Phenotypic characteristics and risk factors in a multi-ethnic cohort of young adults with type 2 diabetes

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ABSTRACT

Background

Early onset of type 2 diabetes (T2DM) is associated with prolonged exposure to hyperglycaemia and increased propensity to chronic complications. The aim of this study was to characterise and compare the phenotypic characteristics and risk factors in a multi-ethnic cohort of young adults with type 2 diabetes (T2DMY).

Methods

100 young adults (White European [WE], South Asian [SA] and African-Caribbean [AC]) diagnosed with T2DM before the age of 40 years were recruited. Demographics, family history, diabetes related complications, co-morbidities, anthropometry (Body Mass Index (BMI), Body composition), physical activity and biochemistry (HbA1c, lipid profile, liver and renal function) and autoantibodies (anti GAD, anti islet cell) were collected for all participants. Data were analysed for the most represented ethnic groups: (WE, N=36 and SA, N=53) using SPSS version 23.

Results

Mean (± standard deviation) age at diagnosis was 32.5±5.5 years and mean diabetes duration was 7.7±3.8 years. Overweight/obesity was present in 95% of participants, history of maternal diabetes in 68%, deprivation 75%, low physical activity 40%, polycystic ovarian disease 29% (in females), acanthosis nigricans 12%, and non alcoholic fatty liver 11%. There was considerable clustering of risk factors within the cohort with over 75% of all subjects having 3 or more of the above risk factors and

fifty two percent required insulin within 3 years of diagnosis. Two-thirds of the patients had evidence of at least one diabetes related micro-vascular complication.

Conclusion

T2DMY is characterised by a high burden of commonly associated risk factors for both the disease and its long term complications.

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BACKGROUND

Type 2 diabetes (T2DM), once considered a rare condition in youth, is now increasingly diagnosed in children, adolescents and younger adults. The International Diabetes Federation (IDF) estimates that the number of people diagnosed with T2DM worldwide before the age of 40 years has increased from 23 million in 2003 to over 63 million in 2013 (1, 2). Worrying trends of increasing numbers of children and adolescents diagnosed with T2DM have been reported in populations across the globe (3, 4). Type 2 diabetes in young adults (T2DMY) presents a number of challenges. It needs to be differentiated from type 1 diabetes (T1DM) which is more common in younger age groups and also from monogenic forms of the disease. In addition, the earlier the age of onset the longer the exposure to hyperglycaemia resulting in a greater lifetime risk of diabetes related complications (5-8). Moreover, there is evidence that T2DMY has a more aggressive pathology than seen in people diagnosed later in life and this is characterised by a faster decline in pancreatic beta-cell function and enhanced susceptibility to complications (9).

Although T2DM is commonly considered as a disorder of impaired beta-cell function and insulin resistance, there is growing understanding that the mechanisms contributing to chronic hyperglycaemia may be different in different age groups (10). While there is now better understanding of the epidemiology of T2DM in children and adolescents, very few studies have attempted to characterise younger adults. Transition from adolescence to young adulthood is relatively seamless and it is likely that the features observed in childhood and adolescence may have a considerable overlap in younger adults. Additionally, other factors such as ethnicity, deprivation and life events such as puberty and pregnancy may influence susceptibility and course of T2DM in youth. Understanding the phenotypic characteristics and risk factors

associated with T2DMY is therefore important in the prevention of diabetes as well as in managing established disease.

The aim of this study was to characterise and compare the major risk factors predisposing to T2DMY in a multi-ethnic cohort of young adults (aged <40 years at diagnosis) with T2DM.

