Screening for impaired fasting glucose and diabetes mellitus among people with major risk factors for type 2 diabetes mellitus

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CONTEXT: The American Diabetes Association (ADA) has identified the major risk factors for type 2 diabetes mellitus (DM) and recommended that individuals with one or more of these major risk factors should be screened at regular intervals for early detection of the prediabetic/diabetic state. **AIM:** To identify prediabetes or DM among individuals with one or more major risk factors as per the ADA 2004 guidelines. **METHODOLOGY:** This study comprised of 1008 nondiabetic individuals of both genders who were >12 years of age. They were divided into two groups on the basis of the presence or absence of major risk factors for DM as proposed by the ADA 2004 guidelines. Group I included individuals with one or more risk factors for type 2 DM, viz, family history of diabetes, overweight, age >45 years, previously identified impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), hypertension, hyperlipidemia, history of gestational diabetes and habitual physical inactivity. Group II included individuals with no major risk factors for type 2 DM. The screening test of choice was the fasting plasma glucose (FPG) measurements using (GOD/POD) kit, based on the enzymatic detection method. Statistical analysis was done using Z test of proportions. **RESULTS:** There were 585 subjects in group I and 423 in group II. On the basis of FPG values, 88.54% of those screened turned out to be normoglycemic in group I and 97.63% in group II. IFG was seen in 4.61% and 1.41% of group I and group II, respectively; 6.83% in group I and 0.70% in group II had abnormal FPG levels, i.e., ≥126 mg/dl. These differences in the proportions between group I and group II were statistically significant (P <0.01). These results suggest that more individuals were detected to have DM/IFG in group I associated with one or more major risk factors for type 2 DM; these patients were unaware of their disease until they were screened. **Conclusion:** This study confirmed that the screening protocol recommended in the ADA 2004 guidelines was equally effective in Indian population in early detection of the prediabetic or diabetic state among individuals with major risk factors for type 2 DM.

KEY WORDS: American diabetes association, diabetes mellitus, fasting plasma glucose, impaired fasting glucose, risk factors, screening for diabetes

Diabetes in all of its forms is one of the most important chronic diseases of the developed and developing world. The number of individuals developing type 2 diabetes mellitus (DM) is increasing worldwide and imposing a growing burden on health services. DM is a serious, costly and increasingly common disease.[1,2] From the year 2000 to 2050, the number of persons with diagnosed diabetes is projected to increase by 165%.[3] In light of the dramatic epidemic of type 2 DM, there is great interest in identifying and implementing interventions to prevent or delay its onset.[4] Type 2 DM frequently remains undiagnosed until its complications appear. Early detection and prompt treatment may reduce the burden of disease and its complications.[5] There is a good evidence that screening tests can detect type 2 DM during the early symptomatic phase.[6] However, due to the lack of high-quality cost-effective protocols large-scale screening has not been recommended till recently.

Among adults, it is assessed that specific population subgroups have a much higher prevalence of the disease

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than the population as a whole. These subgroups have certain attributes or risk factors that either directly cause diabetes or are associated with it. Screening for diabetes as part of routine medical care may be appropriate if an individual has one or more of these specific risk factors. Factors that have been shown to increase the risk for type 2 DM to varying degrees include obesity,[7,8] history of gestational diabetes (GDM),[9,10] hypertension,[11,12] and hyperlipidemia.[11,12] Targeted screening among such high-risk individuals with one or more of these known risk factors, is more cost effective than universal screening at all ages.[13]

The American Diabetes Association (ADA) has proposed the major risk factors[11] for type 2 DM and has created guidelines for early screening in individuals with one or more of these high-risk factors, so as to reduce the burden of disease and its complications.

Thus, the present study was planned to validate the effectiveness of the screening protocol defined by the ADA in the detection of the prediabetic or diabetic state among individuals with one or more of the major risk factors for type 2 DM.

Methodology

This was a health care setting-based, cross-sectional study conducted by the Department of Medicine, Gandhi Medical College, Bhopal, over a one year period. In this study, 1008 eligible people were registered. Persons aged 12 years or more, attending the medical OPD at Gandhi Medical College, Bhopal, for treatment of minor medical ailments and their accompanying attendants were included in the study. Patients with DM, chronic diseases, or those who were on drugs that could alter blood glucose level (e.g. long-term corticosteroid therapy, diuretics or nicotinic acid) did not qualify for the study.

