



GLYCATED HEMOGLOBIN AND RBC LIFE SPAN IN CARDIAC PATIENTS.

Rajasree Pai .R	Endocrinology and metabolism, Santa Rosa Clinic, California, United States.
Jayakrishnan	Department of Laboratory Medicine, SK Hospital, Edappazhinji, Thiruvananthapuram 695006.
Jayanthi Bai.N*	Department of Laboratory Medicine, SK Hospital, Edappazhinji, Thiruvananthapuram 695006. *Corresponding Author

ABSTRACT

CBC level, HbA1c were measured in 100 controls and 100 cardiac patients. CBC was measured using Nihon Kohden 5part haematology analyser and HbA1C measured by ion-exchange HPLC technology using D10 instrument. The HbA1c levels were not associated with RBC life span.

KEYWORDS : HbA1c, CBC, RBC

INTRODUCTION

HbA1c has been widely used as a glycemic control indicator or as a diagnostic tool for diabetes mellitus. However, HbA1c is affected by the erythrocyte life span and, therefore, shows falsely low values in hemolytic patients. Erythrocyte creatine (EC) is a sensitive hemolytic marker that reflects the mean erythrocyte age. The relationship of HbA1c, glycated albumin (GA), and 1, 5- anhydroglucitol (1, 5-AG) with different haemolytic markers were investigated in non haemolytic patient. A total of 23 non- diabetic individuals whose CBC and electrolytes were measured via medical examination to examine the correlation of HbA1c with 1,5-AG values and there haemolytic markers .HbA1c but not with GA and 1,5-AG, showed significant correlations with the hemolytic markers. (1)

MATERIALS.

One hundred non cardiac and 100 cardiac patients were included in the study. All the patients were from those attending OP/IP of SK Hospital .Blood was drawn using disposable syringes and needle and serum separated by centrifugation at 3000 rpm for 10 minutes using Kemi centrifuge.

METHODS.

CBC was measured in Nihon Kohden 5part haematology analyser supplied by Bions Medical Systems Pvt Ltd. HbA1C measured by ion-exchange HPLC technology using Bio-Rad D₁₀ instrument supplied by AK Enterprises. All patients were above 65 years and contain both genders.

RESULT

The CBC and HbA1c results are presented in Table I. The HbA1c result has no direct association with Hb level. The HbA1c level was independent of RBC life span Even in haemolytic anemia the HbA1c was higher or lower compared to Hb%.

DISCUSSION

These results suggest that HbA1c does not reflect by mean erythrocyte age and, therefore, accurately reflect the glycemic control. HbA1C is a valuable tool for the monitoring of glucose control in DM over time and has a strong predictive value for risks of DM complications. In general, any condition shortens RBC survival or decreases mean erythrocyte age, such as autoimmune hemolytic anemia, hereditary spherocytosis discrepancies or acute or chronic blood loss will falsely lower

the HbA1C level^[2,3]. Hence, in conditions associated with shortened red cell survival, HbA1C cannot be used to monitor or manage glucose control. A 1982 study established the usefulness of HbA1C as a screening of anemia due to warm and cold antibody immune hemolysis.HbA1C levels are an unreliable index of glycemic control, and other measures glucose and fructosamine, should be used in such cases^[4,10]

Hb variants and chemically modified derivatives of Hb such as carbamylated Hb, which is increased in uremic patients and acetylated Hb can affect the accuracy of HbA1C. (11, 12) Hemoglobinopathies decreased or increased the HbA1C levels .

Other conditions affecting HbA1C results include vitamins C and E, falsely lower HbA1C,Increased HbA1C results have also been reported in iron deficiency anemia, chronic ingestion of aspirin and opiate addiction interfere were increases HbA1C levels.

HbA1C as the preferred diagnostic test for DM has been recommended by an Expert Committee on the Diagnosis of Diabetes. In patients with decreased RBC lifespan and in Hb variants cases, HbA1C cannot be used for diagnosis; fasting glucose, be the best assay of choice.

2010 reported that HbA1c is well associated with glucose level but not with duration of DM .It may be associated with erythrocyte life span in haemolytic anemia.

50samples from non diabetic cardiac patients and 50 controls are measured .All sample showed low HbA1c independent of Hb or RBC levels of the patients. Thus there is poor association between HbA1c and erythrocyte life.

When interpreting the result of HbA1c factors affecting the life span of red blood cells should be taken in mind as it may affect the measurement of HbA1c. Severe hemolysis may result in falsely low HbA1c. In this case, the diagnosis with blood glucose, peripheral blood smear was performed by clinical lab consultation revealed Heinz bodies in erythrocytes, which were deficient in glucose G6PD. In the clinic, the G6PD was considered like most common RBC deficiency affect in the diagnosis of hemolysis with clinical lab results. This study emphasize that an extremely low HbA1c level can serve as a marker of hemolysis.

