

Study Of Hba1c In Non-Diabetic First Degree Relative Of Type 2 Diabetes Mellitus Patient More Than 14 Year Of Age And Its Effect

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Abstract

Background and aims

The Haemoglobin A1c (glycated haemoglobin, glycosylated haemoglobin, HbA1c, or A1c) test is used to evaluate a person's Level of glucose control. Haemoglobin. Type 2 diabetes can be inherited and is linked to family history and genetics. Early Screening of first degree relative of type 2 dm patient will prevent development of Microvascular and Macrovascular complication.

Primary objective

To determine HbA1c in first degree relatives of patients of type 2 diabetes mellitus more than 14 year of age

Secondary objective

To determine the clinical and laboratory parameter in first degree relatives of type 2 diabetes mellitus patients. And To determine target organ damage in first degree relatives of patients of type 2 diabetes mellitus.

Methods and results

A cross-sectional study was carried out over a period of one year. Among 188 1st degree relative of type 2 DM patient, we divided HbA1c in to three group. Out of 188, 110 is Male while 78 are female. Out of 188 people HbA1c of 78(41.5%) comes below 5.7%, 72(38.3%) in pre-diabetic range (5.7-6.4%) and 38(20.2%) in diabetic range ($\geq 6.5\%$).

Conclusion

The present study demonstrated type 2 DM linked with family history and 1st degree relative of type 2 DM patient has high chance of development of diabetes in future. HbA1c is correlated with metabolic syndrome and could be considered as a marker or surrogate of metabolic syndrome in non diabetic, first degree relative of type 2 diabetes patient.

Categories: Public Health, Internal Medicine, Quality Improvement

Keywords: glycated haemoglobin (hba1c), diabetic microvascular complications, family history of diabetes, s: metabolic x syndrome, diabetes type 2

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I. Introduction

The Haemoglobin A1c (glycated haemoglobin, glycosylated haemoglobin, HbA1c, or A1c) test is used to evaluate a person's Level of glucose control.[1] Haemoglobin. Type 2 diabetes can be inherited and is linked to family history and genetics. HbA1c value is proven to be predictive of DM2, this could provide an easy screening tool for subjects who are potential candidates for lifestyle and/or pharmacological primary prevention of 1st degree relative of type 2 diabetes. This is a very convenient and practical (and perhaps cost-effective) approach as a screening tool for high-risk populations for diabetes. .. Early screening of first

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degree relative of type 2 dm patient will prevent development of Microvascular and Macrovascular complication.[2]

II. Materials And Methods

Study center and target population

The present study was carried out at Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, a tertiary care teaching hospital in central India.

Sample size and study design

The calculated sample size was 188. The study thereby incorporated 188 participants for further evaluation and analysis. This was a single-centric cross-sectional study.

Aims and objectives Primary Objective

To determine HbA1c in first degree relatives of patients of type 2 diabetes mellitus more than 14 year of age

Secondary Objective To determine the clinical and laboratory parameter in first degree relatives of type 2 diabetes mellitus patients. And To determine target organ damage in first degree relatives of patients of type 2 diabetes mellitus.

Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Non diabetic first degree relative of Type 2 DM patients	Relative with Known case of Diabetes mellitus
Person >14 year of age	Person <14 year of age
Person with written consent	Haemoglobinopathy
	Anemia
	Reticulocytosis
	Transfusion
	Uremia

TABLE 1: Inclusion And Exculsion Criteria

Techniques

1st Degree relative of Type 2 DM patients were subjected to history taking and thorough general, head-to- toe, and systemic examination. Subsequently, 2 mL venous blood samples were collected and sent in ethylenediaminetetraacetic acid (EDTA) vials for complete blood count and HbA1c studies for each subject. Measurement of Lipid Profile, Renal function test, Fasting blood sugar, Urine Routine Microscopy. In Examination Fundus, Nerve Conduction Study, Electrocardiogram.

Ethical issues

This study was conducted after getting informed written consent from the patients in their local language. The study was approved by the Institutional Ethics Committee, Netaji Subhash Chandra Bose Medical College, Jabalpur, Madhya Pradesh, India.

