudan

<sup>4</sup>Department of Physiology, Gadarif University, Sudan

<sup>5</sup>Department of Physiology, Dongola University, Sudan

**Submission:** February 28, 2018; **Published:** March 19, 2018

**\*Corresponding author:** Ibrahim Abdelrhim Ali, Department of Physiology, Faculty of Medicine, National Ribat University, Sudan,  
Email: [hemamedicine@gmail.com](mailto:hemamedicine@gmail.com)

## Abstract

**Introduction:** Hb A1c is now used largely for DM control, the normal values of Hb A1c in Sudanese must be established for the clinical diagnosis and follow up of DM. The normal value used in Sudanese laboratories is up to 6.5% which is Caucasians.

**Objective:** The study aimed to establishing the normal Sudanese reference range for Hb A1c in Khartoum state.

**Methods:** A Cross sectional study was conducted between 2016-2018 in Khartoum state capital of Sudan on healthy Sudanese subjects of both sexes with age group 20 -60years. 444 Sudanese adult volunteers were included – 91 males 353 were females. All of them were assessed by a questionnaire covering age, gender, past medical history, family history, physical activity, daily caloric intake, smoking history, and body mass index (BMI) was calculated by standard techniques followed by complete clinical examinations. A sample of five ml venous blood was taken for fasting blood glucose to exclude DM and Hb A1c was measured using modified ELISA reader known as COPAS Integra 800.

**Results:** The mean of age was 25.4±9.2 %. The mean of Hb A1c was 4.2±1.8% SD and with range of 1.2-6.5%.

**Conclusion:** This study showed significant variations in the level of Hb A1c of healthy Sudanese in comparison with the reference ranges of international parameters. The study results revealed an urgent need to build national reference ranges for all hematological and other physiological parameters for Sudanese population in the near future

**Abbreviations:** ADA: American Diabetes Association; MENA: Middle East and North Africa; FBG: Fasting Blood Glucose; FMOH: Federal Ministry of Health in Sudan; NRU: National Ribat University; ELISA: Enzyme Linked Immunosorbent Assay; FBS: Fasting Blood Sugar

## Introduction

Hb A1c, is a glycosylated hemoglobin formed by the glycosylation of hemoglobin. The term glycosylated hemoglobin represents the glycaemic status of a person over the last two to three months [1-5]. According to the American Diabetes Association (ADA) Guidelines 2007, the value of Hb A1c should be kept below 7% in all diabetics and according to the same guidelines, Hb A1c is now referred to as A1c [6]. Hemoglobin A1c was first separated from other forms of hemoglobin by Huisman and Meyering in 1958 using a chromatographic column [7]. About 50 years ago Glycosylated haemoglobin (Hb A1c) was initially identified as an “unusual” haemoglobin in diabetic patients by Samuel Rahbar in 1969, then he noticed significance increase in the level of Hb A1c in diabetes [8]. Another cross sectional study conducted

later by Rahbar et al. [9] at Tehran University found a similar abnormality in 57 diabetic patients.

After that discovery, numerous small studies were conducted correlating the Hb A1c level to the blood glucose level resulting in the idea that Hb A1c could be used as a positive objective factor to measure the glycaemic control. In a larger study of diabetic patients, Trivelli et al. [10] found a two-fold increase of Hb A1c over values observed in non-diabetic subjects. Thus, by the mid 1970s, it was clear that Hb A1c was elevated in humans with diabetes mellitus, although the mechanism of this abnormality was not understood. In 1976 Koenig et al. [11] proposed the idea to use HbA1c level for monitoring the degree of control of glucose metabolism in diabetic patients and

described. HbA1c as a useful mean for monitoring the glycaemic control in diabetic patients. Hb A1c was introduced into clinical use in the 1980s and subsequently has become an important test in Clinical practice [12]. Different studies have shown variation in the normal ranges of Hb A1c.

