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Research Article

# Anaemia and Haemoglobin A1c level: Is there a case for redefining reference ranges and therapeutic goals?

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**Abstract**

**Background:** Haemoglobin A1c (HbA1c) has been adopted by physicians as a surrogate for monitoring glycemic control. There exists concern that other factors beyond serum glucose concentration may affect glycation rates and by extrapolation HbA1c levels.

**Study Objectives:** The study attempts to discern clinical differences in HbA1c levels in patients with anaemia compared to patients without anaemia, quantifying and showing the direction of such differences.

**Study Design:** Using a convenient sampling method and a set of inclusion and exclusion criteria, it examined (retrospectively) patterns in [Hb] and HbA1c in non-diabetics with and without anaemia.

**Results:** The study observed a statistically significant 0.4units (8%) difference in the mean HbA1c in anaemia vs. non-anaemic populations. Reference ranges of HbA1c for non-anaemic population and anaemia subtypes was computed. Computed ranges for anaemia group and its subgroups were significantly wider compared to non-anaemia population. Modest but statistically significant correction of anaemia did not result in significant changes in HbA1c.

**Discussion:** i. The linear relationship between [Hb] and HbA1c holds true for anaemic and non-anaemia populations. ii. Non-diabetic, anaemic have a significantly lower mean HbA1c (5.3% vs. 5.7%), but a similar upper limit of reference range due to a higher variance. iii. The variance and proposed reference ranges for anaemia group and its subtypes was greater than in non-anaemia group, perhaps due to homogenization of clinically heterogeneous entities. iv. Modest correction anaemia did not cause significant change in HbAIc, perhaps the increase in [Hb] was too modest or persistence of correction was too short to be impactful.

**Conclusion:** It makes the case for defining HbA1c reference ranges for each anaemia subtype, as well as utilizing other surrogates for monitoring glycemic control in populations with anaemia.

**Keywords:** Anaemia, Haemoglobin A1c, glycosylated Haemoglobin, HbA1c reference range(s), HbA1c therapeutic goals,

**Abbreviations:** Hb Haemoglobin, HbA1c: glycosylated Haemoglobin, delta sin change

## Introduction

The American Diabetic Association (ADA) and the American College of Endocrinology (ACE) recommend HbA1c levels as diagnostic criteria for diabetes mellitus. Physicians have adopted HbA1c levels as a convenient way to screen for diabetes, as well as to monitor therapy. There exists concern that because HbA1c is formed from the glycation of the terminal Valine unit of the β-chain of haemoglobin, it may not be an accurate surrogate to ascertain glycemic control in certain conditions that affect the concentration, structure and function of haemoglobin. It makes logical sense to infer that HbA1c levels should at least in part reflect the average haemoglobin concentration ([Hb]). Kim et al (2010) stated that iron deficiency is associated with shifts in HbA1c distribution from <5.0 to ≥5.5% [1] and significant increases was observed in the patients' absolute HbA1c levels 2 months after treatment of anaemia.[2] There is a dearth of literature on HbA1c levels in the anaemia population, and a reference range for this unique population does not currently exist. There are a few documented studies on this matter, the findings of which are at best, inconsistent.

It is thought that the various types of haemoglobin found in the myriad of haemoglobinopathies may affect haemoglobin-glucose bonding and/or the lifespan of haemoglobin, and by extrapolation, HbA1c level. Hence, extending target HbA1c values to certain haemoglobinopathaties may be erroneous due to potential differences in glycation rates, analytical methods (HbF interfers with the immunoassay method) and some physiological challenges (markedly decreased red cell survival).[3]

There is a significant positive correlation between haemoglobin concentration and HbA1c in the patients with haemolytic anaemia.[4,5] Cohen et al (2008) reported that observed variation in red blood cell survival was large enough to cause clinically important differences in HbA1c for a given mean blood glucose,[6] and haemolytic disorders may cause falsely reassuring HbA1c values.[7] Jandric et al (2012) inferred that in diabetic population with haemolytic anaemia, HbA1c is a very poor marker of both overall glycemia and haemolysis.[8] Mongia et al (2008) report that immunoassay methods for measuring HbA1c may exhibit clinically significant differences owing to the presence of HbC and HbS traits.[9]However, Bleyer et al report that sickle cell trait does not affect the relationship between HbA1c and serum glucose concentration and it does not appear to account for ethnic difference in this relationship in African Americans and Caucasians.[10]