RESEARCH DESIGN AND METHODS

The city of Birmingham, UK has a multi-ethnic population with an estimated diabetes prevalence of around 10% (11) South Asians (people of Indian, Pakistani and Bangladeshi ethnicity) comprise the largest ethnic group after the local white Europeans and account for 19.5 % of its population (12). We recruited a multi- ethnic cohort of young adults diagnosed with T2DM below the age of 40 years to this observational study. Ethnicity classification was based on the UK 2011 census analysis (13). The following ethnic groups were considered: White, Asian/Asian British (Pakistani, Indian, Bangladeshi and other Asian), Black/British (Caribbean, African and other black). Patients were included in the study if they were: aged 18 years and above, had a diagnosis of T2DM before the age of 40 years and able to provide informed consent. Key exclusion criteria were; a known diagnosis of type 1 diabetes, Latent Autoimmune Diabetes in Adults (LADA- defined as *1*) age usually ≥30 years, *2*) positive titer for at least one of the four autoantibodies, and *3*) has not been treated with insulin within the first 6 months after diagnosis)(14), monogenic diabetes or secondary diabetes; diabetes duration >14 years; on going pregnancy; developmental disorders; other significant illness or condition including severe mental health condition. Key inclusion and exclusion criteria are summarised in **Table 1**. The West Midlands National Research Ethics Service approved the study.

Informed consent was obtained from all patients who met the study eligibility criteria and they were invited to attend a baseline visit. Assessments included demographic details, smoking status, medical and medication history; physical examination including anthropometric measurements (body mass index (BMI), waist and neck circumference and body composition as measured using an automated bio-impedance analyser (Tanita BC 420 S MA). Blood pressure was recorded as a mean of three measurements taken in a sitting position after 5 minutes rest. Screening for neuropathy used the Michigan Neuropathy Screening Instrument (MNSI) comprising feet inspection, ankle reflexes, 10g monofilament perception and neuropathic symptoms questionnaire (16). Cardiac autonomic dysfunction was assessed using heart rate variability and analysed using continuous wavelet transform methods to generate numerical and graphical data using ANX-3.0 software (ANSAR Inc., Philadelphia, PA). Screening for retinopathy comprised digital retinal photographs and optical coherence tomography to assess for maculopathy. All patients had a 12 lead ECG performed and completed validated questionnaires for physical activity using International Physical activity Questionnaire,(IPAQ)(17, 18).

Laboratory tests

All patients were requested to attend the baseline visit after an overnight fast (at least 8 hours duration) and 20 ml of venous blood was collected for biochemical tests. All blood tests were analysed in the pathology laboratories of the Heart of England NHS Foundation Trust, Birmingham. Analyses were made using serum, except for glucose which was determined in plasma. HbA1c was measured by liquid chromatography, whereas lipid profile, liver function, creatinine, urea and electrolytes were measured by colorimetric analysis and spectrophotometry. Thyroid function, vitamin D, vitamin

B12 and, follicle stimulating hormone, luteinising hormone (for females only), were determined by immunoassay.

Target definitions

BMI and waist circumference were assessed following the joint WHO 2008 and NICE 2013 guidelines, considering ethnic differences (19, 20). Hypertension was defined as Blood pressure (BP) >130/80mmHg or if taking anti-hypertensive medication(s), according to the ADA guidelines (21). Dyslipidaemia was defined as elevated total cholesterol >4 mmol/L or elevated low-density lipoprotein cholesterol (LDL-C) > 2.6 mmol/L, or low levels of high-density lipoprotein cholesterol (HDL-C) <1 mmol/L in men and <1.2 mmol/Lin women, or elevated triglycerides (TG) > 1.7 mmol/L or taking lipid lowering medications.

Based on guidelines from the ADA, glycaemic control was considered at target with a HbA1c ≤ 53 mmol/mol (DCCT <7%) and optimal with a HbA1c≤48 mmol/mol (DCCT <6.5%). Albuminuria was classified as: normoalbuminuria (Albumin/Creatinine ratio (ACR) <3 mg/mmol), microalbuminuria (ACR 3-30 mg/mmol) and macroalbuminuria (ACR >30 mg/mmol). Physical activity was categorised according to the IPAQ scoring as sedentary, low, moderate and intense. In accordance with NICE guidelines, Non-alcoholic fatty liver disease (NAFLD) was defined by evidence of hepatic steatosis, detected when serum liver enzymes (measured on two consecutive occasions at least 6 weeks apart) were elevated and/or confirmed by an abdominal ultrasound(22). The diagnosis of polycystic ovary syndrome (PCOS) was based on previous medical notes supported by an ultrasound.

