ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 03 | March - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

STUDY OF SENSITIVITY AND SPECIFICITY OF DIFFERENT INVESTIGATION PROFILES IN THE DIAGNOSIS OF DIABETES MELLITUS.

General Medicine

Dr. Abhaysingh Uttam Bhosale MBBS, DNB Medicine, Assistant Professor, Department of Medicine, Government Medical College and Hospital, Miraj.

Dr. Amruta Anandrao Khade MBBS, MD IHBT, Assistant Professor, Blood Bank, Government Medical College and Hospital, Miraj.

Dr. Shraddha Badrinath Chavan MBBS, MD Pathology, Senior Resident, Department of Pathology, Government Medical College and Hospital, Miraj.

ABSTRACT

Introduction- The term diabetes mellitus describes a metabolic disorder with heterogeneous etiologies which is characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both.1. Diabetes is a condition primarily defined by the level of hyperglycemia, which leads to microvascular damage causing significant morbidity, reduced life expectancy and increased macrovascular complications leading to diminished quality of life.6 Thus, early diagnosis of diabetes is very important to prevent diabetes related morbidity, mortality and improve the quality of life.

Aims-

1. To assess sensitivity and specificity of diagnostic cut point of glycated hemoglobin which is 6.5%, in comparison with fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/ liter) and /or two hour plasma glucose ≥ 200 mg/dl (11.1 mmol / liter) after 75 gm oral glucose tolerance test.
2. To find out cut point of optimal sensitivity and specificity of glycated hemoglobin in comparison with fasting and / or 2 hour plasma glucose after an 75 gm oral glucose tolerance test.

Material & Methods- Total 220 subjects were selected to participate in this study conducted over a period of two year from June 2012 to may 2014. Patients coming for executive health check up, diabetic OPD, general OPD and indoor wards were included in this study with their informed consent. This study was conducted in Tata Main Hospital, Jamshedpur, Jharkhand which is 940 bedded multidisciplinary hospital. **Results-** Out of total 203 study subjects, 102 individuals (50.2%) were diabetic, 22 individuals (10.8%) were having IGT, 18 individuals (8.9%) were having IFG, 7 individuals (3.4%) were having both IGT and IFG and 54 individuals (26.6%) were having NFG and NGT. Out of total 102 diabetic individuals, 4 were diabetic by FPG (3.92%), 40 were diabetic by 2 hr OGTT (39.21%) and 58 were diabetic by both FPG and 2 hr OGTT (56.87%). 78 individuals were having HbA1c ≥ 6.5% hence diabetic according to HbA1c criteria. Sensitivity, specificity, PPV and NPV of HbA1c cut off ≥ 6.5% against FPG and/ or 2 hr OGTT criteria to diagnose diabetes was 62.75%, 86.14%, 82.05%, 69.6% respectively. There is moderate agreement between HbA1c and FPG and / or 2 hr OGTT criteria to diagnose diabetes. (kappa index- 0.489) **Conclusion-** The present study shows that HbA1c at cut off 6.5% has reasonably good specificity for diagnosis of diabetes and is in concordance with ADA recommendations. HbA1c cut off point 6.05% has optimal sensitivity and specificity to be considered as screening test.

KEYWORDS

Diabetes mellitus, HbA1c, hyperglycemia, OGTT, FPG.

INTRODUCTION -

The term diabetes mellitus describes a metabolic disorder with heterogeneous etiologies which is characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both.[1]. The long term relatively specific effects of diabetes include development of retinopathy, nephropathy and neuropathy.[2] People with diabetes are also at increased risk of cardiac, peripheral arterial and cerebrovascular disease.[3]

Diabetes and lesser forms of glucose intolerance and impaired glucose tolerance(IGT) and impaired fasting glucose(IFG) can now be found in almost every population in the world and epidemiological evidence suggests that without effective prevention and control programs, the burden of diabetes is bound to continue to increase globally.[4,5]

Diabetes is a condition primarily defined by the level of hyperglycemia, which leads to microvascular damage causing significant morbidity, reduced life expectancy and increased macrovascular complications leading to diminished quality of life.[6] Thus, early diagnosis of diabetes is very important to prevent diabetes related morbidity, mortality and improve the quality of life.