After informed consent was obtained, detailed information of the person was recorded in a pretested and validated proforma; it included data on demographic details, educational status, type of work, addictions and the presence or absence of the following major risk factors as per the ADA 2004 guidelines:[11]

1. Family history of diabetes
2. Overweight (BMI $\geq$ 25 kg/m^2)
3. Age > 45 years
4. Previously identified impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)
5. Hypertension (> 140/90 mm Hg).
6. Hyperlipidemia (HDL < 35 mg/dl or triglyceride > 250 mg/dl, or both)
7. History of GDM or delivery of a baby over 9lb or 4.1 kg
8. Habitual physical inactivity.
9. Race or ethnicity with high risk of diabetes.

For habitual physical inactivity, the WHO[14] criteria was adopted, which is as follows:

Light work: (75% of time spent sitting and 25% of time spent working)

Moderate work: (40% of time spent sitting and 60% of time spent working)

Heavy work: (25% of time spent sitting and 75% of time spent working)

In this study, race / ethnicity as a risk factor could not be studied as all the study subjects were of the same ethnic origin.

After recording these details in the proforma, the subjects were divided into 2 groups: group I included individuals with one or more risk factors for type 2 DM as per ADA 2004 guidelines and group II included persons with no major risk factors for type 2 DM.

The registered subjects were counseled about the screening test. The screening test chosen was the FPG test, as recommended by the ADA 2004 guidelines.[11] The FPG was preferred because it was easier and faster to perform, convenient, acceptable to patients and inexpensive.[15] The OGTT, although considered the 'gold standard,' was more costly and time consuming than the FPG test and was less reproducible.[16] Fasting was defined as 'no caloric intake for at least 8 h before testing.' Venous blood samples of the subjects in the fasting state were collected on the same day and those who were not fasting were motivated to report in the fasting state on the next day. Laboratory measurement of plasma glucose concentration was performed on venous samples with enzymatic assay techniques using Trinder's method, in which glucose oxidase (GOD) and peroxidase (POD) are used along with phenol and 4-aminoantipyrine.

For the purpose of quality control of the test, 5% of the blood samples collected were also tested in a different lab by a different technician so that reports could be compared for any error.

On the basis of the ADA 1997 revised criteria[17] for diagnosis of diabetes, individuals registered for the study were divided into three categories depending

upon FPG levels:

I. Individuals with a FPG < 110 mg/dl were considered to be normoglycemic.
II. Individuals with FPG ≥ 110 mg/dl but <126 mg/dl were considered to have IFG. IFG is a risk factor for future diabetes, hence they were motivated for a repeat test or OGTT on a different day for the definitive diagnosis.
III. Individuals with FPG ≥126 mg/dl levels were considered as having abnormal FPG and were invited for retesting. They were informed about the results and motivated for a repeat test on a different day to confirm the diagnosis.

During this screening study, we explained the results of the screening test to the subjects and made it clear that follow-up evaluation and treatment would be made available to them.

Results

In the present study, group I included individuals with one or more of the ADA 2004 defined major risk factors for type 2 DM and group II had individuals without any of those risk factors [Figure 1]. There were 585 persons in group I and 423 in group II. In group I, 57.0% were men and 43.0% were women, while in group II 39.0% were men and 61.0% were women. In group I, most subjects were >55 years age and in group II all persons were ≤ 45 years.

The distribution of major risk factors in group 1 is shown in Figure 2.