Statistical analysis

Sample size and power calculations were not performed as this was a feasibility study. Data were entered in Excel sheet and cleaned, validated and analysed using SPSS version 23. Quantitative variables were summarized using mean, standard deviation and median (if data was not normally distribution) while categorical variables were tabulated using frequencies and percentages. Student's t-test and Mann-Whitney U test were used to test the significance of differences between mean values of two continuous variables. Chi-square test was carried out to test the difference between two or more categorical variables. The probability (p) level of < 0.05 was considered significant. All statistical testing was two tailed.

RESULTS

Between November 2012 and April 2014, 100 subjects were recruited (men N=42; women N=58) with a clinical diagnosis of T2DM and age of onset less than 40 years. Five participants were then excluded after antibody tests confirmed a diagnosis of T1DM (N=2) or LADA (N=3). Data were analysed for the remaining 95 subjects (53 South Asian, 36 white European and 6 African Caribbean). Ethnicity comparisons were made between the two ethnic groups predominantly represented in the cohort and included the 36 patients of White European (WE) and 53 of South Asian (SA) ethnicity. Median age at diagnosis was 34 years. More than two thirds of the patients (65.2%) were diagnosed below the age of 35 years with a majority (58.4%) being female. Clinical characteristics of the participants are shown in **Table 2**.

Metabolic profile

The mean BMI of the T2DMY cohort was 35.05±9.54 kg/m^2 and was similar between genders: 21.3% were overweight (9 females and 10 males) and 75.3% were obese (41 females and 26 males). Of those in the obesity range, 22.5% (13 females and 7 males) were morbidly obese (BMI $\geq$ 40kg/m^2). There was no significant association between BMI and age at diagnosis with diabetes (rho=0.03,p=0.74).

Mean waist circumference was above the recommended target among both genders (111.5±20.7cm and 113.9±17.5cm respectively for females and males). Total body fat (TBF) was considerably above the healthy range among females compared to males (41.9±9.5 % vs 33.1±12.2 %, p<0.001). In contrast, visceral fat (VF) rating was lower amongst females compared to males (11.7±7.9 vs 15.2±5.8, p 0.03). SA ethnicity was significantly associated with a lower BMI (mean 32.67±9.10kg/m^2; p=0.004), lower TBF (35.9±11.4, p 0.025), lower waist circumference (108.9±19.6cm; p=0.034), lower muscle mass (40.1±19.3kg; p=0.02) and lower VF rating (11.2±5.5; p=0.013).

Family history of diabetes and gestational diabetes

The majority of participants (N=72, 80.9%) had at least one first degree family member (parent and/or sibling) diagnosed with diabetes: among these, 49 (68.1%) had a history of maternal diabetes. A first-degree family member diagnosed with diabetes was more common for SA than WE participants (92.5% vs 63.9%, p <0.001) as well as high rate of maternal diabetes (75.5% vs 52.2%, p <0.002). Seventeen females (32.7%) had a previous diagnosis of gestational diabetes, mainly among SA participants. WE women with history of GDM had a mean BMI of 46.7 kg/m^2, compared to a mean BMI of 29.6 kg/m^2 for SA women.

Lifestyle

Across the cohort, 40.4% of patients reported a low intensity physical activity or were not active at all. There was, however, no significant difference in physical activity levels between the genders or ethnic groups. The majority of the cohort were non-smokers (58.4%), whereas 15 (16.9%) were ex-smokers and 22 (24.7%) were still smoking cigarettes. The proportion of active smokers was significantly higher in males compared to females (29.7% v 21.2%; $p<0.05$). Amongst ethnic groups, smoking rates were higher in WE than SA participants (30.6% vs 20.8%).

Similarly, regular alcohol consumption was higher in males than in females and (27% vs 9.6%) and in WE than in SA participants (34.3% vs 3.8%).

