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ORIGINAL RESEARCH

Screening for type 2 diabetes in a multiethnic setting using known risk factors to identify those at high risk: a cross-sectional study

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Introduction: Screening enables the identification of type 2 diabetes mellitus (T2DM) during its asymptomatic stage and therefore allows early intervention which may lead to fewer complications and improve outcomes. A targeted screening program was carried out in a United Kingdom (UK) multiethnic population to identify those with abnormal glucose tolerance.

Methods: A sample of individuals aged 25–75 years (40–75 white European) with at least one risk factor for T2DM were invited for screening from 17 Leicestershire (UK) general practices or through a health awareness campaign. All participants received a 75 g oral glucose tolerance test, cardiovascular risk assessment, detailed medical and family histories and anthropometric measurements.

Results: In the 3,225 participants who were screened. 640 (20%) were found to have some form of abnormal glucose tolerance of whom 4% had T2DM, 3% impaired fasting glucose (IFG), 10% impaired glucose tolerance (IGT) and 3% both IFG and IGT. The odds of detecting IGT was approximately 60% greater (confounder-adjusted odds ratios [OR] 1.67 [1.22–2.29]) in the South Asian population.

Conclusions: Around one in five people who had targeted screening have IGT, IFG or T2DM, with a higher prevalence in those of South Asian origin. The prevalence of undetected T2DM is lower in South Asians compared to previously published studies and maybe due to increased awareness of this group being at high risk.

Keywords: type 2 diabetes, screening, cardiovascular risk, impaired glucose regulation

Introduction

By 2025 an estimated 4.2 million adults in the United Kingdom (UK) will have type 2 diabetes mellitus (T2DM).[1,2] If current clinical practice continues the majority of these cases will go undetected for many years, and over 50% will be destined to develop potentially devastating vascular co-morbidities.[3–5] The implications of an emerging disease pandemic on this scale, affecting around 1 in 15 of the working population are almost unimaginable and present a major threat to future healthcare and economic prosperity.

Screening enables the identification of T2DM in the lag phase between the onset of latent hyperglycemia and clinical diagnosis. This approach simultaneously reduces exposure to the deleterious effects of glucose whilst providing an opportunity to perform population-level vascular risk assessments. Early data from the United Kingdom Prospective Diabetes Study (UKPDS) supported this view by demonstrating an inverse relationship between fasting plasma glucose at diagnosis, and adverse clinical outcomes.[6] Subsequent long-term follow-up of this cohort demonstrates that in fact many years of glucose lowering intervention are required to influence cardiovascular outcomes in T2DM again indicating earlier intervention maybe beneficial.[7]

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Recent large intervention trials have clearly demonstrated that treatment of individuals with abnormal glucose regulation with structured lifestyle or pharmacological interventions may lead to fewer complications or even prevent T2DM.[8–10] Indeed, glucose thresholds for the development of atherosclerosis remain contentious but are likely to be significantly lower than existing diagnostic cut-offs for T2DM.[11] Therefore, screening activity aimed primarily at preventing large vessel cardiovascular disease (CVD) should possibly include "pre-diabetes" (impaired glucose regulation) which World Health Organization (WHO) define as impaired fasting glycemia (IFG) and impaired glucose tolerance (IGT) glucose categories.[12]

Despite clear theoretical advantages for earlier detection and intervention there is currently no systematic screening program for T2DM in the UK and no evidence that T2DM cases identified through screening have improved outcomes. As a result the National Screening Committee does not currently advocate universal screening for T2DM and instead recommend strategies targeting populations at "high-risk".[13] Acknowledging this and the multi-factorial nature of cardiovascular risk in this population they have pursued a national agenda in producing a vascular check handbook incorporating screening advice and suggesting a T2DM assessment for individuals over 45 years of age, an elevated body mass index (BMI) or hypertension.[14,15]

Black and Minority Ethnic (BME) groups are at particularly high risk of abnormal glucose tolerance and T2DM, with reported prevalence 2–6 times that of the background white European population.[1,16–21] To be effective national screening programs must adequately represent these groups by adapting to their specific needs and identifying barriers to the detection of disease and delivery of care early.[22] There is currently little data describing the likely consequences of targeted T2DM screening in BME UK populations. In particular the burden of unidentified cardiovascular risk and glucose dysregulation is crucial to appropriate planning and implementation of screening programs in these populations.

The aims of the STAR (Screening Those At Risk) study were to describe the clinical characteristics and cardiovascular risk factor profile of a multiethnic population screened for T2DM with a targeted oral glucose tolerance test (OGTT).