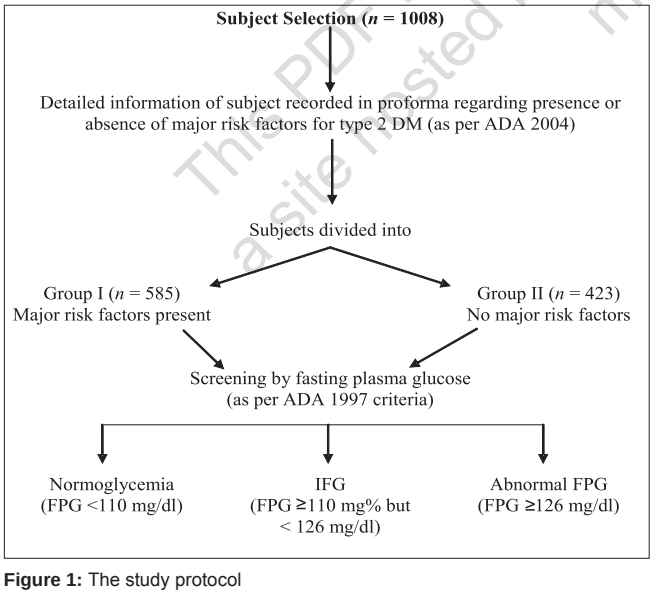

Figure 1: The study protocol

Individuals from both groups underwent screening by the FPG test. FPG was normal in 88.54% cases in group I and in 97.63% in group II. While 4.61% and 1.41% of the study subjects had IFG in group I and group II, respectively, 6.83% cases in group I and 0.70% cases in group II had abnormal FPG levels, i.e. ≥126 mg/dl. Differences in these proportions were statistically significant as calculated by the Z test of proportions ($Z=3.7857$, $Z>2.58$:$P<0.01$).The FPG values clearly proved that presence of the ADA defined major risk factors directly contribute to increased prevalence of IFG and abnormal FGP in group I as compared to group II [Figure 3].

Results of IFG and abnormal FPG in group I were analysed to detect any association between the presence of major risk factors and the prevalence of the prediabetic or diabetic state. The results are depicted in Figure 4. Among persons aged more than 45 years, 15.0% had abnormal FPG / IFG. In subjects with BMI >25 kg/m^2, 14.58% had abnormal results. Out of all individuals with hypertension, family history of diabetes and

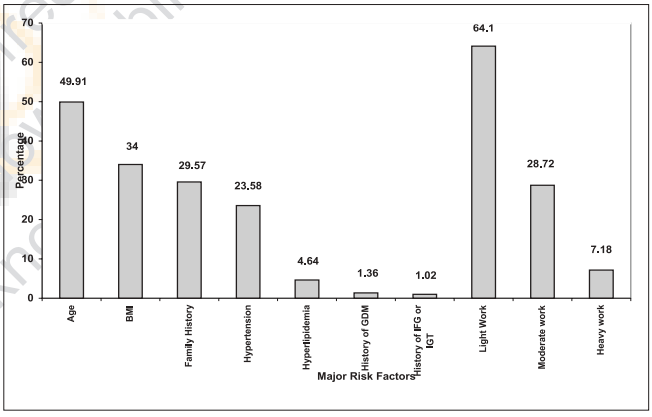

Figure 2: Distribution of cases in group I (n=585) according to major risk factors