In Brazil, Buffarini et al. [13] performed a two cohort studies in 1982 and 1993 which were published later in 2016. It aimed at describing the distribution of Hb A1c levels according to early-life and contemporary factors in adolescents and adults without diabetes mellitus and found the distribution of the Hb A1c was approximately 5.10% ( $\pm 0.43$ ), and 4.89% ( $\pm 0.50$ ) respectively. In United Kingdom in 1989, Simon et al. [14] reported the distribution of Hb A1c in 3240 healthy adult population. They found that the approximately normal distribution of Hb A1c was 5.03% ( $\pm 0.53$ ). In England at 2001 Gulliford and Ukoumunne performed a Cross-sectional survey and found a mean Hb A1c of 6.34% ( $\pm 0.85$ ) in a general population of 9,772 non-diabetic, white European subjects aged 16 years and older [15]. In 2010 Ghazanfari et al. [16] in Iran performed a study to measure the association between Hb A1c and Fasting Blood Sugar (FBS) through a cross-sectional population-based study, and found the mean of Hb A1c in non-diabetics was 5.61% ( $\pm 0.73$ ) and in diabetics was 7.88% ( $\pm 1.92$ ).

In 2011 Nathan et al. in UK reported the normal range of Hb A1c for non diabetic people was found to be between 3.6 – 5.5% [17]. According to a report published in 2009 by an International Expert Committee on the role of Hb A1c in the diagnosis of diabetes, Hb A1c can be used to diagnose diabetes and that the diagnosis can be made if the Hb A1c level is 6.5% or more and Hb A1c level below 6% is considered normal [18], although in Iran Hb A1c in diabetics was found to be 7.88% ( $\pm 1.92$ ) [16]. Hb A1c results in the UK have usually been aligned to the assay used in the Diabetes Control and Complications Trial (DCCT), expressed as a percentage (DCCT-Hb A1c)-non-diabetic 'normal' range being 4-6% [19,20]. Diagnostic criteria for diabetes that made by (WHO report 2011) determined that Hb A1c of 6.5% was considered as the cut-off point for diagnosing diabetes.

A value <6.5% does not exclude diabetes diagnosed using glucose tests. Faerch et al. & Gulliford et al. [15,21] both found somewhat higher levels of Hb A1c in men compared to women, but other studies found no sex-related differences in Hb A1c [22,23]. According to report published by the international diabetes federation- The IDF - Middle East and North Africa (MENA), there was over 1.4 million cases of diabetes in Sudan in 2015 [24]. Although the HbA1c reference intervals for the general population in western countries are well established, reference intervals for healthy Sudanese people are not clearly defined. Most of the studies about Hb A1c that conducted in Sudan was pilot studies that done in small samples or studies considering abnormal Hb A1c such as Hb A1c in Diabetes Mellitus, anemia, pregnancy, or patient with abnormal Hb

structure. These abnormal values of Hb A1c were compared to the international normal one.

It is well known that the normal values used in Sudanese laboratories are mainly derived from European studies. Differences in the normal values in Sudan have been documented in some hematological values [25] and respiratory function tests parameters [26]. As Hb A1c is now used largely for DM control, the normal values of Hb A1c in Sudanese must be established for the clinical diagnosis and followup of DM. In Khartoum state at 2016 Ali et al. performed a Cross-sectional study on 20 non-diabetic adult males of ages between 35-45 years and found a mean Hb A1c of 3.8%  $\pm 1.17$  with a range of (1.2%-5.4%) [27]. Another cross-sectional study also done in Khartoum state at 2016 by Fadul et al. [28] on 20 non-diabetic adult females, their ages was between 35-45 years and found a mean Hb A1c of 3.43%  $\pm 1.17$  with a range of (1.4-5.3%). Despite this variation the normal level of Hb A1c was generally taken as less than 6% and these values were applied to diabetic patients in Sudan, could there be a difference in the normal level of Hb A1c in Sudanese population is clearly a valid a question.