Methods

The STAR study was designed to identify the prevalence of glucose disorders including T2DM using a predetermined targeted strategy. This screening study was conducted in Leicestershire with a population of over 950,000, approximately one third of whom are resident in Leicester city, Leicestershire, United Kingdom. South Asians make up 24% of the population. Individuals aged 40–75 years inclusive (25–75 for South Asians, Afro-Caribbeans and other races due to the reported higher risk of T2DM), who had at least one recognized risk factor for diabetes (identified from general practice computer records) from 17 general practices across Leicestershire were invited to attend screening. Individuals on the practice list and fulfilling the entry criteria were sent a letter and information pack in English or a flyer in four languages (Gujarati, Hindi, Urdu and Punjabi) advising patients how to get details in their native language. Non respondants were sent a second letter. In addition people were recruited in an opportunistic fashion by canvassing at local retail centers during a health awareness campaign "Be a star campaign".

Risk factors for inclusion into the study included a documented clinical history of coronary heart disease, hypertension, dyslipidemia, cerebrovascular disease or peripheral vascular disease (PVD), previous history of IGT, gestational diabetes, polycystic ovary syndrome in those with a body mass index (BMI) > 25 kg/m^2, a first-degree relative with T2DM or BMI > 25 kg/m^2, and current or ex smokers. Exclusion criteria were patients who were housebound, had a terminal illness or were already known to have diabetes. All patients provided written informed consent. The screening was conducted within the general practice, on a mobile screening unit or at one of the local hospitals. Ethical approval was obtained from the local ethics committee.

Screening visit

All individuals attended after at least an eight-hour fast, and venous blood samples were taken for glucose, HbA_{1c} lipids and renal function. A 75-g oral glucose tolerance test (OGTT) (388 mls Lucozade) was given and a venous blood sample taken after 120 minutes. HbA_{1c} was analyzed using the BIORAD Variant II HPLC system (DCCT aligned.) All samples were analyzed in the same laboratory using stable methodology standardized to external quality assurance reference values. Further assessment included blood pressure, height and weight (BMI calculated) to a set of standard operating procedures by a trained member of research staff. Maximum waist and hip measurements were taken. Early morning urinary albumin and creatinine levels were measured and the albumin:creatinine ratio calculated. A ratio ≥ 2.5 mg/mmol in males and 3.5 mg/mmol in

females was taken as microalbuminuria. A twelve-lead electrocardiograph was performed and classified according to the Minnesota classification.[23] All individuals were asked to self-complete an ethnicity (Census classification) and general health questionnaire. A qualified nurse obtained patients' past medical and medication history.

Individuals found to have glucose results within the diabetes range, using the WHO 1998 criteria, were invited for a repeat OGTT.[24] The diagnosis of T2DM was made on the agreement of two OGTTs. In the event of discordant OGTT results (eg, baseline T2DM followed by rescreen IFG/IGT) a diagnosis of "pre diabetes" (impaired glucose regulation) was made. Patients found to have diabetes were invited for a full clinical assessment and were seen by the same physician.

Statistical analysis

Analyses were carried out using Stata software (version 11; Stata Corp, College Station, TX). Data are presented for the total screened group and also by ethnicity (white European versus South Asian). Statistical differences between ethnicities are given both unadjusted and adjusted for age. Odds ratios (OR) (95% confidence intervals [CI]) for the comparison of glucose abnormalities by ethnic group are calculated using logistic regression adjusted for age and separately adjusted for age, sex, smoking status, BMI, waist, HbA_{1c}, total cholesterol, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol. Results are presented as mean (SD) or as count and percentage. A P-value < 0.05 was considered statistically significant.

Results

3,225 participants with at least one risk factor aged between 40–75 (25–75 for South Asians) attended for screening. 66% were of white European origin, with South Asians (mostly of Indian origin) accounting for 30%. The remaining 4% was made up of African, Caribbean, and Chinese origins. The mean age of the total screened population was 55 years (SD 11.2), with 46% being male.