Fatty liver and polycystic ovary syndrome

Non-alcoholic fatty liver disease (NAFLD) was diagnosed in 11.2% patients, with WE participants showing higher rates of NAFLD compared to SA participants (16.7% vs 7.5%, $p =0.18$). NAFLD was associated with obesity and higher VF. 28.8% of all women were clinically diagnosed with PCOS. PCOS was more common in WE participants and was associated with higher BMI (39.0 ± 11.1 kg/m^2 vs 33.0 ± 7.9 kg/m^2, $p=0.030$) and VF (12.5 ± 5.6 vs 9.3 ± 4.6, $p= 0.046$) compared to those not diagnosed with the disease. Acanthosis nigricans was detected in 12.4% of the cohort and was observed in females only with those of SA ethnicity having greater propensity than WE ethnicity.

Socio-economic data

Data on the relative level of deprivation of the area from where patients were recruited were obtained calculating the Index of Multiple Deprivation (IMD) 2015. This is the official measure of relative deprivation for small areas in England, called

Lower-layer Super Output Areas (LSOAs)(23). The average rank for the T2DMY cohort was 5730.5±7714.9, ie. 75% of patients recruited were from the most deprived 10% to 20% LSOAs (2nd decile).

Risk factor clustering

There was a considerable clustering of diabetes risk factors within the cohort with over 75% of all subjects having 3 or more of the following risk factors: obesity, family (maternal) history of diabetes, low physical activity, deprivation, acanthosis nigricans and NAFLD **(Table 3)**.

Glycaemic control and vascular disease

More than two-thirds of the patients (67.4%) had evidence of at least one diabetes microvascular complication. All patients had at least one cardiovascular (CV) risk factor in addition to diabetes and almost two-thirds (64%) had two CV risk factors. Established CV disease (including angina, acute coronary syndromes, myocardial infarction and coronary revascularization) was recorded in 11 (11.6%) patients **(Table 4).**

Hypertension was diagnosed in 53.9% of participants, and the recommended target for both systolic and diastolic BP (<130/80 mmHg) was reached in 66 (74.2%) patients while 70 (78.7%) had evidence of dyslipidaemia. Mean $HbA1_C$ of the cohort was 74.3±21.2 mmol/mol (8.9±4.1 %), with only 23.6% of patients achieving the recommended target for HbA1c. Almost two thirds of patients were receiving a combination of OAD(s) and insulin (60.7%) therapies. The mean duration from diagnosis to insulin start was 4.5(±3.5) years and more than a half of the patients (52.8%) started insulin treatment in the first three years after diagnosis **(Table 4).**

DISCUSSION

This study shows that T2DMY comprises a particular sub group of T2DM characterised by a high burden of commonly associated risk factors for both the disease and its long term vascular complications. Susceptibility to develop T2DM at a younger age appears to be related to a confluence of several risk factors: obesity, family (particularly maternal) history of diabetes, low physical activity, deprivation, acanthosis nigricans and non-alcoholic fatty liver disease, and is further enhanced in those from minority ethnic groups and by female gender. These characteristics bear considerable similarity to that observed in children and adolescents suggesting that features seen in paediatric age groups tend to persist in early adulthood (24).

Obesity is a major risk for T2DM and almost all (96.6%) subjects in the present cohort of T2DMY were overweight or obese (25). Obesity rates continue to rise in young people: 1 in 5 children in school year 6 (age ~10 years) in England has been classified as obese (26) and amongst young adults aged 16-24 years, 10% and 12% of males and females respectively are obese (BMI>30 kg/m^2), rising to 18% and 20% respectively for ages 25-34 years (26).

While there are parallel trends between rising levels of obesity and T2DM, the extent to which onset of diabetes at a younger age could be explained by the severity of obesity is unclear. In our cohort, we found a negative but non-significant trend between the degree of adiposity (as measured by BMI at the time of entry into the study) and age of onset of diabetes. As our subjects had a mean duration of 7 years, it is likely that the BMI would have changed during this period making it difficult to explore the association between BMI and age of onset with certainty. Interestingly, however, studies in obese adolescents and children have shown that it is a deteriorating capacity for beta-cell compensation over time and not obesity per se that

has a greater effect on progression from NGT to IGT/diabetes in susceptible individuals (27-29). It is possible that these effects persist in young adulthood. Also, obesity can lead to increased insulin resistance placing further demand on beta-cells thereby unmasking and worsening underlying beta-cell deficiency (30). Thus the mechanisms through which obesity contributes to development of T2DMY are complex and need further investigation. Given that overweight/obesity is present in most individuals with T2DMY and that it is an important modifiable risk factor, prevention and good management when this occurs should remain a high priority to defer or prevent T2DMY.