Koga & Kasayama (2010) advise that caution should be entertained when diagnosing pre-diabetes and diabetes in people with low or high haemoglobin concentration when the HbA1c level is near 5.7% or 6.5% respectively, citing the implication of changes in erythrocyte turnover. They further assert that the trend for HbA1c to increase with iron deficiency does not appear to necessitate screening for iron deficiency to ascertain the reliability of HbA1c in this population.[11]

In the light of the uncertainty in the influence of anaemia and haemoglobinopathies on HbA1c, it is imperative that clinicians are aware of the caveats with HbA1c values when they make management decisions in the anaemic population.[12] There is currently a call for the use of other surrogates for ascertaining average glycemic control in pregnancy, elderly, non-Hispanic blacks, alcoholism, in diseases associated with postprandial hyperglycemia, genetic states associated with hyperglycation, iron deficiency anaemia, haemolytic anaemias, variant haemoglobin states, chronic liver disease, and end-stage renal disease (ESRD).[13,14]

**Study objectives and hypothesis**

The study attempts to discern clinical differences in HbA1c levels in patients with anaemia compared to non-anaemic population, as well as to quantify and show the direction of such difference if they indeed exist. We hypothesize that as glucose is covalently bound to haemoglobin in glycosylated haemoglobin, HbA1c levels in non-diabetic anaemic population is significantly lower than in non-diabetic, non-anaemic population.[2] However, this relationship may not hold true for certain anaemias, haemoglobinopathies and hyperglycation states in some genetic syndromes.

**Study design and method**

The study is a retrospective chart review of patients with and without anaemia who underwent haemoglobin concentration and HbA1c level testing at The Brooklyn Hospital Center (TBHC) from July, 2009 to June, 2013. Using Cohen (1987) power table, assuming a power of 0.8, alpha level of 0.05, and a small effect size of 0.2 standard deviations (SD), sample size estimation of 461 was computed. A convenient sampling method was used to select patients who meet inclusion criteria, absent exclusionary conditions. In using this sampling method, we queried the electronic medical record at the TBHC using the below-listed inclusion and exclusion criteria. The query generated a list of "potential subjects". We then reviewed the electronic chart of each patient on this list to confirm that they indeed meet all study criteria (excluding further if any exclusion criteria was identified on "second look". We continued the selection until the computed minimum sample size of 461 was significantly exceeded. During this process, we had to examine every patient on the "potential subject" list generated by the initial query to achieve this goal. For the purpose of the study, anaemia is defined as haemoglobin concentration <11g/dl.

Inclusion criteria:

- Study participant must be at least 21 years of age. We adopted this age criteria because at TBHC, electronic medical records was only available for the non-pediatric population over the study period. Patients below 21 years were managed at the pediatrics department using paper charts until the recent adoption of the EMR system. It would have been difficult conducting the study using paper charts.
- Study participant must have at least one documented HbA1c level obtained within a month of a haemoglobin concentration assay. This criterion was adopted to allow for more inclusiveness in the study. It is our experience that haemoglobin assays may not be available on the same day as HbA1C assays considering the retrospective nature of the study.

Exclusion criteria:

- Confirmed cases of diabetes mellitus (using two or more of the following: presence of symptoms related to diabetes, fasting blood glucose, 2 hours post-prandial glucose, and oral glucose tolerance test).
- Documented history of gestational diabetes (GDM)
- Documented history of endocrinopathy with affect for glycemic control
- Current or prior use of medication with potential to increase or decrease HbA1c (includes, but not limited to antidiabetics, corticosteroids, statins, and antipsychotics)
- Pregnancy or pregnancy-related condition within three months of HbA1c assay
- Haemoglobin concentration <6 g/dl or >16g/dl.
- Blood loss or blood transfusion within two months of HbA1c assay

The study assumed a consistent HbA1c assay method at the study center over the study period. 482 (229 anaemic and 253 non-anaemic) were selected. The study reviewed electronic medical records of selected patients, extracting data on HbA1c, fasting blood glucose (FBG), 2-hour post-prandial serum glucose (2HPPG), 2-hour oral glucose tolerance test (OGTT), haemoglobin concentration and electrophoresis, and anaemia work-up results when available. Subsequent measures of HbA1c two months after correction of anaemia was also documented and compared to pre-treatment levels.