Data analysis plan

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 28 software (IBM Corp., Armonk, NY). Descriptive analyses were used for variables in groups. The chi-square test, Student's t-test, and ANOVA test were applied for the determination of the relation between the variables. The Pearson correlation test was used to study the correlation between parametric variables. P- values < 0.05 were accepted as statistically significant.

III. Results

This study included 188 person who is 1st Degree relative of Type 2 diabetes mellitus patient. In which 110 is male and 78 is female. In these subject HbA1c were investigated and correlated with other metabolic parameter.

HbA1c	Population	Percent
<5.7%	78	41.5
5.7-6.4%	72	38.3
≥6.5%	38	20.2

TABLE 2: . HbA1c of 1st degree relative of Type 2 DM patient

HbA1c	MALE (n=110)	FEMALE (n=78)
<5.7%	47(42.7%)	31(39.7%)
5.7-6.4%	47(42.7%)	25(32%)
>=6.5%	16(14.5%)	22(28.2%)

TABLE 3: Sex wise Distribution of HbA1c in 1st degree relative of Type 2 DM patient

MEAN +/-SD	<5.7%	5.7-6.4%	≥6.5%	P value
AGE(Year)	31.3 ± 3.8	30.1 ± 3.1	31.1 ± 3.5	0.11
BMI(kg/m ²)	21.3 ± 0.4	22.3 ± 0.7	23.9 ± 0.4	0.00
Waist circumference(cm)	90.5 ± 5.5	96.2 ± 6.6	101.6 ± 5.8	0.00
SBP(mm/hg)	101.0 ± 3.0	116.9 ± 6.8	137.7 ± 3.9	0.00
DBP(mm/hg)	70.0 ± 0.0	78.7 ± 6.2	88.9 ± 5.2	0.00

TABLE 4: .Distribution of HbA1c in Study population in Clinical Parameter

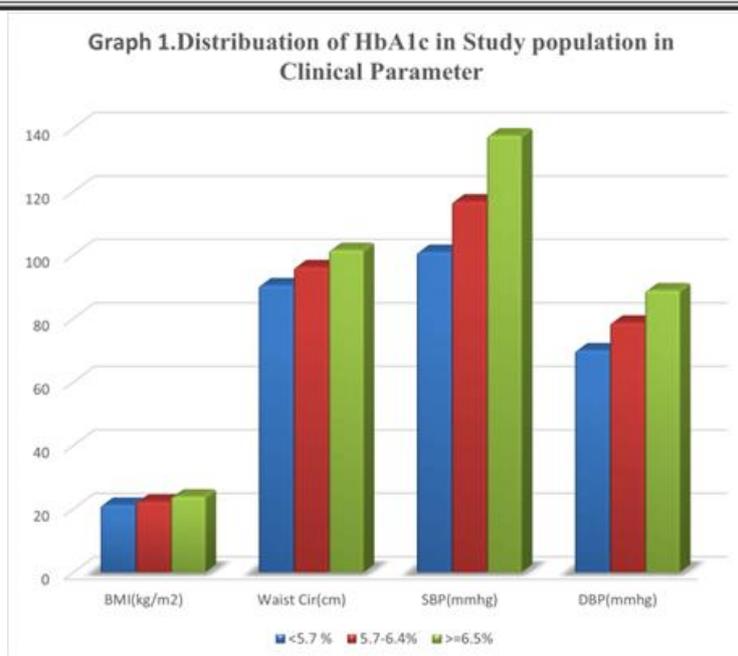


FIGURE 1: Distribution of HbA1c in Study population in Clinical Parameter

MEAN +/-SD	<5.7%	5.7-6.4%	≥6.5%	P value
FBS (mg/dl)	90.8 ± 4.7	111.3 ± 6.4	137.1 ± 5.4	0.00
Serum Cholestrol (mg/dl)	151.7 ± 15.3	187.6 ± 9.8	220.3 ± 6.0	0.00
Serum Triglyceride (mg/dl)	122.9 ± 7.5	143.9 ± 6.8	172.7 ± 8.2	0.00
HDL(mg/dl)	54.0 ± 3.6	46.6 ± 5.0	40.2 ± 5.1	0.00
LDL-C (mg/dl)	104.8 ± 10.2	129.0 ± 8.9	139.6 ± 5.8	0.00