An important finding in this cohort is the large number of subjects with a strong family history of diabetes and, in particular, a history of maternal diabetes. Earlier studies have shown that family history predicts future risk of T2DM and the likelihood of developing diabetes at a younger age(31). Indeed, for every 10% increase in the number of relatives with diabetes, the age of onset decreased by 1.7 years (32). Studies in PIMA Indians have shown that children born to mothers with a history of obesity or diabetes at the time of pregnancy were 10 times more likely to develop diabetes in youth (33). In another study involving sibling pairs who were born before and after their mothers were diagnosed with diabetes, the risk of diabetes at a younger age was greater amongst those siblings who were exposed to maternal diabetes (34). A high prevalence of maternal diabetes was also seen in participants involved in the TODAY study (multiethnic, multicenter randomized trial in the United States to compare 3 treatment approaches in obese youth with new-onset T2DM) in 10-17 year-olds with T2DM (35). The mechanisms through which maternal diabetes may influence the risk of developing diabetes in childhood are

complex and involve a potentially modifiable interaction of environmental and epigenetic factors.

Consistent with other studies in T2DMY, participants in our study had an adverse risk factor profile similar to or worse than described for older adults with T2DM. Despite the young age, all patients had at least one CV risk factor (in addition to diabetes) and almost two-thirds had two or more. The high burden of risk factors raises important questions regarding the optimal management of these patients. Currently, most risk engines for cardiovascular risk estimation are based on studies in individuals aged above 40 years (36) and their utility in younger people is not validated. Further, most policies and guidelines advocate active screening and the use of cardio-protective agents such as statins in those aged above 40 years (37-39). As a result, many younger patients are likely to not receive adequate cardiovascular protection. These concerns were also highlighted in a recently published Swedish cohort study (40).

More than two thirds of participants had glycated haemoglobin above the recommended levels and over 50% of all subjects were on insulin treatment within 3 years of diagnosis-much earlier than the average of 6 years reported in subjects in the UKPDS(41). Previous studies in adolescents and young adults have identified difficulties in achieving good glycaemic control in this age group (42, 43). The reasons are likely to be multifactorial and include issues such as poor adherence to treatment regimens, lack of data relating to efficacy and therapeutic inertia. Another important reason for poor glycaemic control may be the faster progression of diabetes in younger individuals. Studies in adolescents and children with T2DM have reported a rapid loss of beta-cell function in this age group (10, 27, 29, 44). Indeed, clamp studies in children with T2DM have shown the rate of decline in beta-cell function is almost 3 times faster than in adults (27). These findings have been supported by the

recent evidence from the TODAY trial and the RISE study which also showed a faster decline in beta cell function in youth compared with studies in older adults (45, 46). Our findings support the likelihood of a faster decline in beta-cell function in youth and are consistent with the findings of the UKPDS, which also reported a faster decline in beta-cell function in younger individuals (47).

A striking feature of the cohort was that only a third were on oral hypoglycaemic agents alone with the rest requiring a combination of oral agents and insulin or insulin alone. Metformin was the most commonly prescribed oral agent followed by glitptins and sulfonylureas whereas the use of glitazones, GLP-1RA and SGLT2 inhibitors was negligible. This may reflect the general trend in the prescription of oral agents at the time of commencement of recruitment to the study. Given the effects of glitazones on insulin resistance and the metabolically favourable effects of GLP-1RA and SGLT2 inhibitors these classes of drugs may be more suitable in this age group and may potentially delay the need for insulin treatment (48). The true effectiveness of these agents on disease progression, however, needs to be explored in future trials.

