ORIGINAL ARTICLE

Ethnic Differences in Glycaemic Control and Complications: The Adult Diabetes Control and Management (ADCM), Malaysia

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SUMMARY

Introduction: Ethnicity is an important factor in diabetes care. The understanding of its effect in this country may help to improve diabetes care, glycaemic control and diabetic complication rates. This study was to determine the diabetes control profile in relation to complication rates between the three main ethnics group in Malaysia.

Methods: This nested cross-sectional study was part of the Audit of Diabetes Control and Management (ADCM), an ongoing cohort patient registry focused on diabetes control and management in the primary care setting in Malaysia. This registry registers all diabetes patients aged 18 years old and above. Demographic data, diabetes duration, treatment modalities, as well as various risk factors and diabetes complications are reported. Data was handled by statisticians using STATA version 9.

Results: A total of 20330 patients from 54 health centers were registered at the time of this report. The majority were type 2 diabetics (99.1%) of whom 56.6% were female. The mean age was 57.9 years (SD 11.58). Malay accounted for 56.3%, Chinese 19.5% and Indian 22.5%. There were 30.3% who attained HbA1c < 7%. Among three main races more Chinese had HbA1c < 6.5% (Chi-square: $X2=71.64$, $p< 0.001$), but did not show less complications of nephropathy (Indian suffered significantly more nephropathy, Chi-square: $X2=168.76$, $p< 0.001$), ischaemic heart disease (Chi-square: $X2=5.67$, $p = 0.532$) and stroke (Chi-square: $X2=15.38$, $p = 0.078$).

Conclusion: This study has again emphasized the existence of ethnic differences in glycaemic control and complication profiles. The Chinese diabetics suffer as many diabetes-related complications despite better glycaemic control. Further studies will need to look into other socio-genetic factors in order to provide a more personalized effective diabetes care.

INTRODUCTION

Ethnicity has long been recognized as an important health risk factor in many illnesses including diabetes mellitus [1].

True differences in an individual's genetic make-up may lead to real variations in multiple physiologic, metabolic and pathologic manifestations of a particular condition or disease[2-8]. Most of the current body of evidence shows that ethnicity is a surrogate determinant of the complex socio-cultural background of the diabetic patient[9-12]. Thus, though lacking in specificity, the fact that ethnicity is a surrogate determinant may turn out to be a summative factor in determining whether an individual may contract the disease, be useful as a prognosticator for a country like Malaysia which is struggling to contain the increasing prevalence of this disease[13].

Glycaemic control has been well documented as being significantly associated with diabetic complications with clear differences attributable to ethnicity[14]. Indians in Singapore were found to be more insulin resistant and had a higher prevalence for type 2 diabetes when compared to the Chinese and the Malays[15-16]. Among those who developed macrovascular complications, the Indian ethnic group was also the largest sufferers of ischaemic heart disease (IHD), despite equivocal differences in glycaemic control and risk factors[16]. In an Australian study comparing six different ethnic groups including Chinese and Indians with Anglo-Celtics, both Chinese and Indian diabetics were found to have a higher risk of albuminuria[17]. When compared to their Caucasian counterparts, Latino-American, African-American and Mexican-American type 2 diabetics were reported to have a higher mean HbA1c, and in the case of African-American and Mexican-Americans, a higher incidence of proteinuria as well[11,18]. African-American type 2 diabetic patients were also reported to have a 2.6-fold higher adjusted risk of developing end-stage renal disease as compared to Caucasians[19]. D'Costa et al. reported that Pakistanis and Indians in Edinburgh were 4-6 times more likely to develop type 2 diabetes and had a higher risk of developing diabetic complications, with 40% higher mortality rate when compared to their Caucasian neighbors[20,21].

There have been some Malaysian studies that also reported ethnic differences in glycaemic control[22-24]. However, most of these were from big tertiary hospitals and there have been almost none done with a large cohort at the primary care level[25]. Unearthing the background information about ethnic differences in glycaemic control laid the foundation for this study which seeks to examine the differences in diabetes

control and susceptibility to diabetic complications between the three major ethnic groups in Malaysia in a large primary care level cohort.