Clinical characteristics of screened cohort by ethnicity

Table 1 shows the characteristics of those who attended screening. There were substantial differences between the white European and South Asian screened populations, irrespective of the differential age inclusion criteria. White Europeans had significantly higher waist circumference and BMI, and higher levels of total cholesterol. White Europeans also had slightly higher levels of systolic and diastolic blood pressure, but differences in blood pressure were not maintained after adjustment for age. South Asians had significantly higher levels of HbA_{1c}, 5.9% (0.8%) versus 5.7% (0.6%), $P < 0.0001$, this remained significant after adjustment for age. Independent of age there were higher levels of both current and ex smokers in the white European group. There were also differences in the co-morbidity profile of the two ethnic groups (Table 2). White Europeans

Table 1 Demographics and biomedical data of those screened

	Total	White European	South Asian	*P*-value	Age adjusted *P*-value
	3225	2138 (66.3)	963 (29.9)		
Age	55.1 (11.2)	58.4 (9.7)	48.3 (11.1)	<0.0001	–
Sex, male	1495 (46.4)	948 (44.3)	500 (51.9)	<0.0001	<0.0001
Ethnicity, WE	2138 (66.3)	–	–	–	–
Ethnicity, SA	963 (29.9)	–	–	–	–
Ethnicity, Other	124 (3.8)	–	–	–	–
Smoking, current	803 (24.9)	647 (30.3)	117 (12.2)	<0.0001	<0.0001
Smoking, ex	696 (21.6)	609 (28.5)	76 (7.9)	<0.0001	<0.0001
Weight	77.5 (16.1)	79.6 (16.5)	72.4 (13.8)	<0.0001	<0.0001
BMI	28.1 (5.1)	28.5 (5.3)	27.2 (4.7)	<0.0001	<0.0001
Waist	95.1 (13.1)	96.1 (13.6)	93.0 (11.7)	<0.0001	0.004
Systolic blood pressure	132.8 (20.7)	135.1 (20.8)	127.8 (19.8)	<0.0001	0.57
Diastolic blood pressure	80.0 (10.8)	80.3 (10.7)	79.3 (11.0)	0.02	0.68
HbA_{1c}	5.8 (0.7)	5.7 (0.6)	5.9 (0.8)	<0.0001	<0.0001
Cholesterol	5.4 (1.0)	5.5 (1.1)	5.1 (0.9)	<0.0001	<0.0001
LDL	3.3 (0.9)	3.4 (0.9)	3.2 (0.8)	<0.0001	<0.0001
HDL	1.3 (0.5)	1.4 (0.4)	1.2 (0.6)	<0.0001	<0.0001

Abbreviations: WE, white European; SA, South Asian; BMI, body mass index; LDL, cholesterol, low-density lipoprotein; HDL, high-density lipoprotein.

Table 2 Co-morbidities of those screened

	Total	White European	South Asian	*P*-value	Age adjusted *P*-value
	3225	2138 (66.3)	963 (29.9)		
Known history CHD	415 (12.9)	328 (15.3)	82 (8.5)	<0.0001	0.29
Hypertension	1294 (40.1)	965 (45.1)	282 (29.3)	<0.0001	0.17
Cerebrovascular disease or peripheral vascular disease	91 (2.8)	75 (3.5)	13 (1.4)	0.001	0.62
Impaired glucose tolerance	47 (1.5)	33 (1.5)	14 (1.5)	0.85	0.73
Gestational diabetes	57 (1.8)	37 (1.7)	19 (2.0)	0.64	0.14
Polycystic ovary syndrome	8 (0.3)	6 (0.3)	2 (0.2)	0.71	0.09

Abbreviation: CHD, coronary heart disease.

had significantly higher levels of coronary heart disease, hypertension, CVD and PVD; these differences were driven by the age disparity and were not statistically significant when adjusted for age. No difference was seen for previous history of IGT, gestational diabetes or polycystic ovary syndrome.

Prevalence of abnormal glucose tolerance

Of the 3,225 patients screened 640 (20%) were found to have abnormal glucose tolerance, 4% had T2DM, 3% impaired fasting glycemia (IFG) and 10% IGT and 3% had both IFG and IGT (Table 3). The prevalence of abnormal glucose tolerance varied by ethnic group. There was a greater prevalence for South Asians compared to white Europeans across all glucose classifications apart from IFG. For example South Asians had a 70% greater age adjusted odds of having IGT (OR = 1.71, 95% CI: 1.28–2.26; $P < 0.0001$), and a twofold greater odds of having both T2DM (OR = 2.05, 95% CI: 1.35–3.12; $P = 0.001$) or any form of abnormal glucose tolerance (OR = 1.99, 95% CI: 1.61–2.45; $P < 0.0001$). When adjusted for all confounding factors significant differences between South Asians and white Europeans remained for IGT, IGT or IFG and IGT and/or IFG.