The multi ethnic nature of our cohort allowed us to explore the differences between two ethnic groups. In our cohort, south Asians were predominantly female, and were more likely to have a positive family history and maternal history of T2DM than WE subjects. South Asian participants were also more likely to have features of insulin resistance such as acanthosis nigricans. Although the overall rates of obesity, when adjusted for ethnic specific cut offs, were similar there were subtle differences in anthropometry and body composition between the groups with SA subjects having a lower BMI, waist circumference and lower muscle mass than WE subjects. Interestingly, however, we did not find any significant differences in visceral fat scores between the groups. We suggest that lower muscle mass, rather than fat mass,

could be associated with increased insulin resistance in this ethnic group. These findings are consistent with studies in older T2DM populations, which have shown that an older age at diagnosis is associated with a greater decline in muscle mass (48) and that reduced muscle mass and function is strongly associated with insulin resistance (49, 50). It is well known that certain ethnic groups are disproportionately susceptible to T2DM. In the United Kingdom, people of south Asian and African origin have a 2-4 times greater risk of developing diabetes than local white European population (51). Studies in youth with T2DM have supported these findings and have shown that this predisposition is exaggerated in younger individuals belonging to Hispanic, African American and south Asian ethnic groups (52, 53). Our data provide further evidence that these differences persist in younger individuals and that the distinct phenotypic characteristics of each ethnic group can help to identify people at risk within those groups.

In recent years there has been a significant drive to screen and prevent diabetes (54). Although there is good guidance for screening those aged above 40 years, the criteria for screening in youth are less clear and the relative rarity of the condition requires identification of people at highest risk. Besides obesity and family history, we also observed a higher prevalence of other known risk factors such as lack of physical activity and deprivation in this cohort. Indeed, less than 46 % engaged in recommended levels of physical activity. Physical activity levels were lower amongst SA and more noticeably amongst SA women. Lower levels of physical activity are strongly associated with insulin resistance and risk of T2DM and the observations made in our cohort mirror those seen in older adults with T2DM (51). Given the importance of regular physical activity in the prevention of diabetes, interventions targeted to improve physical activity in this age group would be highly useful.

A remarkably high proportion of individuals (75% in top 2 deciles for most deprived) in our cohort was from deprived backgrounds. These figures are higher than expected and may to some extent be attributed to the catchment area of the hospital where the bulk of recruitment was undertaken. Nevertheless, many studies have shown a close association between socio-economic status and T2DM prevalence (55-57) and this association appears to be stronger in younger age groups as evidenced from studies in children and adolescents (24, 58). The relationship between deprivation and T2DM, and particularly its effect on susceptibility to T2DMY, needs to be explored in greater detail.

Using a combination of 6 main risk factors (obesity, family history, low physical activity, deprivation, acanthosis nigricans and NAFLD), we found that 97 % of the patients had 2 or more risk factors and 77% had 3 or more risk factors. In determining the criteria for screening individuals at risk of T2DMY we recommend using the presence of these risk factors as a guide. Younger individuals presenting with two or more of these factors should be actively screened for T2DMY.

To our knowledge, this is the first study to undertake a detailed characterisation of young adults with T2DM. Further, the ability to compare the differences in phenotypes between ethnic groups adds to the usefulness of these data for identification and characterisation purposes. Our study, however, has certain limitations. It was an exploratory study and sample size was relatively small and also, given that subjects had differing durations of diabetes, we were unable to study the natural history of T2DMY. Further, given the small sample size and also small number of subjects within each ethnic group, the observations and differences seen in our study should be seen as indicative and will need to be confirmed in larger cohorts of well matched ethnic populations. We believe our preliminary findings are of

sufficient interest, however, to promote further studies in this under-researched group of patients.

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Author contributions

Drs Bellary, Prof Barnett, Prof Bailey, Prof Pattison and Mr Raymond contributed to the study design. Dr Lascar and Dr Altaf recruited subjects and collected data. Dr Bellary and Dr Lascar produced the first draft of the manuscript. All authors were involved in the revision of the manuscript and agreed on the final version of the manuscript.