Understanding these ethnic differences in diabetes at a primary care level where the disease is largely managed in Malaysia may help us to be more patient-centered and relevant in terms of giving counseling, screening for complications and redistribution of campaign strategies. The mindset and strategy changes resulting from this study may well help curtail the rampage of diabetes on the Malaysian population.

MATERIALS AND METHODS
This nested cross-sectional study was part of the Audit of Diabetes Control and Management (ADCM), an ongoing cohort patient registry focused on diabetes control and management in the primary care setting in Malaysia. The study adheres to Ministry of Health Malaysia guidelines and has received approval from the Ministry's Medical Research Ethics Committee (MREC). ADCM was begun as a pilot project in the state of Negeri Sembilan in May 2008 to monitor the provision of diabetes care in order to formulate better treatment modalities for patients as well as providing factual evidence for economic planning and policy making. It originally began with less than 30 source data providers (SDPs) which were mainly government health clinics and some hospitals and now has expanded to cover nine states and federal territories with 303 SDPs. This study utilized data from 54 SDPs over three states from May 2008 to December 2008.

Trained nurses, medical assistants, medical officers and family medicine specialists at the SDP register their patients aged 18years old and above annually via an online system with a case report form (CRF) [26-27]. The CRF covers variables such as demographical, diabetes history, treatment modalities, risk factors for complications of diabetes and complications themselves when present. The detailed methodology of this study had been described elsewhere [28].

Patients with Type 2 Diabetes (T2D) were defined as those who fulfilled all these criteria: (1) either documented diagnosis of diabetes mellitus according to the World Health Organisation (WHO) criteria or (2) those who were on treatment for diabetes, either via lifestyle modification, oral anti-diabetics or insulin. Estimated glomerular filtration rate (eGFR) was calculated using Cockroft-Gault formula. Percentages of each diabetic complication was calculated based on the total number of each ethnic group as the denominator and not the number of tests done or examinations performed. This was to avoid over-estimation of certain complication rates because there is a general rule of being more selective with screening for complications or examinations for symptomatic patients due to cost and staff constraints in our current practice. Data was analysed using Data Analysis and Statistical Software (Stata) version 9. Chi-square or Fisher's Exact tests or ANOVA (analysis of variance) were used to determine the association of categorical data. Test of significance were two-tailed, and a significance level was set at $p < 0.05$.

RESULTS
A total of 20330 patients were registered in ADCM as of 31st December 2008 with the demographic data breakdown as shown in Table I. The majority were T2D (99.1%). The proportion of the three main ethnic groups was not similar to the distribution of the Malaysian national population as evidenced by over-representation of Indians (22.5%) in this study.[29] The proportion of patients whose HbA1c was at targeted treatment levels of < 7% and < 6.5% was 30.3% and 18% respectively out of the total who underwent this test as compared to Table I which shows the proportion who achieved both the HbA1c targets out of the total number of patients in the registry. The prevalence of those with complications from diabetes from the study population for stroke, IHD, foot problems, retinopathy and nephropathy was 2.5%, 8.1%, 3%, 4.2% and 9.5% respectively (see Figure 1). The proportion of each ethnic group screened for diabetic complications were as shown in Table II.

Table I: Demographic Data of the ADCM by 31st December 2008, n= 20330 (100%)

Clinical Profiles	n (%)
Age, mean (SD)	57.9 (11.6)
Female	11504 (56.6)
Malay	11443 (56.3)
Chinese	3969 (19.5)
Indian	4567 (22.5)
Others	351 (1.7)
HbA1c done	
Malay	
Chinese	
Indian	13041 (64.1)
7743 (67.7)	
2301 (58)	
2823 (61.8)	
HbA1c, mean (SD)	8.34 (2.16)
HbA1c < 7%	3950 (19.4)
HbA1c < 6.5%	2350 (11.6)

ADCM Audit of Diabetes Control and Management

Table II: Proportion of Diabetic Complications Documented for each Ethnic Group in the past one year, n (%)