Table - I

S. No	Bill	Age /Gen	Hb (g/dL)	WBC (10 ⁹ /L)	DC					PCV%	Plt (10 ⁹ /L)	RBC (10 ¹² /L)	MCV (fL)	MCH (pg)	MCHC (g/dL)	ESR (mm/Hr)	Hb A1c %
					Poly %	Lym %	Eosi n%	Mono	Baso %								

1	3764221	35/M	13.2	9.7	64	31	2	3	0	41.2	90	4.94	83.4	26.7	33	46	9.9
2	944619	72/M	10.5	9	77	18	1	4	0	30.3	286	3.37	89.9	31.2	34.7	98	6
3	922316	99/M	11.3	3.8	55	38	3	4	0	34.1	191	3.93	86.8	28.8	33.1	10	5.6
4	2874913	53/F	13.1	8.70	52	41	4	3	0	38.5	259	4.68	82.3	28	34	54	6.7
5	4440013	72/M	14	10.2	54	29	13	4	0	40.3	268	4.56	88.2	30.5	34.5	22	6.7
6	3360721	53/M	15.1	6.2	49	44	3	4	0	44	225	5.31	82.9	28.4	34.3	18	9.5
7	3780621	64/M	14.4	8.8	52	37	7	4	0	41.6	150	4.46	93.3	32.3	34.6	18	6.3
8	432614	74/M	13.3	7	65	28	4	3	0	38	190	4.31	88.2	30	35	17	6.5
9	3109219	78/M	15	6.4	46	45	5	4	0	44.5	202	5.31	83.8	28.2	33.7	10	8.4
10	3782821	53/F	10.1	10.7	45	42	8	5	0	31.4	278	4.4	71.4	22.5	31.6	80	13.7
11	3786321	86/M	13.6	11	58	36	2	4	0	39.7	225	4.46	89	30.5	34.3	63	6.6
12	4799618	70/M	13.5	7.7	76	18	2	4	0	39.7	180	4.48	88.6	30.1	34	11	6.5
13	3779821	41/F	12.3	7.4	53	42	1	4	0	36.3	351	4.95	79.1	26.8	33.9	53	6
14	2340019	24/M	15.1	5.9	43	44	8	5	0	43.9	151	4.9	89.6	30.8	34.4	8	5.2
15	3789521	80/M	15.4	8.8	71	21	3	5	0	45.1	183	5.21	89	29.6	34.1	51	7.8
16	935321	60/F	8.5	8	44	47	6	3	0	25.6	335	3.13	64.8	21.1	32.6	74	9.1
17	3080515	69/M	14	11.9	62	35	1	2	0	41.2	262	4.95	83.2	28.3	34	33	9.8
18	4312912	59/M	14.6	4.8	37	56	4	3	0	42.8	214	4.6	93	31.7	34.1	22	6.3
19	2962718	67/M	13.2	8.6	61	37	8	4	0	38.5	285	4.38	87.9	30.2	34.3	38	7.7
20	2424420	53/F	11.5	6.6	48	47	3	2	0	36.6	252	4.39	83.4	26.2	31.5	57	7.7
21	2993317	70/M	15.7	5.4	54	38	4	4	0	45.5	150	5.31	85.7	29.6	34.5	12	5.8
22	5025713	68/M	13.4	5.4	51	41	4	4	0	39.5	161	4.53	87.2	29.6	33.9	21	6.5
23	1143111	61/M	15.4	6.6	53	39	4	4	0	44.9	210	5.34	84.1	28.8	34.3	17	6.5
24	2259211	74/F	12.8	7.7	55	39	2	4	0	40.8	191	4.66	87.6	27.5	31.5	44	7.2
25	3535621	75/F	13.7	8.1	57	39	1	3	0	40	255	4.6	87	29.8	34.3	48	12.4
26	3780721	67/M	13.4	5.7	64	32	1	3	0	39.4	197	4.47	88.1	30	34	19	6.8
27	3784921	75/F	11.3	11.7	57	31	10	2	0	32.8	310	4.3	76.3	26.3	34.5	36	9.5
28	3350921	68/F	10.9	5.2	61	31	4	4	0	32.5	96	3.43	94.8	31.8	33.5	19	6.6
29	2423713	47/F	13.2	7.2	45	48	4	3	0	40.1	262	4.39	87.9	30.2	34.3	20	6
30	269420	74/M	10.8	10.3	70	24	2	4	0	31.6	339	3.78	83.6	28.6	34.2	83	7.3
31	3783821	67/M	14.3	5	36	61	2	2	0	41.3	221	4.8	86	29.8	34.6	10	9.2
32	2572216	56/F	13.6	9.1	49	45	2	4	0	39.8	350	4.5	88.4	30.2	34.2	36	6.1
33	3798321	42/F	13.3	7.4	45	40	10	5	0	38.8	257	4.46	87	29.8	34.3	15	5.5