In this study, the normal level in healthy Sudanese people will be investigated. Most of the studies about normal Hb A1c were obtained in Western countries. These countries have totally different environment, ethnic groups, nutritional habits and body mass index, compared to Sudan. Currently, there are no known big scale studies conducted to investigate the normal reference range of Hb A1c in Sudanese people, and the normal reference range of Hb A1c in Sudanese hospitals and clinics is obtained from non-Sudanese subjects depending on the international American and British Guidelines.

### Methods

A Cross sectional study conducted in Khartoum state capital of Sudan between 2016-2018 on Healthy Sudanese subjects of both sexes with age group 20 -60 years. 444 Sudanese adult volunteers were included – 91 males, 353 were females. All subjects had normal fasting blood glucose (FBG). The exclusion criteria of this study include Pregnant ladies, abnormal FBG, Diabetes mellitus, Hypertension, Renal failure, Liver disease, Cancer, Chronic diseases (cardiac diseases, TB, asthma, thyroid disorders), Hematological disorders., Recent acute diseases (Malaria, typhoid fever ...etc), Lactation, History of recent surgery (splenectomy), History of schistosomiasis and Subjects not consenting. Written consents were obtained from all participants after fully explaining to them the project. A questionnaire was filled by all volunteers to obtain the data about name, age, address, medical history, drug use, and lifestyle.

Weight, height, and blood pressure were measured with standard techniques. Complete clinical examination was performed. After informed consent, five ml of venous blood was collected by a standard procedure from each participant

under complete aseptic conditions in the morning and after an overnight fasting. 2.5ml was placed in fluoride oxalate containers, and then used for FBG measurement with auto analyzer A15. The other 2.5ml was placed in EDTA container and used for Hb A1c analysis. (Icteric, lipemic, hemolyzed or bacterially contaminated samples were not used). Hb A1c was measured using modified ELISA reader known as COPAS Integra 800 using commercial reagent kits from Roche Company. All techniques and equipment were standardized. All data collected in this study was analyzed using the SPSS computer programs, (t-test for mean and p. value  $P \leq 0.05$  for significance).

### Ethical consideration

Ethical Approval of this study was obtained from the Federal Ministry of Health in Sudan (FMOH) and The National Ribat University (NRU). The objectives of the study were explained to all individuals participating in the study. An informed consent was obtained from each participant in the study.

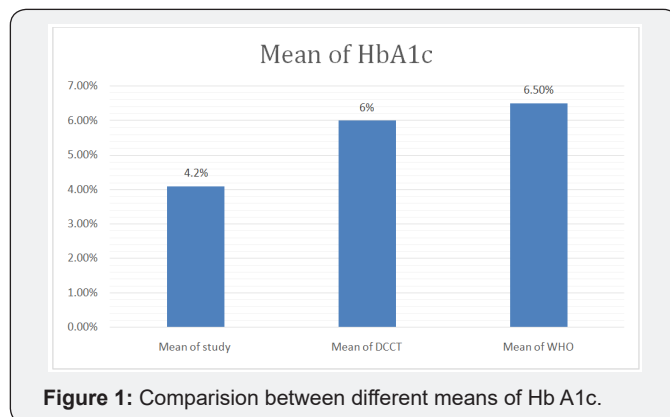
### Results

444 participants were included in this study 91 males and 353 females their ages between 20-60 years old.

- The mean of age was  $25.4 \pm 9.2$  %
- The mean of Hb A1c was  $4.2 \pm 1.8$ % and with a range of 1.2-6.5%
- The mean of Hb A1c in males was  $4.2 \pm 1.8$ %
- The mean of Hb A1c in females was  $4.2 \pm 1.8$ % (Table 1) (Figure 1).