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Table 1. Inclusion and exclusion criteria

Inclusion criteria	Able to give informed consent for the study
	Diagnosed with T2DM according to American Diabetes Association (ADA) criteria (15)
	Diagnosed between age 18 to 40 years
Exclusion criteria	Secondary diabetes e.g. cystic fibrosis- , transplant- or thalassaemia-related diabetes
	Diagnosis of Type 1 diabetes, monogenic diabetes
	Other significant organ system illness or condition (including psychiatric or developmental disorder) that, in the opinion of the investigator, would prevent participation.
	Duration of diabetes $\geq$ 14 years

Table 1: Summary of the key inclusion and exclusion criteria for eligibility to participate in the study.

Table 2. Characteristics of the T2DMY cohort.

Total Cohort N=89. White European (WE) N=36(40.4%); South Asian (SA) N=53(59.6%). Data for African-Caribbean participants not included in analysis due to low numbers but shown separately in appendix 1. Data are *N (%)* unless otherwise specified. *Data are *mean*±*SD.* The probability (p) level refers to differences between the two ethnic groups. ** Overweightness and obesity were calculated considering the different BMI reference ranges by ethnic group (WHO 2004)[14] respectively: WE BMI≥25 kg/m^2 and BMI≥30 kg/m^2; SA BMI≥23 kg/m^2 and BMI≥27.5 kg/m^2. ***Physical activity questionnaire was completed by 78 patients (36WE and 42SA). **** Results for fasting UPCR were available for 62 patients (22WE;40SA) at baseline and for 58 (17WE;41SA) after OGTT. *NAFLD=non-alcoholic fatty liver disease; PCOS=polycystic ovary syndrome; UCPCR=urinary c peptide/creatinine ratio; OGTT=oral glucose tolerance test*

	Total	**WE**	**SA**	***p***
Age (years)*	40.2±7	40.6±6.9	39.9±7.0	*0.64*
Men	37 (41.6)	17 (47.2)	20 (37.7)	*0.50*
Women	52 (58.4)	19 (52.8)	33 (62.3)	
Diabetes Age at diagnosis (years)*	32.5±5.5	33.4±4.9	32.0±5.9	*0.22*
Age diagnosis < 35 years	58 (65.2)	21 (58.3)	37 (69.8)	*0.11*
Diabetes Duration (years)*	7.7±3.8	7.2±4.0	7.9±3.6	*0.39*
Body composition				
BMI (kg/m^2)*	35.05±9.54	38.56±9.21	32.67±9.10	*0.004*
Overweight**	19 (21.3)	6 (16.7)	13 (24.5)	*0.10*
Obese**	67 (75.3)	30 (83.3)	37 (69.8)	*0.100*

Total body Fat*	38.2±11.5	41.6±11.1	35.9±11.4	*.025*
Muscle mass (kg)*	44.4±18.2	50.2±15.1	40.1±19.3	*0.020*
Visceral fat*	13±7.4	15.5±8.9	11.2±5.5	*0.013*
Waist circumference (cm)*	112.5±19.3	117.9±17.9	108.9±19.6	*0.034*
Neck circumference (cm)*	41.5±5.9	43±7.2	40.4±4.8	*0.06*
At least 1 first degree family member with T2DM	72 (80.9)	23 (63.9)	49 (92.5)	*0.001*
Maternal diabetes	49 (55.1)	12 (33.3)	37 (69.8)	*0.002*
History of gestational diabetes	17 (32.7)	5 (26.3)	12 (36.4)	*0.56*
Lifestyle				
Current cigarette smokers	22 (24.7)	11 (30.6)	11(20.8)	*0.001*
Current alcohol drinkers	14 (15.7)	12 (33.3)	2 (3.8)	*<0.001*
Physical activity intensity*:**				
Low	36 (46.2)	13 (40.6)	23 (50)	
Moderate	26 (33.3)	15 (41.7)	11 (26.2)	*0.48*
High	16 (20.5)	8 (22.2)	8 (19.0)	
AcanthosisNigricans	11 (12.4)	1 (2.8)	10 (18.9)	*0.032*
NAFLD	10 (11.2)	6 (16.7)	4 (7.5)	*0.18*
PCOS	15 (28.8)	8 (42.1)	7 (21.2)	*0.23*
Vitamin D (nmol/L)*	35.5±20.9	40.8±21.1	33.0±20.9	*0.10*
UCPCR (nmol/mmol)**:** Fasting* 30 min post-OGTT* 30 min post-OGTT in patients on insulin*	 0.40±0.69 1.0±1.5 0.80±1.00	 0.41±0.38 1.01±1.35 1.01±1.35	 0.40±0.82 1.01±1.59 0.69±0.79	 *0.94* *0.85* *0.11*
% of those in top 2 deciles for most deprived (IMD)	65 (73)	25 (69.4)	40 (75.5)	*0.73*