34	3208217	72/F	10.3	3.5	53	38	5	4	0	30.2	265	3.71	81.4	27.8	37.1	29	5.4
35	4755417	53/F	11.1	9	9	35	3	3	0	32.7	320	4.1	79.8	27.1	33.9	57	6.5
36	3798421	45/F	12.6	8.1	62	31	3	4	0	37.2	335	4.57	81.4	27.6	33.9	17	6
37	1498920	73/M	16.7	9.5	51	37	7	5	0	47.5	175	5.29	89.8	31.6	35.2	14	6.1
38	2141320	23/F	12.4	9.4	72	21	2	5	0	37.1	260	4.89	75.9	25.4	33.4	35	5.8
39	535112	66/F	10.2	8.9	66	28	3	3	0	29.6	217	3.7	80	27.6	34.5	84	12.6
40	800715	67/F	7.8	10.8	71	18	8	3	0	23.9	586	3.69	64.8	21.1	32.6	109	10.7
41	3812221	44/F	13	7.3	46	47	4	3	0	38.7	316	4.51	85.8	28.8	33.6	22	6.1
42	2830414	41/M	14.4	7	61	34	2	3	0	42.2	185	4.86	86.8	29.6	34.1	5	5.4
43	4140212	60/F	12.5	10	59	35	3	3	0	36.1	326	4.37	82.6	28.6	34.6	22	10.5
44	4196716	68/M	14.7	7.2	58	34	4	4	0	42.8	272	4.65	92	31.6	34.3	6	5.9
45	3812521	60/F	12.9	8.8	48	46	3	3	0	40.4	291	4.73	85.4	27.4	32	36	9.1
46	2332613	63/F	12.2	9.4	61	32	4	3	0	37	278	4.25	87.2	28.8	33	36	9.5
47	1998016	57/F	11.6	7.6	58	38	2	2	0	34.8	311	4.36	79.9	26.7	33.4	75	12.8
48	2588921	79/F	12.8	7.2	51	43	1	5	0	38.8	371	4.36	89	29.4	33	40	6.2
49	3816121	71/F	7.7	3.6	57	37	2	4	0	23.5	217	4.59	88.3	30.1	34.1	36	6.3
50	1569312	58/M	15.2	7.4	62	33	3	2	0	46.4	202	5.35	86.8	28.5	32.8	8	12.5
51	3564312	78/M	11.9	5.8	74	23	2	1	0	37.3	217	4.13	90.3	28.9	32	10	7.6
52	1522	81/F	12.5	6.7	66	29	3	2	0	37.9	156	4.31	87.9	28.9	32.9	14	7.4
53	429621	32/F	11.1	7.7	52	42	3	3	0	34.2	346	3.88	88.3	2.7	32.6	9	6
54	4253311	70/F	12.3	5.7	55	34	6	5	0	38.7	232	4.15	93.3	29.6	31.8	14	5.7
55	3814921	71/M	4.3	8.5	76	18	1	5	0	14.8	285	2.58	57.5	16.7	29	13	5.4
56	1877117	57/M	9	6.4	83	14	1	2	0	27.4	202	3.52	77.9	25.6	32.9	89	13.6
57	7022	64/F	12.3	10.6	92	5	1	2	0	37.9	150	4.36	86.9	28.3	32.6	61	6.8
58	5052814	71/F	11.2	3.9	60	35	2	3	0	34.6	162	3.96	87.4	28.3	32.4	5	7.1
59	574318	52/M	17.4	7.9	64	30	2	4	0	53.6	179	6.02	89.1	28.9	32.5	5	5.5
60	5062415	86/M	11.9	7	51	42	3	4	0	35.8	186	3.94	90.9	30.1	33.1	16	7.5
61	8922	48/F	9.8	6.9	40	54	3	3	0	29.5	258	3.41	86.4	28.7	33.3	40	5
62	9922	92/F	11.8	5	74	20	2	4	0	36.6	230	4.07	89.9	29	32.3	22	6.9
63	13522	63/M	13.2	6.4	56	36	4	4	0	41	150	4.8	85.5	27.6	32.2	18	6.1
64	13422	58/M	15.2	8.1	78	17	1	4	0	46.1	140	5.15	89.6	29.6	33	25	8.3
65	1355011	66/F	12.4	8.8	46	48	2	4	0	37.8	261	4.27	88.5	29.1	32.8	6	6.3
66	3222611	72/M	10.8	9.4	58	36	3	3	0	35.1	249	4.62	75.8	23.4	30.8	23	8.8
67	1447914	60/F	11.9	5.8	55	40	2	3	0	36.7	262	4.15	88.5	28.8	32.5	25	7.7
68	40518	59/F	11.5	8.1	75	22	1	2	0	35.8	256	4.07	87.9	28.2	32.1	12	5.6

