A COMPARATIVE STUDY OF ORAL GLUCOSE TOLERANCE TEST AND GLYCATED HAEMOGLOBIN IN HIGH RISK PATIENTS FOR DIABETES MELLITUS

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Abstract

Aims: To ascertain which is a better screening test to diagnose diabetes mellitus, OGTT or HbA_{1c}. Method : 100 high risk patients for diabetes and 35 controls (none a known diabetic) were screened by OGTT and HbA_{1c}. 1980 WHO criteria for diagnosing diabetes and HbA_{1c} ³ 7% (cation exchange chromatography) were followed to categorise patients as diabetics. Results : 17% of the patients were hound to be diabetic by OGTT criteria and 49% by HbA_{1c} criteria. Sensitivity and specificity of OGTT and HbA_{1c} (³ 7%) were 24.5%, 90.2%, 89.5%, 56.6% respectively. Besides essential hypertension and obesity - coronary artery disease and central obesity have been found to be significantly associated with diabetes. Conclusion : HbA_{1c} is a more sensitive screening test than OGTT, but lacks specificity. OGTT is more specific. All high risk patient should be screened by HbA_{1c} and if HbA_{1c} is ³ 7%, they should undergo an OGTT to confirm the diagnosis.

KEY WORDS : Type 2 Diabetes Mellitus; HbA_{1c}; OGTT; High risk groups for diabetes mellitus; Essential hypertension; CAD; Obesity; Central obesity.

INTRODUTION

Diabetes mellitus will be the major non-communicable disease in this millennium. It is estimated that in the next decade, another 100 million diabetics will be added to the 100 million diabetics existing today [1]. Between 1995 and 2025 the number of adult diabetics in the developing countries is projected to grow by 170%. Further, 76% of the diabetics will be from the developing countries. India will have the greatest burden, with an increase of approximately 170% or more. Most of these diabetic individuals will be in the most productive years of their lives.

It is estimated that 50% of persons with diabetes in the United States are undiagnosed [2]. 25% of the newly diagnosed type 2 diabetes mellitus have diabetic retinopathy. One of the main reasons for this under diagnosis is the difficulty encountered in adhering to the guidelines for its diagnosis [2]. Currently diabetes is diagnosed by one of the tow criteria. (1980 WHO) 1. Fasting plasma glucose ³ 140 mg/dl (two occasions); 2. Following ingestion of > 75 g of glucose, venous plasma glucose ³ 200 mg/dl at 2 hour and on one other occasion during the 2 hour oral glucose tolerance test.

Recently, the American Diabetes Association (ADA) has proposed a simplified diagnostic criteria for diabetes (any one of the three criteria) [3].

1. A FPG (fasting plasma glucose) ³ 126 mg/dl, after no caloric intake for at least 8 hours; or

2. A casual plasma glucose (Taken at any time of day without regard to the time of last meal) ³ 200 mg/dl, combined with classic diabetes symptoms of increased urination, increased thirst and unexplained weight loss; or

3. OGTT value ≥ 200 mg/dl in the 2 hour sample. The ADA has not recommended the HbA_{1c} test for diagnosis [3].

In addition to the routine diabetes testing in all adults aged 45 years or older, and repeat testing every three years, the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [3] recommended earlier and/or more frequent testing for diabetes in individuals who 1) are obese (> 20% above their ideal body weight); 2) have a first degree relative with diabetes; 3) are member of a high risk ethnic group (African-American, Hispanic, Native America, Asian); 4) deliver a baby weighing more than 9 lb. or have been previously diagnosed with gestational diabetes mellitus; 5) are hypertensive, blood pressure ³ 140/90 mmHg; 6) have a high density lipoprotein cholesterol level £ 35mg/dl and / or a triglyceride level ³ 250 mg/dl; 7) or on previous testing and impaired fasting glucose or impaired glucose tolerance [3].