**Table 1:** Show the mean of Hb A<sub>1c</sub> in males and females.

Gender	Mean	N	Std. Deviation
Females	4.2%	353	1.86003
Males	4.2%	91	1.83495
Total	4.2%	444	1.85286



### Discussion

In previous pilot studies we have found that HbA<sub>1c</sub> level was lower in sudanese compared to the international values [27,28]. The result of this study in khartoum state with a bigger

sample has confirmed that the Hb A1c in sudanese is lower than the international. In this study the normal mean distribution of HbA1c in Sudanese adult males was 4.2% ( $\pm 1.8$ %) and the range was 1.2-6.5% which is lower than in international range (3.6-6.5%) [18-20]. These differences may be due to ethnic and genetic differences because all these comparable studies were performed in Western countries, although the nutritional differences need further investigations. This study showed that the normal mean distribution of Hb A1c is not different between the males and females which is in contrast to Faerch et al. & Gulliford et al. [15,21] who found somewhat higher levels of Hb A1c in men compared to women, but in agreement with Kilpatrick et al. & Modan et al. [22,23].

These variations can be related to exact physiological role of Hb A1c which has not been addressed. In conclusion, this study showed significant variations in the level of Hb A1c of healthy Sudanese in comparison with the reference ranges of international parameters. The study results re-vealed an urgent need to build national reference ranges for all hematological and other physiological parameters for Sudanese population in the near future. Further studies to confirm these results and establish reference range for Hb A1c in different age groups, Hb A1c in pregnancy, Hb A1c in different category of BMI, Hb A1c in different Sudanese tribes and Hb A1c in athletes are highly recommended.

### Acknowledgement

Our great gratitude goes to the participants for accepting to come in their private time for the study and for the National Ribat University for providing fund for the project.

### References

- Telen MJ, Kaufman RE, JP, Foerster J, Rodgers G (2004) The mature erythrocyte, editors. Wintrobe's (Clinical Hematology). (11<sup>th</sup> edn), Lippincot : Williams and Wilkins, Philadelphia, USA, pp. 1-230.
- Roth M (1990) "Glycated hemoglobin," not "glycosylated" or "glucosylated". Clin Chem 36(6): 1254-1255.
- Bunn HF, Haney DN, Gabbay KH, Gallop PM (1975) Further identification of the nature and linkage of the carbohydrate in hemoglobin A<sub>1c</sub>. Biochem Biophys Res Commun 67(1):103-109.
- David B Sacks, Mark Arnold, George L Bakris, David E Bruns, Andrea Rita (2002) Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 48(3): 436-472.
- Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A (2002) Defining the relationship between plasma glucose and Hb A<sub>1c</sub>: analysis of glucose profiles and Hb A<sub>1c</sub> in the Diabetes Control and Complications Trial. Diabetes Care 25(2): 275-278.
- American Diabetes Association (2007) Standards of medical care in diabetes 30(suppl 1): S4-S41.
- Huisman TH, Martis EA, Dozy A (1958) Chromatography of hemoglobin types on carboxymethylcellulose. J Lab Clin Med 52(2): 312-327.
- Rahbar S (1968) An abnormal hemoglobin in red cells of diabetics. Clin Chim Acta 22(2): 296-298.