**Results and Analysis**

The mean age of the anaemic and non-anaemic was 51.8 and 64.6 years respectively. Using the student's t-test and $x^2$analysis respectively, the difference in mean age of both groups (anaemia and non-anaemic) was significant at p0.05 while gender distribution was similar (p>0.05), see table 1. The mean HbA1c for anaemic and non-anaemic groups was 5.35% and 5.74%

respectively, amounting to a 0.4 unit difference in (8%) in mean HbA1c. This difference was statistically significant (p0.02). A significantly higher variance was observed in the anaemia group (0.79 vs. 0.64).

**Table 1:** Gender and age distribution and statistics

| Age in years | #(%) | Gender (M/F) | Mean Age (in yrs) |
|---|---|---|---|
| Anaemia | | | |
| 21-44 | 20(8.7) | 17/41 | |
| 45-64 | 76(33.2) | 43/86 | |
| ≥65 | 133(58.1) | 10/32 | |
| Total | 229(100.0) | 70/159 | 64.6 |
| Non-anaemic | | | |
| 21-44 | 64(25.3) | 23/42 | |
| 45-64 | 134(53.0) | 58/81 | |
| ≥65 | 55(21.7) | 18/31 | |
| Total | 253(100) | 99//154 | 51.8 |

p-Values: Age=0.023, Gender=0.061

Assuming that 95% of the population is normal, computation of HA1c reference range (mean ±1.96SD) for the anaemia and non-anaemic group yielded 3.8-6.9 and 4.5-7.0 respectively. There was a significantly positive spearman correlation between [Hb] and HbA1C (r=0.28, p0.00). The mean HbA1c level and proposed reference ranges for the five anaemia subgroups (anaemia of chronic disease [ACD], iron deficiency anaemia [IDA], mixed anaemia, macrocytic anaemia and sickle-cell disease) are shown in table 2. Using one-way ANOVA analysis, the difference in the mean [Hb] and HbA1c across anaemia subtypes was not statistically significant (p0.08 and p0.36 respectively), see table 2.

**Table 2:** Anaemia subtypes with HbA1c statistics

| Anaemia Type | # | Mean [Hb] | Mean HbA1c | 95% CI (HbA1c) | Ref. range (HbA1c) |
|---|---|---|---|---|---|
| ACD | 92 | 9.23 | 5.41 | 5.24-5.59 | 3.5-7.1 |
| IDA | 78 | 9.41 | 5.38 | 5.22-5.54 | 3.9-6.8 |
| Mixed | 11 | 9.11 | 5.21 | 4.82-5.59 | 3.9-6.5 |
| Macrocytic | 43 | 8.83 | 5.14 | 4.92-5.37 | 3.7-6.6 |
| SCD | 5 | 9.12 | 5.55 | 4.84-6.26 | 3.8-7.3 |
| Anaemia (all types) | 229 | 9.21 | 5.35 | 5.24-5.44 | 3.8-6.9 |
| Non-anaemic | 253 | 12.87 | 5.735 | 5.66-5.81 | 4.5-7.0 |

p-values: [Hb] for anaemia subtypes=0.08, HbA1C for anaemia subtypes=0.36, HbA1C anaemia vs. non-anaemia=0.02. ACD: anaemia of chronic disease, IDA: iron deficiency anaemia, SCD: sickle cell disease.

The study also examined the anaemia group to document the effect of anaemia correction on HbA1c levels. Only 62 of the 229 anaemic participants had documented [Hb] and HbA1c after interventions to correct anaemia, see table 3 and 4.