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The OGTT is the 'gold standard' for the diagnosis of diabetes mellitus. It is an useful epidemiological tool and has been used to determine the prevalence of diabetes in different cultures and communities. However, on an individual basis, for both the clinician and the patient, the test has drawbacks. The patients must fast and then undergo a non-physiological stress and wait for 2 hours before the test is over. This is far from ideal. On the other hand it is poorly reproducible [4]. Although ADA has recently recommended that two abnormal OGTT's are required to diagnose diabetes, such an approach can be labour intensive and inconvenient for the patients. Naturally a simple, one-off diagnostic test, has always been the goal.

A meta-analysis by Peters et al [2] suggested that a single measurement of glycated hemoglobin could be used in place of the OGTT. This group analysed previous studies in which both HbA_{1c} values and OGTT values were recorded. Date were available for over 8000 individuals. They recommended a HbA_{1c} ^{3} 7% to diagnose treatment requiring diabetes.

In view of the diabetes epidemic in our country, a high risk approach for early diagnosis of diabetes will be cost-effective rather than a population based approach.

We undertook this study to see the prevalence of undiagnosed diabetes mellitus among certain non-diabetic high risk groups to ascertain which is a better screening test, OGTT or $HbA_{1c.}$

MATERIAL AND METHODS

The study was conducted in M. G. M. Medical College and M. Y. Hospital, Indore, amongst high risk groups, between July 1998 to December 1999. 100 patients and 35 controls were selected. Controls were non-diabetic, without having any risk factors for diabetes. All denied family history of diabetes mellitus. They were age and sex matched. All underwent a 75 g OGTT after an overnight fast. HbA_{1c} was measured from a blood sample obtained on the same day by an automated ion-exchanged chromatography (BIO-RAD mini column).

The high risk groups selected were:

1. Hypertension (≥ 140/90 mmHg)
2. Coronary artery disease – characterized by:
   a) typical anginal pain.
   b) Documented myocardial infarction (at least three months old) having any two of the following.
      i. Severe chest pain > 30 min.
      ii. Elevated cardiac enzymes.
      iii. Progressive ECG changes consistent with myocardial infarction with or without echocardiographic or angiographic evidence of myocardial infarction.
   c) ECG suggestive of myocardial infarction or coronary artery disease.
4) Obesity (BMI > 25 kg/m^2 for males: for 24 kg/m^2 females)
5) Women with bad obstetric history such as recurrent abortions, history of pre-eclampsia, small for date babies or still births.
6) Women with a history of a baby > 4.5 kg. at birth.

Interpretation of results :

1. 1980 WHO criteria for diagnosing diabetes was followed.
2. HbA_{1c} ^{3} 7% was interpreted as treatment requiring diabetes.
3. Obesity was defined by BMI (weight in kg / height in m^2) – Males > 25 kg/m^2, Females >24 kg/m^2
4. Waist / hip ratio > 0.85 for males and 0.9 for females were interpreted as diagnostic of central obesity.

RESULTS

The prevalence of diabetes was found to be 17% by OGTT and 49% by HbA_{1c} (Table 1). The prevalence of diabetes was almost the same amongst males and females diagnosed by OGTT; more in males than females diagnosed by HbA_{1c} (52.5% and 43.9% respectively). (Table 2 and 3).

Table 1. Positive OGTT and increased HbA_{1c} ^{3} 7% compared between age groups

Age Group	No. of	Diabetes Mellitus		$HbA_{1c} \geq 7\%$	
	Patients	No.	%	No.	%
20-30 years	7	1	14.2	1	14.2
31-40 years	6	-	-	4	66.7
41-50 years	25	6	24	20	80
51-60 years	32	6	18.8	15	46.9
61-70 years	30	4	13.3	9	30
Total	100	17	17	49	49

Table 2. Positive OGTT and increased HbA_{1c} ³ 7% amongst male patients of different age groups

Age Group	No. of	Diabetes Mellitus		$HbA_{1c} \geq 7\%$	
	Patients	No.	%	No.	%
20-30 years	-	-		-	
31-40 years	5	-		3	60
41-50 years	10	4	40	8	80
51-60 years	21	4	19.0	12	57.1
61-70 years	23	3	13.0	8	34.8
Total	59	11	18.6	31	52.5