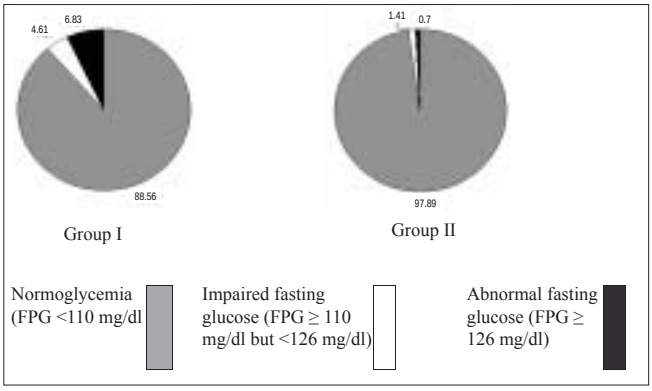

Figure 3: Glucose intolerance in group I and group II

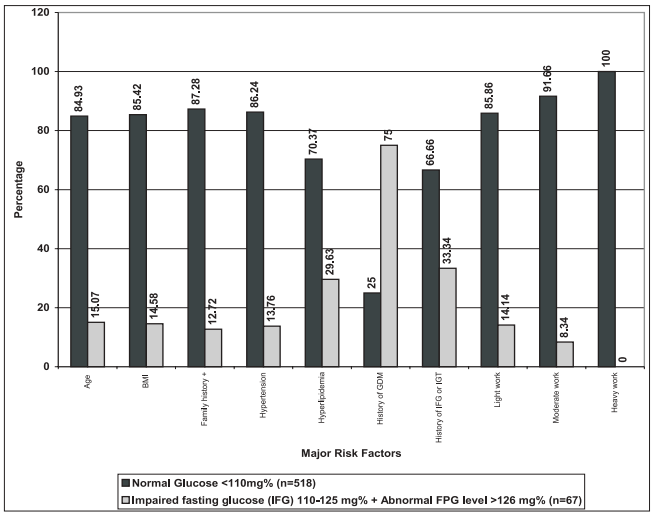

Figure 4: Prevalence of prediabetic or diabetic state in cases with major risk factors

hyperlipidemia, 13.76, 12.72, and 29.63% had abnormal FPG, respectively. Among women with a history of GDM, 75% showed abnormal FPG. Abnormal FPG was detected in 33.34% of persons with previous history of IFG or IGT and in 14.14% of individuals with a sedentary lifestyle. The results of this univariate analysis could not be entirely attributed to any one particular risk factor as most of the individuals had more than one risk factor present, and these high percentages could have been confounded because of the coexistence of other risk factors.

When the number of risk factors present in cases with IFG was studied, it was found that the majority of the cases with IFG (FPG ≥ 110 mg/dl but < 126 mg/dl), i.e., 12 cases (44.44%) had two major risk factors, 6 (22.22%) had three major risk factors for diabetes, 7 (25.90%) had only one risk factor, 1 (3.70%) subject had 4 and 1 (3.70%) subject had 5 risk factors for type 2 DM. In group I, when the number of risk factors present in cases with abnormal FPG (FPG ≥ 126 mg/dl) were studied, it was found that the maximum cases, i.e. 16 (40%) had 2 risk factors for type 2 DM, 8 (20%) subjects had 4 risk factors, 5 (12.5%) had 5 risk factors, 4 (10%) had 1 risk factor, 4 (10%) had 3 risk factors, and 3 (7.5%) had 6 risk factors for type 2 DM.

Discussion

The detection of diabetes in a patient calls for efforts (in addition to glycemic control) to screen for diabetes-related complications and to intensify cardiovascular risk reduction. Detecting IFG or abnormal FPG in asymptomatic individuals warrants such efforts to prevent or delay their progression to diabetes and its related complications.

Though various advisory groups[18] have suggested many risk factors for type 2 DM and various studies have been done since 1993, most of them were based on questionnaires and few have included chemical blood tests. All these studies were community-based studies but few have given any clear-cut guidelines for screening for type 2 DM.

The ADA, in 2004, had prepared an exhaustive list of the major risk factors for type 2 DM and recommended that individuals with these risk factors should be screened regularly so as to detect prediabetes or diabetes at the earliest. In the present study the screening protocol recommended by the ADA 2004 guidelines was followed and results were analyzed.

It was found that the male: female ratio was higher among individuals with major risk factors when compared to those without any major risk factors. Drobae[19] had also noticed that males predominate among those having major risk factors for type 2 DM. In group 1 of the present study population, 29.75% of the individuals had a family history of diabetes, and on assessment of their FPG it was seen that 2.90% had IFG and 9.80% had abnormal FPG levels. Because family history reflects genetic susceptibility in addition to other factors, it may be a useful public health tool for diabetes prevention.[20] It was also suggested by one study[21] that onset of diabetes was delayed in individuals without family history of diabetes and they had better HDL levels, when compared with individuals with family history of diabetes, who had higher BMI and associated hypertension.