69	378217	62/M	15.2	6.1	74	21	1	4	0	45.8	246	5.1	89.6	29.7	33.1	10	5.3
70	15522	56/F	14.6	6.3	52	43	1	4	0	45.9	282	4.95	9236	29.5	31.8	24	6.4
71	4633014	70/F	11.5	10.3	56	40	1	3	0	36.1	356	3.98	90.8	28.9	31.8	14	6.6
72	2953718	52/F	11.2	8.1	46	49	3	2	0	35.2	172	4.07	86.7	29.4	31.7	41	7
73	995819	76/M	11.9	4.1	60	32	3	5	0	36.5	175	4.18	87.2	28.4	32.6	15	8.7
74	3222	58/F	11.8	10.1	48	47	2	3	0	37.3	235	4.66	80.1	25.3	31.6	30	10.4
75	14022	74/F	12.4	2.7	40	55	1	4	0	38.6	179	4.16	92.8	29.8	32.1	43	5.9
76	3344812	70/F	12.1	8.7	64	32	1	3	0	38.4	204	4.53	84.9	36.7	31.5	56	9.5
77	2777912	88/M	11.2	6.4	56	39	1	4	0	33.9	142	3.76	90.3	29.7	32.9	5	8.4
78	19922	48/F	11.9	8.2	59	37	1	3	0	37.8	264	4.41	85.9	27.1	31.5	16	5.5

CONCLUSIONS

An attempt was made in the present study to evaluate the correlation between age of RBC and HbA1c. It is observed that both are independent and have no direct association. HbA1c does not depend on life span of RBC. Even haemolytic anemia patient this HbA1c level can be high.

REFERENCES

- [1] Kuniwa N, Okumiya T, Tokuhira S, Matsumura Y, Matsui H, Koga M. Hemolysis causes a decrease in HbA1c level but not in glycated albumin or 1,5-anhydroglucitol level. *Scand J Clin Lab Invest.* 2019 Oct; 79(6):377-380. doi: 10.1080/00365513.2019.1627577. Epub 2019 Jun 17. PMID: 31204512.
- [2] Sacks DB, Bruns DE, Goldstein DE, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem.* 2002;48:436-472.
- [3] Panzer S, Kronik G, Lechner K, et al. Glycosylated hemoglobins (Ghb): An index of red cell survival. *Blood.* 1982;59:1348-1350.
- [4] Tack CJJ, Wetzels JFM. Decreased HbA1C levels due to sulfonamide-induced hemolysis in two IDDM patients. *Diabetes Care.* 1996;19:775-776.
- [5] Herranz L, Grande C, Janez M, et al. Red blood cell autoantibodies with a shortened erythrocyte life span as a cause of lack of relation between glycosylated hemoglobin and mean blood glucose levels in a woman with type 1 diabetes. *Diabetes Care.* 1999;22:2085-2086.
- [6] Baynes KCR, McIntosh C, Feher MD. Artefactually low glycated haemoglobin is a potential pitfall in diabetes measurement: Consider congenital haemolytic anaemias. *Pract Diab Int.* 2001;18:103-106.
- [7] Liew CF, Cheah JS. Hereditary spherocytosis, a pitfall in the assessment of glycaemic control. *Singapore Med J.* 2003;44:94-97.
- [8] Kutter D, Thoma J. Hereditary spherocytosis and other hemolytic anomalies distort diabetic control by glycated hemoglobin. *Clin Lab.* 2006;52:477-481.
- [9] Diop ME, Bastard JP, Meunier N, et al. Inappropriately low glycated hemoglobin values and hemolysis in HIV-infected patients. *AIDS Res Hum Retroviruses.* 2006;22:1242-1247.
- [10] Arnold JG, McGowan HJ. Delay in diagnosis of diabetes mellitus due to inaccurate use of hemoglobin A1C levels. *Amer J Fam Med.* 2007;20:93-96.
- [11] Bry L, Chen PC, Sacks DB. Effects of hemoglobin variants and chemically modified derivatives on assays for glycohemoglobin. *Clin Chem.* 2001; 47: 153-163.
- [12] Factors that interfere with GHB (HbA1C) Test Results, Updated 8/09. National Glycohemoglobin Standardization Program. Available at: www.NGS.Porg./prog/factors.htm.