Table 3: Showing the % of people with the number of risk factors associated with T2DMY. The six risk factors included are: obesity, family (maternal) history, low physical activity, deprivation (20% most deprived), acanthosis nigricans and non-alcoholic fatty liver disease

N° OF RISK FACTORS	**WE N(%)**	**SA N (%)**	**Total N (%)**
1	1(2.8)	1(1.9)	2 (2.2)
2	10(27.8)	8(15.1)	18 (20.2)
3	10(27.8)	16(30.2)	26 (29.2)
4	13(36.1)	20(37.7)	33 (37.1)
5	2(5.6)	7(13.2)	9 (10.1)
6	0	1(1.9)	1 (1.2)
Total	36	53	89

Table 4: The proportion of patients with known risk factors in the whole cohort and also in the WE and SA ethnic groups. Data are *N (%)* unless otherwise specified. *Data are *mean±SD* . ** includes patients with Cardio vascular risk factors for atherosclerotic cardiovascular disease (ASCVD) in addition to diabetes. CV risk factors included having at least one of the following: smoking, overweight/obesity, LDL>2.6mmol/L, hypertension [ref ADA2012]. *** 0 indicates none of the patients. *OAD= Oral Anti Diabetes agents; NIIA= Non-Insulin Injectable Agents*

	Total	White Europeans	South Asians	*P value*
Hypertension	48 (53.9)	23(63.9)	25(47.2)	*0.18*
Dyslipidaemia	70 (78.7)	31 (86.1)	39 (73.6)	*0.25*
HbA_{1c} (mmol/mol)*	74.3±21.2	74.1±24.3	73.4±19.1	*0.89*
HbA1c≤53 mmol/mol	21 (23.6)	11 (30.6)	10 (18.9)	*0.31*
Treatment				
OAD alone	32 (36)	13 (36.1)	19 (35.8)	*1.00*
OAD + Insulin	54 (60.7)	21 (58.3)	33 (62.3)	*0.71*
Insulin alone	2 (2.2)	2 (5.6)	0***	*0.31*
OAD + NIIA				
Metformin	*82 (92.1)*	*33 (91.7)*	*49 (92.5)*	1.00
DPP4 inhibitor	*34 (38.2)*	*15 (41.7)*	*19 (35.8)*	0.74
Sulphonylurea	*18 (20.2)*	*6(16.7)*	*12 (22.6)*	0.68
GLP1 analogue	*8 (9)*	*6 (16.7)*	*2 (3.8)*	0.09
Glitazones	*3 (3.4)*	*2 (5.6)*	*1 (1.9)*	0.73
SGLT2 inhibitor	*1 (1.1)*	*0***	*1 (1.9)*	1.00
Microvascular complications				
Retinopathy	33 (37.1)	11 (30.6)	22 (41.5)	*0.41*
Nephropathy	31 (34.8)	12 (33.3)	19 (35.8)	*0.73*
Neuropathy	31 (34.8)	11 (30.6)	20 (37.7)	*0.64*
ASCVD* **				
One CV risk factor	89 (100)	36 (100)	53(100)	
At least two CV risk factors	57 (64)	26 (72.2)	31 (58.5)	*0.27*
Established CV disease	5 (5.6)	3 (8.3)	2 (3.8)	*0.65*
Established cerebrovascular disease	7 (7.9)	2 (5.6)	5 (9.4)	*0.79*