According to recently published report in 2009, the International Expert Committee recommends that, diagnosis of diabetes can be made if HbA1c level is 6.5% or more. Revised ADA 2010 criteria for diagnosis of diabetes also include HbA1c, which is:

1. Symptoms of diabetes plus random blood glucose ≥ 200 mg/dl (11.1 mmol/l).
2. FPG ≥ 126 mg/dl (7 mmol/l)
3. HbA1c ≥ 6.5%
4. 2 hr plasma glucose ≥ 200 mg/dl (11.1 mmol/l) after 75 gram OGTT

Thus HbA1c has emerged as a new diagnostic tool.

The present study is to study and observe the accuracy of HbA1c to diagnose type 2 diabetes in Indian population taking FPG only, 2hr plasma glucose after 75 gm oral glucose tolerance test(OGTT) only and FPG and / or 2 hr OGTT as reference tests and to find out optimal HbA1c cut off point at which it can be used as screening and diagnostic test in Indian population.

AIMS & OBJECTIVES -

1. To assess sensitivity and specificity of diagnostic cut point of glycated hemoglobin which is 6.5%, in comparison with fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/ liter) and /or two hour plasma glucose ≥ 200 mg/dl (11.1 mmol / liter) after 75 gm oral glucose tolerance test, taking as reference standard, for diagnosis of type 2 diabetes in individuals of Jamshedpur.
2. To find out cut point of optimal sensitivity and specificity of glycated hemoglobin in comparison with fasting and / or 2 hour plasma glucose after an 75 gm oral glucose tolerance test, in diagnosing type 2 diabetes in individuals of Jamshedpur.

MATERIAL & METHODS -

Study Design & Setting -

This was hospital based prospective study. Patients coming for executive health check up, diabetic OPD, general OPD and indoor wards were included in this study with their informed consent. This study was conducted in Tata Main Hospital, Jamshedpur, Jharkhand which is 940 bedded multidisciplinary hospital.

Period Of Study-

The study was conducted over a period of two year from June 2012 to may 2014.

Sample Size-

Total 220 subjects were selected to participate in this study out of which 14 subjects were subsequently lost to follow up and 3 subjects were unable to complete the OGTT as they could not tolerate the procedure and they were not included in study (sample size of 220 selected depending upon such study previously undertaken, reference no. 98 the prevalence of diabetes in that study was 58.9%). So total 203 subjects were included in this study.

Inclusion Criteria -

All patients coming to executive health check up, general OPD, diabetic OPD and indoor patients were screened and those who satisfy following criteria were included in study group.

1. Patients showing symptoms suggestive of diabetes i.e. increased thirst, increased urination, unexplained weight loss, increased hunger, ulcers that do not heal fatigue.
2. Asymptomatic individuals who were at high risk of developing diabetes (these category of patients underwent at least one time previous routine health check up) i.e.

- FPG ≥ 100 mg/dl(5.6mmol/l).
- 2 hr OGTT 140 mg/dl (7.8 mmol/l) or more
- HbA1c in the range 5.7-6.4%.

Exclusion Criteria –

1. Pregnant females.
2. Type I diabetes mellitus.
3. Vitamin B12 and iron deficiency anemia.
4. Hemoglobinopathies.
5. Chronic kidney disease
6. Alcoholism and chronic liver disease
7. Patients taking certain drugs like steroids, antiretroviral drugs, dapsone etc.
8. Hypertriglyceridemia.

Investigations-

1. Fasting and 2 hour post load glucose after 75 gm oral glucose tolerance test.
2. HbA1c.
3. Renal function test.
4. Hemoglobin count.