TABLE 5: Distribution of HbA1c in Study population in Metabolic Parameter

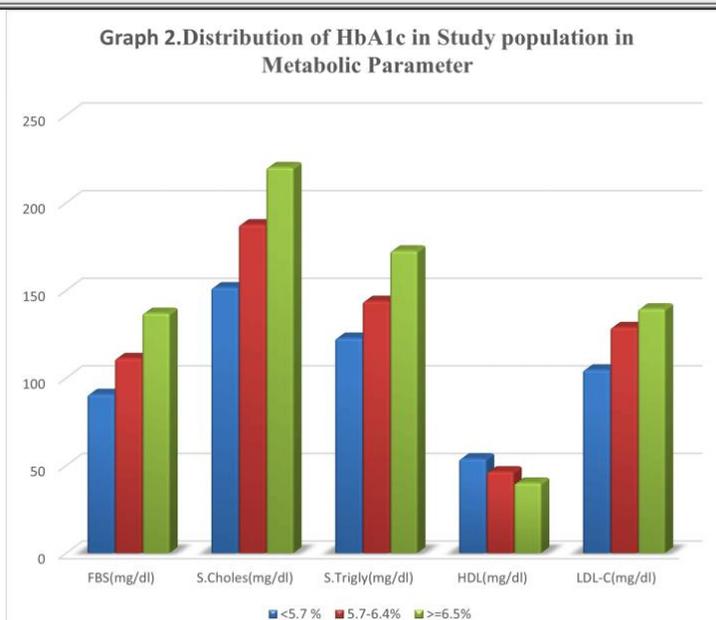


FIGURE 2: Distribution of HbA1c in Study population in Metabolic Parameter

HbA1c	MEAN	SD	P value
<5.7%	17.5	1.0	0.003
5.7-6.4%	17.8	1.5	
>=6.5%	18.8	3.6	

TABLE 6: Blood urea (mg/dl)of study population in relation to HbA1c

HbA1c	MEAN	SD	P value
<5.7%	0.89	0.70	0.53
5.7-6.4%	0.80	0.09	
>=6.5%	0.84	0.07	

TABLE 7: Serum creatinine(mg/dl) of study population in relation to HbA1c

HbA1c	
<5.7%	Nil
5.7-6.4%	Nil
>=6.5%	Nil

TABLE 8: Urine routine microscopy of study population in relation to HbA1c

HbA1c	Fundus
<5.7%	Normal
5.7-6.4%	Normal
>=6.5%	Normal

TABLE 9: Fundus of study population in relation to HbA1c

HbA1c	NCS
<5.7%	Normal
5.7-6.4%	Normal
>=6.5%	Normal

TABLE 10: Nerve Conduction study(NCS) of study population in relation to HbA1c

HbA1c	ECG
<5.7%	Normal
5.7-6.4%	Normal
>=6.5%	Normal

TABLE 11: Electrocardiogram (ECG)of study population in relation to HbA1c

IV. Discussion

In our study of 188 1st degree relative of type 2 DM patient, we divided HbA1c in to three group. Out of 188, 110 is Male while 78 are female. Out of 188 people HbA1c of 78(41.5%) comes below 5.7%, 72(38.3%) in pre- diabetic range (5.7-6.4%) and 38(20.2%) in diabetic range ($\geq 6.5\%$). Other studies also reported similar result done by Dr.S.M.Mahamudul Hassan Rizvi[3] in 2022 found that 46 % of first degree relative of Diabetes patients have diabetes in family. The finding in our study is also consistent with those described by Hong Ma [4] in 2011 found that 26.6 % 1st degree relative are diabetic ($\geq 6.5\%$) and 15% in pre diabetic range (5.7- 6.4%).