9. Rahbar, Blumenfeld O, Ranney HM (1969) Studies of an unusual hemoglobin in patients with diabetes mellitus. *Biochem Biophys Res Commun* 36(5): 838-843.
10. Trivelli LA, Ranney HM, Lai HT (1971) Hemoglobin components in patients with diabetes mellitus. *New Engl J Med* 284(7): 353-357.
11. Koenig RJ, Peterson CM, Jones RL, Saudek C, Lehrman M (1976) Correlation of glucose regulation and haemoglobin A<sub>1c</sub> in diabetes mellitus. *Eng J Med* 295(8): 417-420.
12. Massi Benedetti M (2006) Changing targets in treatment of type 2 DM. *Curr Med Res Opin* 22(suppl 2): S5-S13.
13. Romina Buffarini, Mara Clara Restrepo-Méndez, Vera M Silveira, Jaime J Miranda, Helen D Gonçalves (2016) Distribution of Glycated Haemoglobin According to Early-Life and Contemporary Characteristics in Adolescents and Adults without Diabetes: The 1982 and 1993 Pelotas Birth Cohorts. *PLOS ONE* 11(9): e0162614.
14. Simon D, Senan C, Garnier P, Saint-Paul M, Papoz L (1989) Epidemiological features of glycated haemoglobin A<sub>1c</sub>-distribution in a healthy population. *The Telecom Study. Diabetologia* 3(12): 864-869.
15. Gulliford MC, Ukoumunne OC (2001) Determinants of glycated haemoglobin in the general population: associations with diet, alcohol and cigarette smoking. *Eur J Clin Nutr* 55(7): 615-623.
16. Zahra Ghazanfari, Ali Akbar Haghdoost, Sakineh Mohammad Alizadeh, Jamileh Atapour, Farzaneh Zolala (2010) A Comparison of Hb A<sub>1c</sub> and Fasting Blood Sugar Tests in General Population. *Int J Prev Med* 1(3): 187-194.
17. Nathan R Hill, Nick S Oliver, Pratik Choudhary, Jonathan C Levy, Peter Hindmarsh, et al. (2011) Normal Reference Range for Mean Tissue Glucose and Glycemic Variability Derived from Continuous Glucose Monitoring for Subjects Without Diabetes in Different Ethnic Groups. *Diabetes Technol Ther* 13(9): 921-928.
18. (2009) International Expert Committee report on the role of the A<sub>1c</sub> assay in the diagnosis of diabetes. *Diabetes Care* 32(7): 1327-1334.
19. Weykamp C, John WG, Mosca A (2009) A Review of the Challenge in Measuring Hemoglobin A<sub>1c</sub>. *J Diabetes Sci Technol* 3(3): 439-445.
20. World Health Organization (2011) Use of Glycated Haemoglobin (Hb A<sub>1c</sub>) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation. World Health Organization, Geneva, Switzerland.
21. Faerch K, Borch-Johnsen K, Vaag A, Jorgensen T, Witte DR (2010) Sex differences in glucose levels: a consequence of physiology or methodological convenience? The Inter 99 study. *Diabetologia* 53(5): 858-865.
22. Kilpatrick ES, Dominiczak MH, Small M (1996) The effects of ageing on glycation and the interpretation of glycaemic control in Type 2 diabetes. *Q J Med* 89(4): 307-312.
23. Modan M, Meytes D, Rozeman P, Yosef SB, Sehayek E (1988) Significance of high Hb A<sub>1c</sub> levels in normal glucose tolerance. *Diabetes Care* 11(5): 422-428.
24. International federation- The IDF- Middle East and North Africa (MENA), Sudan.
25. Hamad IM, Musa OA (2013) Reference Hb value in apparently healthy Sudanese children in Khartoum state. 37<sup>th</sup> Congress of IUPS (Birmingham, UK) Proc 37th IUPS, PCA297, Birmingham, UK.
26. Amir A Bashir, Omer A Musa (2012) Reference spirometric values in Sudanese. *Cohort EMHJ* 18(2): 151-158.
27. Ali IA, Abdalarhim HM, Musa OA (2016) Reference values for hemoglobin A<sub>1c</sub> in males living in Khartoum state pilot study, Sudan *Med Monit* 11(3): 91-96.
28. Fatima Ahmed Fadul, Hisham Mohammed Abdelrhim, Ibrahim Abdelrhim Ali, Omer Abdelaziz Musa (2017) Normal Values of Hemoglobin A<sub>1c</sub> among Women in Khartoum State: (A Pilot Study, 2016). *IJSR* 6(9): 6-391.



This work is licensed under Creative Commons Attribution 4.0 License  
DOI: [10.19080/APBIJ.2018.04.555644](https://doi.org/10.19080/APBIJ.2018.04.555644)

### Your next submission with Juniper Publishers will reach you the below assets

- Quality Editorial service
- Swift Peer Review
- Reprints availability
- E-prints Service
- Manuscript Podcast for convenient understanding
- Global attainment for your research
- Manuscript accessibility in different formats ( Pdf, E-pub, Full Text, Audio)
- Unceasing customer service

**Track the below URL for one-step submission**  
<https://juniperpublishers.com/online-submission.php>