**Table 3:** Trend in [Hb] and HbA1c

| | N | Mean | SD | SEM | Change | p-Value |
|---|---|---|---|---|---|---|
| $[Hb]_1$ | 62 | 9.2 | 1.07 | 0.14 | | |
| $[Hb]_2$ | 62 | 10.1 | 1.98 | 0.25 | [Hb]=0.9 | 0.00 |
| $HbA1c_1$ | 62 | 5.37 | 0.69 | 0.88 | | |
| $HbA1c_2$ | 62 | 5.35 | 0.66 | 0.83 | HbA1c=0.02 | 0.78 |

$[Hb]_1$ and $[Hb]_2$: haemoglobin concentration pre- and post-treatment for anaemia. $HbA1c_1$ and $HbA1c_2$: HbA1c pre- and post-treatment for anaemia

Using the student's t-test, analysis, a 0.9g/dl mean improvement in [Hb] in the anaemia group (significant at p0.00) did not result in a statistically significant change in HbA1c (-0.02 units, p0.78). Similar results were obtained with anaemia of chronic disease and iron deficiency anaemia (ICD: change [Hb] =+0.6g/dl, change HbA1c=0.09, p0.31; IDA: change [Hb]=+1.3g/dl, change HbA1c=0.03, p0.79).

**Discussion**

There was an over-representation of the elderly in the anaemia group (58.1% vs. 21.7%). This is not unexpected as nutritional anaemia and anaemia of chronic disease increase in prevalence with the increasing co-morbidities associated with increasing age. The linear relationship between [Hb] and HbA1c holds true for anaemic and non-anaemia populations. There is a statistically significant difference of 0.4units (8%) in the mean HbA1c between the anaemic and the non-anaemic population. This difference is even more marked when the lower limit of the range is compared (3.8 vs. 4.5, difference of 0.7unit, 18%), the significance of which is not as clinically impacting as the upper limit of the range (diabetes mellitus diagnostic criteria). However, the relatively lower limit of normal for HbA1c in anaemic subgroups (especially of anaemia of chronic disease) may make low values of HbA1c in these patients less indicative of over-enthusiastic glycemic control, as well as less predictive of the increase in mortality associated with such tight control.

The upper range of normal for HbA1c for the anaemia and the non-anaemic groups and by extrapolation the proposed diagnostic criteria for diabetes, is however more similar (6.9 vs. 7.0%). This result appear consistent with Koga and Kasavama (2010) assertion that the trend in HbA1c does not appear to necessitate screening for iron deficiency to ascertain the reliability of HbA1c in this population.[11] Our observation is explained by the greater variance associated within the anaemia group. The significantly higher variance observed in the anaemia may be explained by the convenient homogenization of clinically heterogeneous anaemia entities in the anaemia group. Perhaps a prospective study that avoids this may report differently.

The significantly higher variance (23%) in the anaemia is explained by the heterogeneity of the subtypes within the anaemia group. The myriad of pathophysiologies (from variant

**Table 4:** Trend in [Hb] and HbA1c for anaemia subtypes

| | N | Mean [Hb]1 | Mean [Hb]2 | Δ Hb | p Value | Mean HbA1c1 | MeanHbA1c2 | Δ A1c | p Val |
|---|---|---|---|---|---|---|---|---|---|
| ACD | 33 | 9.1 | 9.7 | 0.6 | 0.0 | 5.44 | 5.35 | 0.09 | 0.3 |
| IDA | 21 | 9.4 | 10.7 | 1.3 | 0.0 | 5.30 | 5.33 | 0.03 | 0.8 |
| Mixed | 1 | | | | | | | | |
| Macrocytic | 6 | | | | | | | | |
| SCD | 1 | | | | | | | | |
| Total | 62 | 9.2 | 10.1 | 0.9 | 0.0 | 5.37 | 5.35 | 0.02 | 0.8 |

ΔHb: change in haemoglobin concentration ([Hb]), ΔA1c: change in HbA1c

haemoglobin affecting structure and function, and perhaps glycation rates of haemoglobin, to shortened erythrocyte lifespan due to intravascular and extravascular haemolysis) accounts for a less precise HbA1c reference range for the anaemia group. Separating the anaemia group into unique anaemia subtypes created less heterogeneity, reduced some within group variance and yielded a more precise references range for some anaemia subtypes.