RESULTS -

Table 1 - Age Distribution Of Study Subjects

Age (years)	No. of subjects	Percent
30-45	51	25.1
46-60	77	37.9
61-75	56	27.6
76-90	19	9.4
Total	203	100.0

From above table it is seen that maximum number of subjects were in 46-60 years age group (37.9% of total study population) followed by 61-75 years age group (27.6% of total study population) and minimum number of subjects were in 76-90 years age group (9.4%). 25.1% study population was in 30-45 years age group.

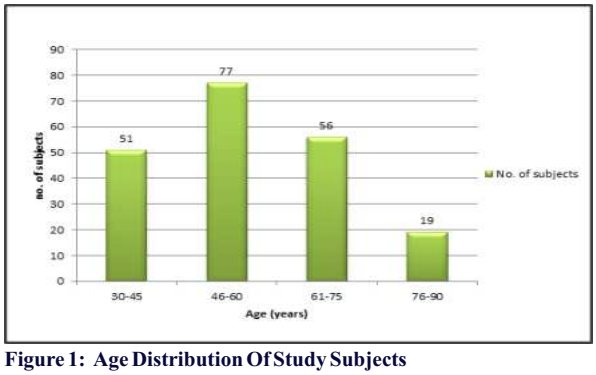

Figure 1: Age Distribution Of Study Subjects

Table 2 - Gender Distribution Of Study Subjects

Sex	No. of subjects	Percent
Male	109	53.7
Female	94	46.3
Total	203	100.0

In present study 109 subjects were males (53.7%) and 94 subjects were females (46.3%).

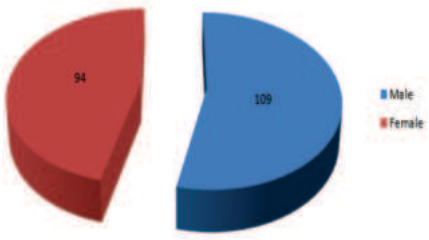

Figure 2: Gender Distribution Of Study Subjects

Table 3 - Distribution Of Study Subjects According To Diagnosis

Diagnosis	No. of subjects	Percent
Diabetic	102	50.2
IGT	22	10.8
IFG	18	8.9
IGT & IFG	7	3.4
NGT & NFG	54	26.6
Total	203	100.0

Out of total 203 study subjects, 102 individuals (50.2%) were diabetic, 22 individuals (10.8%) had impaired glucose tolerance, 18 individuals (8.9%) had impaired fasting glucose, 7 individuals (3.4%) had both impaired fasting glucose and impaired glucose tolerance and 54 individuals (26.6%) had normal glucose tolerance and normal fasting glucose.

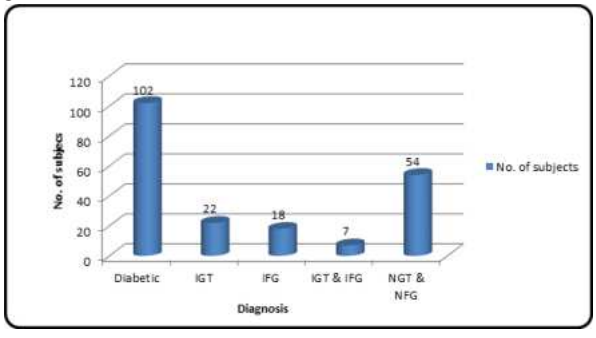

Figure 3: Diagnosis Of Study Subjects

Table 4-Distribution Of Diabetic Subjects According To Diagnostic Test

Diagnostic Test	No. of diabetic individuals	Percent
FPG (≥126 mg/dl)	4	3.92
2 hr OGTT (≥ 200 mg/dl)	40	39.21
Both FPG and 2 hr OGTT	58	56.87
Total	102	100

Out of total 102 diabetic individuals, 4 were (3.92%) diabetic by FPG, 40 were (39.21%) diabetic by 2 hr OGTT and 58 individuals (56.87%) were diabetic by both FPG and 2 hr OGTT.