Out of 188 patients, 110 patient were male HbA1c of 47(42.7%) comes below 5.7%, 47(42.7%) in pre-diabetic range and 16(14.5%) in diabetic range. While in female HbA1c of 31(39.7%) comes below 5.7%, 25(32%) in pre-diabetic range and 22(28.2%) in diabetic range. The finding in our study is not consistent with those described by Yuan Gong[4] in 2011 found that 28.5% of male and 25.5 % female have HbA1c of diabetic range while 13.7 % male and 15.9% female have HbA1c in pre-diabetic range which were first degree relative of type 2 DM patients. The finding in our study is consistent with study done by Benja Muktabhant[5] in 2014 reported

among the newly diagnosed Type 2 DM 60 % has 1st degree relative, predominantly as their mother. Gender has conflicting data regarding 1st degree relative of Diabetes mellitus patient .This suggestive of 1st degree relative who has family history of Type 2 DM has higher chance of being prediabetic and diabetic in future.

Further We correlated these group of HbA1c with anthropometric and metabolic parameter. In anthropometric parameter we examined Body weight (in kg), Height (in meter), BMI(in kg/m²), Waist circumference(cm), Blood pressure(mm/hg)

Body mass index (BMI) in study population shows mean of BMI is 21.3(kg/m²) in relative whose HbA1c in normal range ,in prediabetic range BMI is 22.3,in diabetic range BMI is 23.9. P value of BMI were found to be significant.The finding in our study is also consistent with those described by Susana Siewert[6]2017 that BMI higher in 1st degree relative of Type 2 DM patients. Similar result shown by Fahd Ahmed[7]2021 reported mean of BMI in 1st degree relative of Type 2 DM is 22.9kg/m². our finding are also consistent with Sadeghi E[8]2020 reported that mean of BMI in 1st degree relative of Type 2 DM is 28.8 kg/ m². The finding in our study is also consistent with those described by Dr.S.M.Mahamudul Hassan Rizvi[3] in 2022 reported that mean of BMI in 1st degree relative of Type 2 DM patient is 24 kg/ m².This shows that BMI in 1st degree relative of Type 2 DM patient whose HbA1c in prediabetic and diabetic range have higher value.

In Waist circumference(cm) mean is 90.5 cm in relative whose HbA1c in normal range ,in prediabetic range 96.2cm,in diabetic range 101.6cm. The finding in our study is also consistent with those described by Fahd Ahmed[7]2021 reported mean of Waist circumference in 1st degree relative of Type 2 DM patients is higher.similar result shown by Irma Gonzalez[6]that mean of Waist circumference in 1st degree relative Type 2 DM is 89.4 cm. In male population Waist circumference(cm) mean is 94.4 cm in relative whose HbA1c in normal range ,in prediabetic range 100.5cm,in diabetic range 107.4cm .while in Female population Waist circumference(cm) mean is 84.8 cm in relative whose HbA1c in normal range ,in prediabetic range 88.1cm,in diabetic range 97.3cm.. Similar result were found by Susana Siewert[6]2007 that in male mean of Waist circumference in 1st degree relative Type 2 DM is 104.4 cm while female has mean of Waist circumference 91.7 cm. This is suggestive of that 1st degree relative of type 2 DM in diabetic range has high value of Waist circumference.

In Systolic blood pressure(mmhg) shows mean of BMI is 101mmhg in relative whose HbA1c in normal range, in prediabetic range it is 116.9mmhg, in diabetic range 137.7mmhg. while Diastolic blood pressure mean is 70mmhg in relative whose HbA1c in normal range ,in prediabetic range it is 78.7mmhg,in diabetic range 88.9mmhg. The finding in our study is also consistent with those described by Dr.S.M.Mahamudul Hassan Rizvi³ in 2022 reported that 18 % study subject who had history of diabetes in family have SBP of >130mm hg while 8% have DBP >90 mmhg.similar result shown by Fahd Ahmed [7] 2021 that 1st degree relative of Type 2 DM have mean of SBP 117 mmhg while DBP is 77mmhg.1st degree relative who has high HbA1c has higher Systolic and Diastolic Blood pressure in comparison to those who have low HbA1c.These patient have higher tendency to develop Metabolic syndrome related complication in future.