The widened 95% CI of mean and reference ranges observed with mixed and sickle cell anaemia (95% CI of mean =4.82-5.59 and 4.84-6.26 respectively) may be attributable in part to the small number of participants in these subgroups (11 and 5 respectively, the normal curve is less robust in these circumstances [when n<30])). Furthermore, the marked variability in the type, severity, and the number of chronic morbidities and deficiencies causing mixed anaemia may be contributing. The imprecision of HbA1c observed with the sickle cell may be compounded by the unstable clinical course of sickle disease, marked by periodic crises with fluctuating [Hb] associated with intermittent or chronic haemolysis. These observations make the case for defining HbA1c reference ranges for each anaemia type.

A modest correction of anaemia (Δ [Hb] of +0.9g/dl, i.e <1g/dl) did not appear to cause a significant change in HbA1c levels. It is possible that higher increments in [Hb] may produce significant change in HbA1c (we predict in the direction of increment). A similar pattern was observed with anaemia of chronic disease and iron deficiency anaemia subtypes, where improvements in [Hb] of 0.6 and 1.3g/dl respectively did not cause a significant change in HbA1c. We propose that with anaemia of chronic disease, the change in [Hb] concentration was too modest to cause a significant change in HbA1c. The relative small size of participants (33) examined also makes type II statistical errors highly likely. We further propose that with anaemia of chronic disease, the myriad of functional cellular and system abnormalities (many, potentially affecting cellular homeostasis, especially acid-base balance and haemoglobin molecule covalent binding) associated with the primary disorder may impact on the potential for increase in HbA1c with increasing [Hb]. In view of the retrospective nature of the study, we could not ascertain the timelines of certain interventions and hence accurately determine the persistence of anaemia correction. Theoretically, a recent correction in [Hb] is less likely to impact on HbA1c. As alluded to above Kim et al (2010) evaluated for changes in HbA1c two months after correction of anaemia. Similar explanations are offered for the observation with iron deficiency anaemia. There were only 21 participants in the iron anaemia subgroup (i.e. <30, probable violation of a rule for use of parametric tests), making the parametric statistical tests less robust for the analysis. We did not study patterns with mixed, macrocytic and SCD, as each subtype had <7 (1,6,1) participants.

The study examined a large volume of data, eliminating as much as possible, potential extraneous factors in the relationship between [Hb] and HbA1c levels. However, the retrospective nature of the study made the control of other extraneous variables and certain patient attributes infeasible. It was also difficult to discern critical timelines and hence eliminate the potential impact of certain therapeutic interventions. Also, our exclusion of the younger population of patients (i.e. 16-20 years) does not necessarily indicate the result of the study may not be extended to this population of anaemia patients. In fact the similar human haemoglobin physiology in this group advises that the results may be extended to this younger population without concern. Due to the retrospective nature of the study, and in our attempt to increase inclusiveness, we allowed haemoglobin concentration and HbA1c assays done within a month of each other. In reality though, the majority (57%) had same day assays and even a greater majority (79%) had within same week assays. We recommend a larger scale prospective study with participants representative of all anaemia subtypes and ages so that the results can be extrapolated to the general population of anaemia patients.

**Conclusion**

The study emphasizes the need to exercise caution when applying HbA1c reference ranges to anaemic populations. It makes the case for defining HbA1c reference ranges and thus, therapeutic goals for each anaemia subtype. Redefining such reference ranges may increase the sensitivity of HbA1c in diagnosing diabetes in anaemic population if indeed the lower mean HbA1c (observed in this study) translates into significantly lower upper limits of references ranges (not

observed in this study). Also, the realized reduced lower limits of reference range in this population will lead to appropriate clinical tolerance for lower HbA1c levels, with avoidance of inappropriate intervention for erroneous perception of over-enthusiastic control of diabetic hyperglycemia. We recommend that, absent risks factors for and symptoms relatable to diabetes, marginal elevations in HbA1c levels (i.e. HbA1c >6%) in anaemic patients should warrant confirmation of diagnosis using fasting blood glucose and 2HPPG or OGTT. The use of other surrogates of glycemic control, immune to the blur associated with haemoglobin type and concentration, may circumvent the problem associated with use of HbA1c in this special population. To this end, fructosamine and glycated albumin assays are currently being examined. [1,15]