Distribution Of Study Subjects According To Diagnostic Cut Off Values Of Fpg, 2hr Ogtt And Hba1c

Table 5 - Distribution Of Study Subjects According To Fpg

FPG (mg/dl)	No. of subjects	Percent
< 126	141	69.5
≥ 126	62	30.5
Total	203	100.0

Total 62 individuals had FPG ≥ 126 mg/dl and hence diabetic by FPG test and total 141 subjects had FPG < 126 mg/dl and hence nondiabetic by FPG test.

Table 6 - Distribution Of Study Subjects According To 2 Hr Ogtt

2 hr OGTT (mg/dl)	No. of subjects	Percent
< 200	105	51.7
≥ 200	98	48.3
Total	203	100.0

98 subjects (48.3%) had 2 hr OGTT ≥ 200 mg/dl, hence diabetic according to 2 hr OGTT and 105 subjects (51.7%) had 2 hr OGTT < 200 mg/dl, hence nondiabetic according to 2 hr OGTT.

Table 7 - Distribution Of Study Subjects According To Hba1c

HbA1c (%)	No. of subjects	Percent
< 6.5	125	61.6
≥ 6.5	78	38.4
Total	203	100.0

78 individuals (38.4%) had HbA1c ≥ 6.5% so diabetic according to HbA1c and 125 (61.6%) subjects having HbA1c < 6.5% so nondiabetic according to HbA1c criteria.

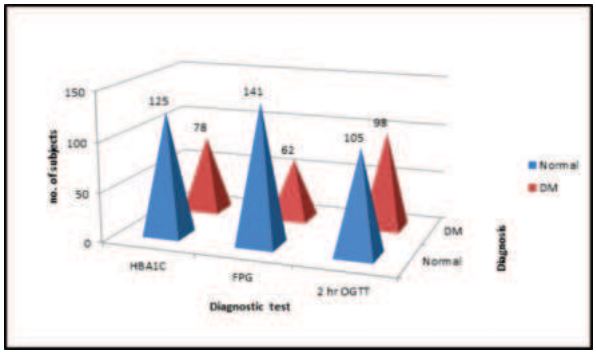

Figure 4: Number Of Diabetic Subjects According To Test

Table 8- Evaluation Of Hba1c At Cut Off Point ≥ 6.5% In Diagnosing Diabetes In Comparision With Fpg And/ Or 2hr Ogtt

HBA1C (%)	No. of diabetic subjects (FPG ≥126mg/dl and/ or 2hr OGTT ≥ 200 mg/dl)	No. of nondiabetic subjects (FPG<126 mg/dl and 2 hr OGTT <200 mg/dl)	Total
≥6.5	64	14	78
<6.5	38	87	125
Total	102	101	203

Performance of HbA1C at cut off point ≥ 6.5% is evaluated in comparison with FPG (≥ 126 mg/dl) and / or 2 hr OGTT (≥ 200 mg/dl) and results are as below:
Sensitivity= 62.75%
Specificity= 86.14%
Positive predictive value = 82.05%
Negative predictive value = 69.6%
From above table kappa coefficient was calculated which was 0.489 and p value was <0.001.

This suggests moderate agreement between HbA1C cut off value of ≥ 6.5% and WHO 1999 / ADA 1997 criteria to diagnose diabetes (i.e. FPG≥126 mg/dl and / or 2 hr OGTT ≥200 mg/dl).

DISCUSSION -

The present study which was conducted in tertiary care hospital was sincere effort toward evaluating diagnostic usefulness of HbA1C in diagnosing new onset diabetes in comparison with WHO 1999 and ADA 1997 criteria. Total 203 subjects were included in this study which was carried out over period of June 2012 to May 2014. In present study 53.7% were males and 46.3% were females and mean age of study population was 56.66 ± 12.73 years.