The finding in our study is also consistent with those described by Susana Siewert[6],2007 that 1st degree relative of Type 2 DM have mean of SBP 123.6 mmhg while DBP is 81 mmhg.This shows that SBP and DBP in prediabetic and diabetic 1st degree relative of Type 2 DM patients has higher values. So In 41.5 % relative whose HbA1c in normal range has BMI and Waist circumference ,Systolic blood pressure, Diastolic blood pressure comes under normal range.In 38.3 % relative whose HbA1c is in prediabetic range has shows increment in these anthropometric parameter.In 20.2 % relative whose HbA1c is in Diabetic range has shows significant worsening of anthropometric parameter like Waist circumference more than 88cm in female while 102cm in Male and Blood pressure of more than 130/85 mmhg in both sex.

In Metabolic parameter we measured Fasting serum glucose(mg/dl), Serum cholesterol(mg/dl), Serum Triglyceride (mg/dl),High density lipoprotein (HDL),Low density lipid (LDL-C). These parameter like BMI,SBP,DBP were found to be significant with P value <0.05.

Fasting blood sugar(mg/dl) in study population shows mean of FBS is 90.8 mg/dl in relative whose HbA1c in normal range ,in prediabetic range FBS is 111.3 mg/dl,in diabetic range FBS is 137.1 mg/dl. The finding in our study is also consistent with those described by Fahd[7]2021 reported Mean of FBS in 1st degree relative of Type 2 DM patient is 91.8 mg/dl.while person with no family history of diabetes has Mean of FBS 88.2 mg/dl.similar result reported by Sergio Filipuzzi[6]2007 that high FBS in 1st degree relative of Type 2 DM patient .

Serum Cholesterol (mg/dl) in study population shows mean is 151.7 mg/dl in relative whose HbA1c in normal range ,in prediabetic range is 187.6 mg/dl,in diabetic range is 220.3 mg/dl. our

finding are also consistent with Sadeghi E[8]2020 reported that mean of Serum Cholesterol in 1st degree relative of Type 2 DM is 195.1 mg/dl. Serum Triglyceride (mg/dl) in study population shows mean is 122.9 mg/dl in relative whose HbA1c in normal range in prediabetic range is 143.9 mg/dl, in diabetic range is 172.7 mg/dl. similar result reported by Susana Siewert[6]2007 that Mean of Serum Triglyceride in 1st degree relative of Type 2 DM patient is 147.1mg/dl. our finding are also consistent with Sadeghi E[8] 2020 reported that mean of Serum Cholesterol in 1st degree relative of Type 2 DM is 159 mg/dl.. So patients with higher HbA1c have more likelihood of developing dyslipidemia.

High density lipoprotein (HDL) (mg/dl) in study population shows mean is 54 mg/dl in relative whose HbA1c in normal range ,in prediabetic range HDL is 46.6 mg/dl,in diabetic range is HDL 40.2 mg/dl. similar result reported by Susana Siewert[6]2007 that Mean of High density lipoprotein (HDL) in 1st degree relative of Type 2 DM patient is 45.4mg/dl. In male population High density lipoprotein (HDL) (mg/dl) mean is 52.8 mg/dl in relative whose HbA1c in normal range ,in prediabetic range HDL is 43.4 mg/dl,in diabetic range HDL is 37 mg/dl. our finding are also consistent with Hosseini[8] 2020 reported that mean of High density lipoprotein (HDL) in male population who are 1st degree relative of Type 2 DM is 45.3 mg/dl. while in Female population mean of HDL is 55.7 mg/dl in relative whose HbA1c in normal range ,in prediabetic range HDL is 52.5 mg/dl,in diabetic range HDL is 42.6 mg/dl. similar result reported by, Irma Gonzalez⁶ 2007 that Mean of High density lipoprotein (HDL)) in female population who are 1st degree relative of Type 2 DM is 41.4 mg/dl, while in male population Mean of High density lipoprotein (HDL) is 37.8mg/dl.