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**REFERENCES**

1. Kim, C., Bullard K., Herman, W., Beckles, G. (2010). Association Between Iron Deficiency and A1C Levels Among Adults Without Diabetes in the National Health and Nutrition Examination Survey, 1999–2006. Diabetes Care. 2010 April; 33(4): 780–785. Published online 2010 Jan 12. doi: 10.2337/dc09-0836.
2. Sinha, N., Mishra, T., Singh, T., Gupta, N. (2012). Effect of Iron Deficiency Anaemia on Haemoglobin A1c Level. Ann Lab Med. 2012 January; 32(1): 17–22. Published online 2011 Dec 20. doi: 10.3343/alm.2012.32.1.17
3. Higgins, T., Stewart D., Boehr E. (2008). Challenges in HbA1c analysis and reporting: an interesting case illustrating the many pitfalls. Clin Biochem. 2008 Sep;41(13):1104-6. Epub 2008 Jun 19.
4. Koga, M., Hashimoto, K., Murai J, Saito, H., Mukai, M., Ikegame, K., Ogawa, H., Kasayama, S. (2011). Usefulness of glycated albumin as an indicator of glycemic control status in patients with hemolytic anemia. Clin Chim Acta. 2011 Jan 30;412(3-4):253-7. Epub 2010 Oct 18.
5. Ford, E., Cowie C., Li C., Handelsman Y., Bloomgarden Z. (2011). Iron-deficiency anemia, non-iron-deficiency anaemia and HbA1c among adults in the US. J Diabetes. 2011 Mar;3(1):67-73.
6. Cohen, R., Franco, R., Khera, P., Lindsell, S., Ciraolo, P., Palascak, M., Joiner, C. (2008). Red cell life span heterogeneity in hematologically normal people is sufficient to alter HbA1c. Blood. Nov 15; 112(10): 4284–4291.
7. Debard, A., Charmion, S., Ben Ameur S., Gaultier, J., Cathébras, P. (2008). Inappropriate low glycated Haemoglobin and hemolysis. Rev Med Interne. 2009 Jun;30(6):525-7. Epub 2008 Nov 18.
8. Jandrić, B., Lukenda, V., Jandrić, I., Raguž, A., Zukanović, S., Miškić, B. (2012). HbA1C - overall glycemia marker and hemolytic anaemia indicator. Med Glas Ljek komore Zenicko-doboj kantona. 2012 Aug;9(2):406-8.
9. Mongia, S., Little, R., Rohlfing C., Hanson, S., Roberts, R., Owen, W., D'Costa, M., Reyes, C., Luzzi, V., Roberts W. (2008). Effects of Haemoglobin C and S traits on the results of 14 commercial glycated Haemoglobin assays. Am J Clin Pathol. 2008 Jul;130(1):136-40.
10. Bleyer, A., Vidya, S., Sujata, L., Russell, G., Akinnifesi, D., Hire D., Shihabi Z., Knovich, M., Daeihagh, P., Calles, J., Freedman, B. The impact of sickle cell trait on glycated haemoglobin in diabetes mellitus. Diabet Med. 2010 Sep;27(9):1012-6.
11. Koga, M., Kasayama, S. (2010). Clinical impact of glycated albumin as another glycemic control marker. Endocr J. 2010;57(9):751-62. Epub 2010 Aug 17.
12. Nasir, M., Thevarajah, M., Yean, C. (2010). Haemoglobin variants detected by Haemoglobin A1c (HbA1c) analysis and the effects on HbA1c measurements. Int J Diabetes Dev Ctries. 2010 Apr-Jun; 30(2): 86–90.
13. Lippi, G., Targher, G. (2010). Glycated Haemoglobin (HbA1c): old dogmas, a new perspective? Clin Chem Lab Med. 2010 May;48(5):609-14.
14. Youssef D., El Abbassi, A., Jordan, R., Peiris, A. Fructosamine--an underutilized tool in diabetes management: case report and literature review. Tenn Med. 2008 Nov;101(11):31-3.
15. Kim, S., Min, K., Chun, S., Lee, W., Park, H. (2011). Glycated albumin may be a possible alternative to Haemoglobin A1c in diabetic patients with anemia. Clin Chem Lab Med. 2011 Oct;49(10):1743-7. Epub 2011 Jun 17.