Total body adiposity, a central fat distribution and the duration and time course of developing obesity are all established risk factors for type 2 DM in both genders.[22–26] Having BMI >35 kg/m^2 increases the risk of developing diabetes over a 10-year period by a staggering 80 fold as compared with lean individuals (BMI <22 kg/m^2).[27] In our study we considered BMI >25 kg/m^2 as a risk factor for diabetes. In group I, 34% cases had BMI ≥25 kg/m^2, out of which 35.03% were males, which suggested that men were more obese compared to women among undiagnosed diabetic individuals. These results were comparable to that reported by Harris[28] in 1993, who has also reported obesity as being more common among undiagnosed males. The recognition of significant association between obesity and diabetes

in many population studies has also been translated into therapeutic success. In the Swedish Obese Subjects (SOS) study, obese (BMI >34 kg/m^2 for men or 38 kg/m^2 for women) patients treated with gastrointestinal surgery to promote weight loss were compared with matched nonsurgically treated control patients and it was found that in surgically treated patients, 2 to 5 years after surgery diabetes incidence was reduced by up to 97%[29,30] as compared to their counterparts who did not undergo surgery.

IFG and abnormal FPG were also found in those who had other major risk factors for type 2 DM, alone or in combination. Association between hypertension and type 2 DM depends on the presence of various risk factors.[31] In the present study, 23.80% cases in group I had hypertension.

Following a pregnancy with GDM, the mother has an increased risk of developing type 2 DM.[32] Women at greatest risk of developing GDM are those who are obese, older than 25 years, have a previous history of abnormal glucose metabolism or poor obstetric outcome, have first degree relatives with diabetes, or are members of ethnic groups with high prevalence of diabetes.[32] Constan et al., in his study, observed that 30% of women with GDM developed diabetes 7–10 years after the pregnancy.[33] In our study, 75% of women with history of GDM were found to have abnormal FPG levels. Out of them 66% had also other major risk factors for type 2 DM, which suggested that women with history of GDM and with one or more major risk factors for type 2 DM should be screened more regularly for the presence of a prediabetic or diabetic state.

Physical inactivity plays a role in development of type 2 DM independent of other risk factors.[34] It has been observed that leisure-time physical activity was inversely related to the development of type 2 DM[35] and the relative risk of developing type 2 DM decreases progressively as physical activity pattern increases.[36] In our study, 64% of individuals registered in group I had sedentary lifestyles, 28.72% had moderately active lifestyles and 7.18% were heavy workers. IFG or abnormal FPG was found more in persons with a sedentary lifestyle (14%) when compared with moderate (8.34%) and heavy (0%) work lifestyles. The findings of four studies[7,35–37] have also documented the association between physical inactivity and the development of diabetes and supported the hypothesis that type 2 DM can be prevented by adoption of healthy lifestyles, including regular exercise. A study from Malmo (Sweden) also demonstrated the effectiveness of lifestyle changes in preventing diabetes.[38]

The DPP study on people with IGT concluded that the absolute risk of developing diabetes was 11% per year if effective interventions were not undertaken in people with IGT.[39] Thus, interventions in the form of health education, nutrition therapy and intensive lifestyle modification are essential to prevent the risk of type 2 DM amongst people with history of IGT.[39,40]

In the present study, evidence for earlier IFG or IGT was present in 1.05% cases and out of them 33.33% had abnormal FPG levels.

Diabetes is positively and independently associated with increasing age. Advancing age is a predisposing risk factor for type 2 DM, independent of other major risk factors. In our study 49.91% of cases were of age ≥45 years and 15% of them had IFG or abnormal FPG levels.

When all risk factors were considered, it was found that age >45 years and a sedentary lifestyle were the two important risk factors which were present in the maximum number of individuals with IFG or abnormal FPG, along with the presence or absence of other risk factors for type 2 DM. This observation suggested that intervention in lifestyle changes, especially in individuals with major risk factors for type 2 DM, would be a cost-effective measure in the prevention of type 2 DM.

Conclusion

The study concludes that the screening of the high-risk individuals should be done at regular intervals specially in those above 45 years with a sedentary lifestyle and with or without obesity, hypertension or hyperlipidemia. Also, individuals with family history of diabetes or a past history of IFG or females with history of GDM should be screened more frequently for type 2 DM, irrespective of the presence or absence of other major risk factors.

Thus, this study confirmed that the screening protocol as recommended by ADA 2004 guidelines was equally effective in Indian populations in the early detection of the prediabetic or diabetic state among individuals with major risk factors for type 2 DM.

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