The prevalence of newly diagnosed diabetes in the present study was 50.2%. The prevalence of newly diagnosed diabetes in the study carried out by Kim et al [8] was 58.9%. In the study carried out by Yun et al [9] the prevalence of newly diagnosed diabetes was 31.2%. The prevalence of newly diagnosed diabetes in a study carried out by Cavagnolli et al [7] was 23.1%.

In the present study prevalence of newly diagnosed diabetes was high because high risk subjects satisfying inclusion criteria were recruited in study after screening general population from OPD and indoor wards. Similar pattern of diabetes prevalence was observed in studies carried out by Kim et al, [8] Yun et al [9] as their studies also included high risk individuals having FPG ≥ 100 mg/dl. Cavagnolli et al [7] also included high risk subjects in their study which gave high prevalence of diabetes in their study.

In present study 26.6% study subjects had NFG and NGT. In the study carried out by Kim et al [98] 7.1% subjects had NFG and NGT. In the study carried out by Yun et al [9] 22.5% subjects had NFG and NGT. In the study carried out by Cavagnolli et al [7] 24.5% subjects had NFG and NGT.

In present study sensitivity and specificity of HbA1c at cut off 6.5% was 62.75% and 86.14% respectively when FPG and/ or 2 hr OGTT taken as reference standard while positive predictive value (PPV) and negative predictive value (NPV) was 82.05% and 69.6% respectively.

The sensitivity and specificity of HbA1c cut off 6.5% was 73.5% and 89.1%, respectively in the study carried out by Kim et al [8] where they have established diagnosis of diabetes by FPG or 2 hr OGTT criteria.

Sensitivity and specificity of HbA1c cut off 6.5% was 62.7% and 93.5% respectively in the study carried out by Yun et al [9] where they have taken FPG and/ or 2 hr OGTT as reference criteria for establishing diabetes.

The sensitivity and specificity of the HbA1c cut-off value of 6.5% in the study carried out by Cavagnolli et al [7] was 20.9% and 95.3%, respectively, compared with the fasting plasma glucose and / or 2-hr OGTT plasma glucose criteria to establish diagnosis of diabetes. The NPV was 80.5%.

In the study carried out by Cavagnolli et al [7] at cut off level of 7.0% and 8.0% specificities of HbA1C in comparison with FPG only were 99.5% and 99.8% respectively, While in present study specificities of HbA1C at cut off level 7.05% and 8.05% in comparison with FPG only were 91.5% and 97.9% respectively.

An international expert committee report on HbA1c as a diagnostic test chose 6.5% as the cutoff for diagnosis of diabetes based on the study results of The Evaluation of Screening and Early Detection Strategies for Type 2 Diabetes and Impaired Glucose Tolerance (DETECT-2), which is based on moderate retinopathy. Although the ADA 2010 guideline recommends HbA1c level of 6.5% for diagnosis of diabetes, it did not specify its sensitivity and specificity.

The present study showed a specificity of 86.14% at HbA1c cutoff level of 6.5% for diagnosing diabetes and is in concordance with ADA recommendations.

As Indian population is highly heterogeneous community, in order to draw a consensus on optimal HbA1c cut off for screening and diagnosing diabetes and to describe normative distribution of HbA1c in Indian population, there is a need for larger population-based study comprised of composite population groups from different regions of the country. This approach will provide great scope to understand the determinants of HbA1c responsible for inter-individual glycation of hemoglobin and thereby, the different observed relationships between HbA1c and glycaemia.

CONCLUSION –

The present study shows that HbA1c at cut off 6.5% has reasonably good specificity for diagnosis of diabetes and is in concordance with ADA recommendations. HbA1c cut off point 6.05% has optimal sensitivity and specificity to be considered as screening test.

