Artifactually low HbA1c in Hb E disorder.

Artifactually low HbA1c in diabetic patients with hemoglobin E: Surin Hospital, Thailand.

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BACKGROUND

➡ A decreased life-span of erythrocytes is associated with lower concentration of hemoglobin A1C (HbA1c).

➡ The HbA1c concentration is correlated with the developmental stage of erythrocytes.

➡ The most common cause of anemia in endemic area of hemoglobinopathy is hemoglobin E disorder. Therefore, the possibility of the coexistence of DM and hemoglobin E disorder is higher than any other type of anemia in Surin province, Thailand.

The relationship between hemoglobin E homozygote (EE) and HbA1c in DM has not been previously studied.

OBJECTIVES

Objective

➡ This research aims to study effect of hemoglobin E homozygote on HbA1c level of diabetic patients in Surin Hospital.

MATERIALS & METHODS

This cross-sectional study was approved by the institutional review board and conducted in the diabetic clinic at Surin Hospital since January, 2009 to December, 2016. Hemoglobinopathies are routinely screened in the diabetic clinic at Surin hospital. For the laboratory measurements, a blood sample was taken in the morning after an overnight fast and there was a test for dichlorophenol-Indolephenol (DCIP). Subjects were classified into one of three groups; included, negative DCIP (N), homozygous hemoglobin (HbEE) and excluded hemoglobin E trait (HbEA). In patients with hemoglobinopathy hemoglobin typing was compared with liquid chromatography.

HbA1c in each group was compared with fasting plasma glucose measured before breakfast. Statistical analysis was carried out. Descriptive parameters are presented as means with standard deviations, or as percentiles. Unpaired *T- test* analysis was used to compare the mean values among the group defined by different levels of blood glucose and HbA1c. Gaussian regression analysis was used for univariable and multivariable analysis. A *p*-value < 0.05 was considered statistically significant. Statistical analysis was carried out by using STATA 15.0 software.

RESULTS

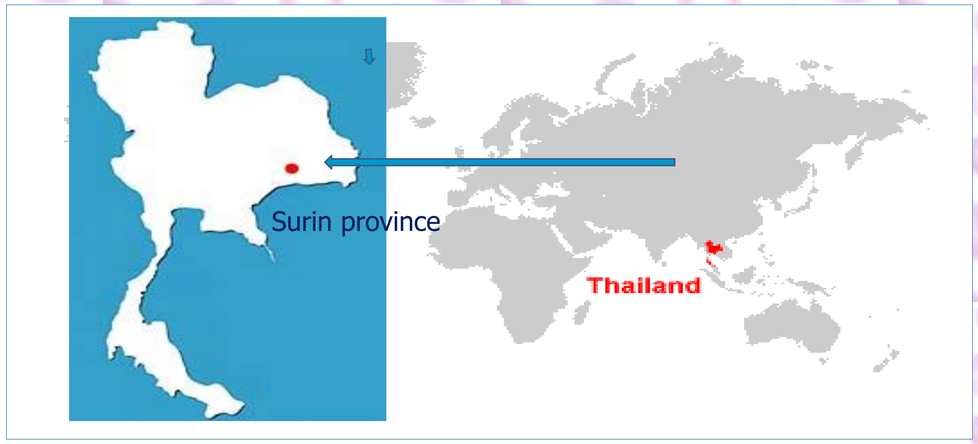


Figure 1. Histogram of HbA1c - -negative DCIP, -- -- Hb EA, ----Hb EE

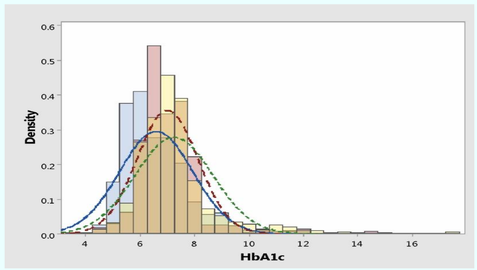


Table2. Combination of fasting plasma glucose and HbA1c in hemoglobin E and negative DCIP group by unpair T-test.

Fasting plasma glucose (mg%)	HbA1c (%)		P-value
	Negative DCIP group	Hb EE	
80-99 mg/dl (4.4-5.5 mmol/l)	6.86 ±0.86 SD	5.98 ± 0.95 SD	<0.001
100-119 mg/dl (5.6-6.6 mmol/l)	6.58 ± 0.99 SD	6.18 ± 1.27 SD	0.001
120-139 mg/dl (6.7-7.7 mmol/l)	6.98 ± 8.12 SD	6.17± 7.55 SD	<0.001
140-159 mg/dl (7.8-8.8 mmol/l)	7.35 ± 1.43 SD	6.60 ± 1.20 SD	<0.001
160-179 mg/dl (8.9-9.9 mmol/l)	7.66 ± 1.45 SD	6.69 ± 1.16 SD	<0.001
180-239 mg/dl (10.0-13.3 mmol/l)	8.56 ± 1.90 SD	7.58 ± 1.34 SD	<0.001

FPG= Fasting plasma glucose; control group= negative dichlorophenol-Indolephenol; Hb EA= hemoglobin E trait; Hb EE= homozygous hemoglobin E; P-value<0.05 significant

Table 1- Characteristics of the patients at baseline.