Low density lipoprotein (LDL-C) (mg/dl) in study population shows mean is 104.8 mg/dl in relative whose HbA1c in normal range,in prediabetic range (LDL-C) is 129 mg/dl,in diabetic range is (LDL-C) 139.6 mg/dl. our finding are also consistent with Vossoughi[8]2020 reported that mean of Low density lipoprotein (LDL- C) in 1st degree relative of Type 2 DM patients is 123.7 mg/dl.This suggestive of Dyslipidemia in 1st degree relative of Type 2 DM patient who are having HbA1c in prediabetic and Diabetic range that can lead complication in future.Metabolic parameter in our study were found to be significant. In 41.5 % relative whose HbA1c in normal range has mean of Fasting serum glucose, other Lipid parameter comes under normal range .In 38.3 % relative whose HbA1c in prediabetic range and also shows high serum triglyceride ,Cholesterol ,LDL-C and low HDL level Suggestive of altered lipid profile in these subject.In 20.2% relative whose HbA1c is in Diabetic range has shows Serum Triglyceride more than 150 mg/dl in both Male and female.Fasting blood sugar more than 100 mg/dl in both sex and HDL less than 40 in male and less than 50 in female.

To see complication of type 2 Diabetes we measured Blood urea(mg/dl),Serum creatinine(mg/dl),Urine routine microscopy, Fundus, Nerve conduction study (NCS), Electrocardiogram (ECG). Blood urea (mg/dl) in study population shows mean is 17.5 mg/dl in relative whose HbA1c in normal range ,in prediabetic range is 17.8 mg/dl,in diabetic range is 18.8mg/dl. Serum creatinine (mg/dl) in study population shows mean is 0.89 mg/dl in relative whose HbA1c in normal range ,in prediabetic range is 0.80 mg/dl,in diabetic range is 0.84 mg/dl. Urine routine microscopy in study population shows absence of glucose and protein in relative whose HbA1c in normal range ,in prediabetic range and diabetic range. Fundus examination in study population shows no changes of diabetic retinopathy in relative whose HbA1c in normal range,in prediabetic range and diabetic range. Nerve conduction study in study population shows no changes of diabetic neuropathy in relative whose HbA1c in normal range,in prediabetic range and diabetic range. Electrocardiogram in study population is within normal limit in relative whose HbA1c in normal range,in prediabetic range and diabetic range.similar study done by Dicky L Thapary[9]2023 .P value was not found to be significant for long term complication in 1st degree relative of type 2 DM patients.

Limitation Of The Study

The period of study conducted was of a finite duration, restricting the number of subject included in the study .in addition , as the study population was restricted to patients presenting to a tertiary healthcare center,the finding may not be suitably applicable or generalized to the whole population.

V. Conclusions

The present study demonstrated type 2 DM linked with family history and 1st degree relative of type 2 DM patient has high chance of development of diabetes in future.HbA1c is

correlated with metabolic syndrome and could be considered as a marker or surrogate of metabolic syndrome in non diabetic ,first degree relative of type 2 diabetes patient. Measuring HbA1c in 1st degree relative of type 2 DM patient serve as surrogate of metabolic syndrome and other micro and macrovascular complication of diabetes. This is very convenient and practical approach as screening tool for non diabetic 1st degree relative of type 2 diabetes patient.

Family history of diabetes and raised HbA1c in 1st degree relative shows an irreversible risk factor for 1st degree relative of diabetes. Early identification of person at high risk of developing DM and metabolic syndrome can be useful in preventing the onset of development of disease and its complication,by primary prevention measures in form of life style modification as doing physical exercise, dietary modification, weight control measures. This study will be helpful in curtailing the incidence of Diabetes burden in the community or delaying the onset of disease and its complication and this will reduce the disease burden in the community.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. NETAJI SUBHASH CHANDRA BOSE MEDICAL COLLEGE AND HOSPITAL issued approval IEC/2022/8629-17. Institutional Ethics Committee approved your following thesis.

Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue.

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work.

Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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