Discussion

One in five of those screened for T2DM through the nationally recommended targeted approach have some form of abnormal glucose tolerance. White Europeans have a greater prevalence of traditional risk factors for T2DM and CVD compared to South Asians but this increased prevalence can mostly be explained by the difference in age inclusion criteria. Irrespective of a similar or in some cases lower risk profile a two fold greater prevalence of T2DM is seen in those from a South Asian origin. This suggests that there are risk factors for T2DM which we have not measured in this study which explain the difference seen in prevalence.

An age-adjusted OR for T2DM of 2.05 (95% CI: 1.35–3.12) in predominantly Indian South Asians is similar to incident estimates from a larger UK primary care data set and the most recent health survey for England.[25,26] Our study adds to the remarkable paucity of published data describing the burden of glucose dysregulation in migrant South Asian populations using the gold standard OGTT.[16,17,27,28]

It is clear that this approach identifies a significant burden of unidentified cardiovascular risk in both white European and South Asian UK populations. Lower rates of traditional cardiovascular-risk factors (blood pressure, smoking, dyslipidemia, BMI) emphasizes the likely

Table 3 Prevalence of type 2 diabetes and impaired glucose regulation. The odds ratios (OR) in bold are statistically significant

	Total	White European	South Asian	*P* value	Age adjusted OR SA versus WE	Fully adjusted OR SA versus WE*
IFG	91 (2.8)	55 (2.6)	30 (3.1)	0.39	1.48 (0.90 to 2.44)	1.56 (0.90 to 2.68)
IGT	315 (9.8)	209 (9.8)	96 (10.0)	0.86	**1.71 (1.28 to 2.26)**	**1.67 (1.22 to 2.29)**
IGT or IFG	406 (12.6)	264 (12.4)	126 (13.1)	0.57	**1.70 (1.32 to 2.19)**	**1.67 (1.26 to 2.23)**
IGT and IFG	111 (3.4)	68 (3.2)	41 (4.3)	0.13	**1.74 (1.13 to 2.69)**	1.44 (0.88 to 2.34)
IGT and/or IFG	517 (16.0)	332 (15.5)	167 (17.3)	0.20	**1.79 (1.42 to 2.25)**	**1.62 (1.25 to 2.10)**
T2DM	123 (3.8)	74 (3.5)	44 (4.5)	0.12	**2.05 (1.35 to 3.12)**	0.66 (0.34 to 1.28)
Abnormal glucose	640 (19.8)	406 (19.0)	211 (21.9)	0.04	**1.99 (1.61 to 2.45)**	1.24 (0.95 to 1.62)

Notes: *Adjusted for age, sex, smoking status, BMI, waist, HbA_{1c}, total cholesterol, LDL, HDL.
Abbreviations: OR, odds ratios; SA, South Asian; WE, white European; IFG, impaired fasting glycemia; IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus; BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

importance of glucose disorders, insulin resistance and other unknown contributors to premature vascular disease in British South Asians.

The significantly increased prevalence of IGT in south Asians after adjustment for confounders also suggests that two-hour glucose levels are important and therefore, although cumbersome and impractical, the OGTT should be used in the screening of these at risk individuals. The utility of measuring HbA_{1c}% or alternative glucose indices to estimate two hour glucose levels in this population is unknown and requires further investigation.

Individuals were recruited into this study if they had one or more risk factors for T2DM in line with recommendations of the UK National Screening Committee.[13] These results are therefore highly applicable to multiethnic screening programs. An additional strength of this study is that all participants received an OGTT and the diagnosis of T2DM was made on the basis of a repeat OGTT. This is a unique and extremely important aspect of STAR as the clinical relevance of glucose intolerance in the patho physiology and prevention of T2DM becomes more apparent especially in populations predisposed to central obesity. A large cohort of people were screened (> 2000) including a significant proportion of South Asians. Although there is some heterogeneity among the South Asian population in Leicester, the majority of those included were of Indian origin.

Conclusion

Earlier identification of dysglycemia may be an effective method of improving vascular outcomes in people with T2DM. Economic modeling suggests targeted population screening for T2DM may be cost effective.[29] Results of these studies may not be directly applicable to ethnic minority populations at risk of T2DM and data describing unidentified cardiovascular risk in these groups is urgently needed. We have described the methodology and characteristics of a large scale targeted screening program for T2DM. The prevalence of unidentified abnormal glucose tolerance is high, particularly within the South Asian ethnic minority.

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Competing interests

KK and MJD are advisors to the National Screening Committee.

Disclosure

The authors report no conflicts of interest in this work.

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