Variable	Control group	HbEA	HbEE	p-value*
Cases(n)	353	193	81	
Blood sample	691	596	580	
Age(years; mean, SD)	60(10.9)	58(10.6)	60(10.4)	0.1156
Sex(Male: Female)	0.43	0.46	0.38	
FPG(mg/dl; mean, SD)	150(85.7)	151(50.1)	146(45.9)	0.5660
HbA1c(%; mean, SD)	7.15(1.24)	6.94(0.96)	6.48(1.17)	<0.001
Hematocrit(%; mean, SD)	39(5.2)	38(4.4)	32(4.1)	<0.001

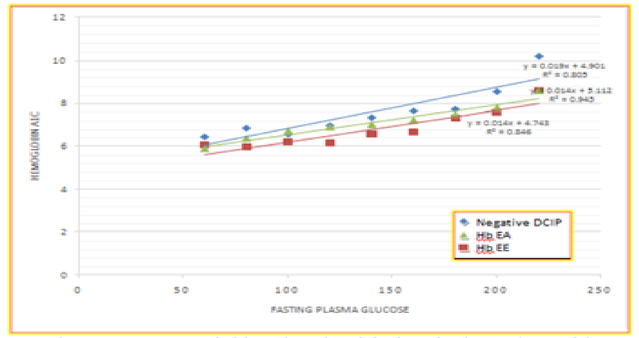
FPG= Fasting plasma glucose; control group= negative dichlorophenol-Indolephenol; Hb EA= hemoglobin E trait; Hb EE= homozygous hemoglobin E; P-value<0.05 significant

Table3. Combination of fasting plasma glucose and HbA1c in hemoglobin EA and negative DCIP group by unpair T-test.

Fasting plasma glucose (mg%)	HbA1c (%)		P-value
	Negative DCIP group	Hb EA	
80-99 mg/dl (4.4-5.5 mmol/l)	6.86 ±0.86 SD	6.35 ± 0.91 SD	<0.001
100-119 mg/dl (5.6-6.6 mmol/l)	6.58 ± 0.99 SD	6.70 ± 0.63 SD	<0.001
120-139 mg/dl (6.7-7.7 mmol/l)	6.98 ± 8.12 SD	6.89± 0.74 SD	<0.001
140-159 mg/dl (7.8-8.8 mmol/l)	7.35 ± 1.43 SD	7.00 ± 0.77 SD	0.005
160-179 mg/dl (8.9-9.9 mmol/l)	7.66 ± 1.45 SD	7.2 ± 0.82 SD	0.019
180-239 mg/dl (10.0-13.3 mmol/l)	8.56 ± 1.90 SD	7.77 ± 1.34 SD	<0.001

FPG= Fasting plasma glucose; control group= negative dichlorophenol-Indolephenol; Hb EA= hemoglobin E trait; Hb EE= homozygous hemoglobin E; P-value<0.05 significant

Figure2. Regression line by mean fasting plasma glucose versus mean HbA1c in hemoglobin EE, hemoglobin EA and control group.



Control group= negative dichlorophenol-Indolephenol; Hb EA= hemoglobin E trait; Hb EE= homozygous hemoglobin E.

Table 4. Effect of fasting plasma glucose and hemoglobinopathy to HbA1c by Gaussian regression.

Variable	Constant	Co-efficient	95% Confidence interval	P-value
FPG	4.98	0.014	0.012-0.015	<0.001
DCIP group	7.19	-0.33	(-0.40)-(-0.27)	<0.001

Table 5. Effect of hemoglobinopathy to HbA1c by Gaussian regression compare with negative DCIP.

Variable	Constant	Co-efficient	95% Confidence interval	P-value
Group 1 Hb EA	7.15	-0.21	(-0.34)-(-0.88)	0.001
Group 2 Hb EE	7.15	-0.67	(-0.80)-(-0.55)	<0.001

Table 6. Effect of fasting plasma glucose and hemoglobinopathy to HbA1c by multivariable regression.

Variable	Constant	Co-efficient	95% Confidence interval	P-value
FPG	5.25	0.014	0.013-0.015	<0.001
Group 1 Hb EA	5.25	-0.23	(-0.34)-(-0.12)	<0.001
Group 2 Hb EE	5.25	-0.70	(-0.81)-(-0.58)	<0.001

HbA1c=5.25+0.014FPG-0.23HbEA-0.70HbEE

SUMMARY

➡ Diabetes mellitus is a frequent disorder affecting individuals of all ages. HbA1c has a key role in the assessment of glycemic control in diabetic patients. These results clearly demonstrate that there is a relationship between the hemoglobinopathy and HbA1c in adult patients with DM.

HbA1c concentrations in diabetic patients with hemoglobin E disorder was found lower than control group when compared to similar glycemic control level.

CONCLUSIONS

➡ FPG is higher than expected because of the artifactually low of HbA1c measurement.

➡ Self monitoring in blood sugar should be performed. Diabetic patients with hemoglobins E disorder should carefully use HbA1c level as an indicator for long-term glycemic control.

➡ Diabetic patients with unexpected by low HbA1c value should be identified hemoglobins variant.

REFERENCES

1. Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M: Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 48:2002; 436–472.
2. Fitzgibbons JF, Koler RD, Jones RT. Red-cell age-related changes of hemoglobins A1a+b and A1c in normal and diabetic subjects. J. Clin. Invest. 1976; 41: 820–4.
3. Weatherall DJ, Clegg JB. Inherited haemoglobin disorders: an increasing global health problem. Bulletin of the World Health Organization 2001; 79:704-712.
4. Fucharoen S, Winichagoon P. Hemoglobinopathies in Southeast Asia. Hemoglobin 1987; 11:65-88.
5. Sattarattanamai C, Thongsuk S, Sutjaritchep P, Thuengsang D, Chomchuen S: Prevalence of thalassemia and hemoglobinopathies in pregnant women at Surin Hospital. Med J Srisaket Surin Buriram Hosp 2000; 15: 1-12.
6. Sueyunyongsiri P: Effect of Hemoglobin E disorder on Hemoglobin A1c in Diabetic patients. Med J Srisaket Surin Buriram Hosp 2008; 23: 637-643.