Table 3. Positive OGTT and increased HbA_{1c} ³ 7% amongst female patients of different age groups

Age Group	No. of	Diabetes Mellitus		$HbA_{1c} \geq 7\%$	
	Patients	No.	%	No.	%
20-30 years	7	1	14.3	1	14.3
31-40 years	1	-	-	1	
41-50 years	15	3	20	11	73.3
51-60 years	11	3	27.3	3	27.3
61-70 years	7	1	14.3	2	28
Total	41	8	19.5	18	43.9

The significance of the association between individual risk groups and diabetes was ascertained by the chi-square test. It was observed that essential hypertension ($p < 0.01$), hypertension with coronary artery disease ($p < 0.05$), coronary artery disease ($p < 0.01$), and central obesity alone ($p < 0.01$) had significant association between obesity (defined by BMI), history of first degree relative with diabetes and bad obstetric history to be statistically significant.

Table 4: Positive OGTT and increased HbA_{1c} 7% compared among patients having hypertension as the only risk factors

No.	Diabetes Mellitus		$HbA_{1c} \geq 7\%$		MBG
	No.	%	No.	%	
20	4	20	5	25	131.9

	Male	**Female**
Number	5	15
Mean age	63.6	55.5
Mean blood glucose (MBG)	131.7	134.9

Table 5: Positive OGTT and increased HbA_{1c} ³ 7% compared amongst patients having hypertension (HTN) and coronary artery disease (CAD) without any evidence of myocardial infarction

Risk	No.	Diabetes Mellitus		$HbA_{1c} \geq 7\%$		MBG
Factor		No.	%	No.	%	
HTN+ CAD	16	7	43.8	9	56.3	131.9

	Male	**Female**
Number	9	7
Mean age	58.1	61.3
Mean blood glucose (MBG)	148.2	147.3

Table 6: Positive OGTT and increased HbA_{1c} ³ 7% compared amongst patients having hypertension (HTN) and myocardial infarction (MI)

Risk	No.	Diabetes Mellitus		$HbA_{1c} \geq 7\%$		MBG
Factor		No.	%	No.	%	
HTN+ CAD-MI	18	3	16.7	9	50	146.7

	Male	**Female**
Number	17	1
Mean age	56.9	69
Mean blood glucose (MBG)	146.7	

Table 7: Positive OGTT and increased HbA_{1c} ³ 7% compared amongst patients having coronary artery disease (CAD) with or without myocardial infarction (MI) not associated with hypertension

Risk	No.	Diabetes Mellitus		$HbA_{1c} \geq 7\%$		MBG
Factor		No.	%	No.	%	
CAD with / without MI	36	5	13.9	22	61.1	152.9

	Male	**Female**
Number	27	9
Mean age	54.2	50.4
Mean blood glucose (MBG)	151.6	156.8

Table 8: Waist Hip ratio compared with positive OGTT; increased HbA_{1c} ³ 7% and mean blood glucose (MBG) amongst male patients

Hip /	No.	%	Diabetes Mellitus		$HbA_{1c} \geq 7\%$		MBG
Waist			No.	%	No.	%	
<0.85	16	27.1	1	6.3	5	31.3	148.1
>0.85	43	72.9	26	20.9	26	60.5	148.0

Table 9: Waist Hip ratio compared with positive OGTT; increased HbA_{1c} ³ 7% and mean blood glucose (MBG) amongst female patients

Waist/ Hip	No.	%	Diabetes Mellitus No.	%	$HbA_{1c} \geq 7\%$ No.	%	MBG
<0.90	9	22.0	1	11.1	4	44.4	134.2
>0.90	32	78.0	5	15.6	14	43.8	142.9

In comparison to controls, hypertension ($t = 9.7179$, $p < 0.001$), coronary artery disease ($t = 12.5455$, $p < 0.001$), central obesity ($t = 11.89$, $p < 0.001$), obesity as defined by BMI ($t = 10.732$, $p < 0.01$), first degree relative ($t = 5.940$, $p < 0.001$), and bad obstetric history ($t = 4.7817$, $p < 0.001$) were significantly associated with diabetes, defined by either OGTT or HbA_{1c}.
The sensitivity, specificity and predictive value of HbA_{1c} and OGTT are as follows (Table 10).