REFERENCES –

1. World Health Organization. *Definition, Diagnosis and classification of Diabetes Mellitus and its complications. Part 1: Diagnosis and Classification of Diabetes Mellitus.* WHO/ NCD/ NCS/ 99.2 ed.Geneva, World Health Organization, 1999.
2. Hanssen KF, Bangstad HJ, Brinchmann-Hansen O et al. Blood glucose control and diabetic microvascular complications: long term effects of near normoglycaemia. *Diabet med*, 1992, 9:697-705.
3. Fox CS, Coady S, Sorlie PD et al. Increasing cardiovascular disease burden due to diabetes mellitus: the Framingham Heart Study. *Circulation*, 2007, 115:1544-1550.
4. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. *Nature*, 2001, 414:782-787.
5. Alberti KG, Zimmet p, Shaw J. International Diabetes Federation: a consensus on Type 2 diabetes prevention. *Diabet Med*, 2007, 24:451-463.
6. *Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia*. Geneva, World Health Organization, 2006.
7. G. Cavagnolli, J. Comerlato, C. Comerlato, P. B. Renz et al. HbA1c measurement for the diagnosis of diabetes: is it enough?, *diebet med*, 2011, 28(1):31-35.
8. Kim HJ, Choi EY, Park EW, Cheong YS, Lee HY. The Utility of HbA1c as a Diagnostic Criterion of Diabetes. *Korean J Fam Med* 2011;32:383-9.
9. Yun yu, Xiao-Jun Ouyang, Qing-Lin Lou, Liu-Bao Gu et al. Validity of Glycated Hemoglobin in Screening and Diagnosing Type 2 Diabetes Mellitus in Chinese Subjects. *Korean J Intern Med.* 2012, 27(1): 41–46.
10. American Association of Clinical Endocrinologists Board of Directors, American College of Endocrinologist Board of Trustees. American Association of Clinical

Endocrinologists/American College of Endocrinology statement on the use of hemoglobin A1c for the diagnosis of diabetes. *Endocr Pract*. 2010, 16:155-56.
11. Tanaka Y, Atsumi Y, Matsuoka K, Mokubo A et al. Usefulness of stable HbA1c for supportive marker to diagnose diabetes mellitus in Japanese subjects. *Diabetes Res Clin Pract*, 2001; 53: 41–45.
12. G. Cavagnolli, J. Comerlato, C. Comerlato, P. B. Renz et al. HbA1c measurement for the diagnosis of diabetes: is it enough?, *diebet med*, 2011, 28(1):31-35.
13. Bennett CM, Guo M, Dharmage SC. HbA1c as a screening tool for detection of Type 2 diabetes: a systematic review. *Diabet Med,* 2007, 24: 333–343.
14. Cohen RM (2009) A1c: does one size fit all? *Diabetes Care* 30: 2756–2758.
15. Young IS (2010) Counterpoint: The reporting of estimated glucose with haemoglobin A1c. *Clin Chem* 56: 547–549.
16. K. Venkataraman, S. L. Kao, A. C. Thai, A. Salim. Ethnicity modifies the relation between fasting plasma glucose and HbA1c in Indians, Malays and Chinese. *Diabetic Medicine*, July 2012; 29: 911–917.
17. CD Saudek, Rita R Kalyani, RL Derr. Assessment of glycemia in diabetes Mellitus: Hemoglobin A1c; *JAPI*. 2005;53 : 299-305.
18. Manisha Nair, Dorairaj Prabhakaran, K.M. Venkat Narayan, Rashmi Sinha, 2011.HbA1c Values for Defining Diabetes and Impaired Fasting Glucose in Asian Indian. *Prim Care Diabetes*,July 2011; 5(2): 95–102.
19. *Principles of diabetes mellitus* (2nd ed.) New York: Springer. p. 3. Editor Leonid Poretsky.
20. Himsworth (1936). "*Diabetes mellitus: its differentiation into insulin-sensitive and insulin-insensitive types.*"Lancet 227 (5864): 127–30.