Table 10 : Sensitivity, Specificity and Predictive Values of different screening tests

Diagnostic Criteria	Sensitivity	Specificity	Predictive Values Positive	Negative
$HbA_{1c} \geq 7\%$	70.6	58.0	24.5	97.1
OGTT	24.5	90.2	70.6	55.4

DISCUSSION

The prevalence of diabetes mellitus amongst high risk groups was estimated as 29% (Jeppson JO et al, 1986), 18% (Hauson RL et al, 1993) 49% (Kanatsuka et al, 1982), 33% (Have PM et al, 1984), 33% (Baucher BJ et al, 1981) 43% (Forrest RD et al, 1987) [2]. We have found a prevalence of 17% by OGTT and 49% and HbA_{1c} and is comparable with the above studies.

We have observed a greater prevalence of diabetes mellitus amongst males. We think this is because of the risk group chosen. The major risk group was coronary artery disease, and males are more prone to coronary artery disease than females.

The observed prevalence of diabetes mellitus amongst hypertensives was 20% and it is in agreement with the Framingham Heart Study [5].

Prevalence of diabetes mellitus in myocardial infarction patients ranged from 4.3% [6] (Oswald GA et al), 6% [7] (Madsen JK et al), to 78% (Sundersen M et al, 1988) [8]. We have observed a prevalence of 43.8% by OGTT and 56.3% by HbA_{1c} in the patients having both hypertension and coronary artery diseases. The prevalence decreased in patients with hypertension and coronary artery disease who had suffered any myocardial infarction (16.7% by OGTT and 50% by HbA_{1c}) ($p < 0.001$). We attribute this to moderate exercise, lifestyle modifications and controlled diet.

In patients with coronary artery disease with/without myocardial infarction 13% were found to be diabetic by OGTT and 61.1 % by HbA_{1c}. But the discrepancy is not significant statistically. We think this discrepancy is due to either intra individual variation of HbA_{1c} levels (Gould BJ) [9] or dyslipidemia associated with coronary artery disease [10] (Ko GT et al, 1998). Several recent studies have documented a relationship between the risk of CAD events and hyperglycemia, increased levels of glycated hemoglobin (HbA_{1c}) and hyperinsulinemia. Whether these metabolic abnormalities play a direct role in the pathogenesis of atherosclerosis or increase the risk of CAD due to frequently associated other vascular risk factors is currently a subject of investigation [11].

72.9% of the males and 78.0% of females had central obesity. The association of central obesity with diabetes mellitus was significant in males ($p < 0.001$) and not significant in females. On the contrary, prevalence of diabetes is less in obese females compared to non-abose ones (35% vs 52.4%), signifying other factors were independently associated with hyperglycemia.

We have also observes that amongst patients with bad obstetric history 10% were diabetic by OGTT and 40% by HbA_{1c}. On the other hand 11.8% of the first degree relatives were diabetic by OGTT, and 23.5% by HbA_{1c}.

We conclude that coronary artery disease and central obesity should be included in the high risk group.

We have observed that the diabetic yield of HbA_{1c} is almost thrice compared to OGTT. HbA_{1c} was more sensitive, whereas OGTT was more specific. We think that a single measurement to diagnose diabetes is unwarranted. We propose a two step approach to diagnose diabetes in the population. We propose that high risk patients should be screened by HbA_{1c} and if the HbA_{1c} ³ 6.5% they should undergo a 2h OGTT to confirm the diagnosis of diabetes. In our opinion the time has not yet arrived to abandon OGTT as a whole.

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