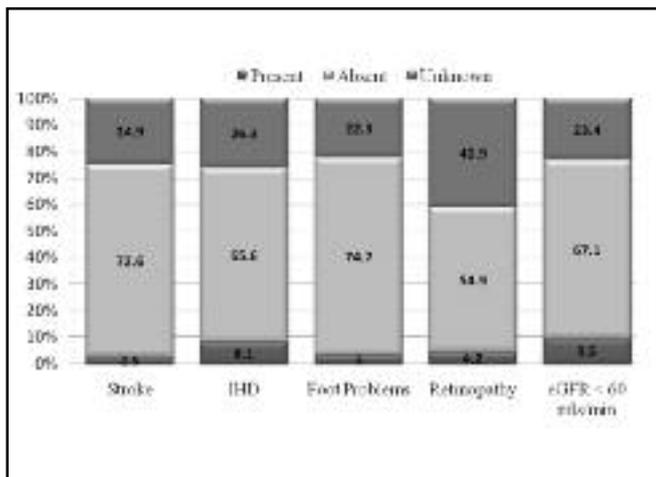| Diabetic Complications	Malay		Chinese		Indian	
	Present	Unknown	Present	Unknown	Present	Unknown
Stroke	8649 (75.6)	2794 (24.4)	2928 (73.8)	1041 (26.2)	3257 (71.3)	1310 (28.7)
IHD8420 (73.6)	3023 (26.4)	2883 (72.6)	1086 (27.4)	3225 (70.6)	1342 (29.4)	
Diabetic foot problems	8932 (78.1)	2511 (21.9)	3120 (78.6)	849 (21.4)	3483 (76.3)	1084 (23.7)
Retinopathy	6943 (60.7)	4500 (39.3)	2358 (59.4)	1611 (40.6)	2493 (54.6)	2074 (45.4)
Nephropathy-						
eGFR < 60 mls/min	9226 (80.6)	2217 (19.4)	2763 (69.6)	1206 (30.4)	3365 (73.7)	1202 (26.3)
Nephropathy-Microalbuminuria	4961 (43.4)	6482 (56.6)	1542 (38.9)	2427 (61.1)	1737 (38)	2830 (62)

Fig. 1: Proportion of Diabetic Complications amongst the ADCM cohorts by 31st December 2008

χ^2 shown are Chi-square tests

Fig. 2: Percentage of complications amongst the three main ethnic groups.

The Chinese, despite having the lowest mean HbA1c (7.8%) amongst three ethnic (ANOVA: F4= 42.18, p < 0.001), did not have lesser diabetic complications when compared to the other ethnic groups, rather, they had the highest prevalence of retinopathy instead. The Indians with the highest mean HbA1c seemed to suffer the most from nephropathy and were the second highest sufferers from IHD, though the associations between these rates and HbA1c were not of statistical significance.

DISCUSSION

Two thirds of the study population managed to have HbA1c tested at least once a year and of these, slightly less than one third achieved a HbA1c of < 7%. There were more Indians as compared to Chinese in the study, which was not representative of the national ethnic composition, but reflects the findings of NHMS III which found that the prevalence of diabetes amongst Indians was 19.9%, almost double that of the other ethnic groups [13]. Another reason to explain the skew in demographics causing it not to reflect the national compositions could be that all the SDPs were government-based health care facilities which are known to be not well-frequented by those of the Chinese ethnic group [13].

There were some ethnic differences in the American study where more of the Caucasian-Americans had their LDL-C tested and eyes checked when compared to the African-Americans. This study showed that there was no difference in the number of different ethnic groups being selected to undergo screening tests or examinations. This came as no surprise as there is a high level of national integration throughout all levels of the healthcare system without any history of ethnic discrimination ever being documented.

Similar ethnic disparities in glycaemic control have been reported before, with one being a study based in major Malaysian hospitals [22] and another in Singapore which found that the Chinese as an ethnic group had the best glycaemic control [16]. These differences could be due to the fact that Indians have been 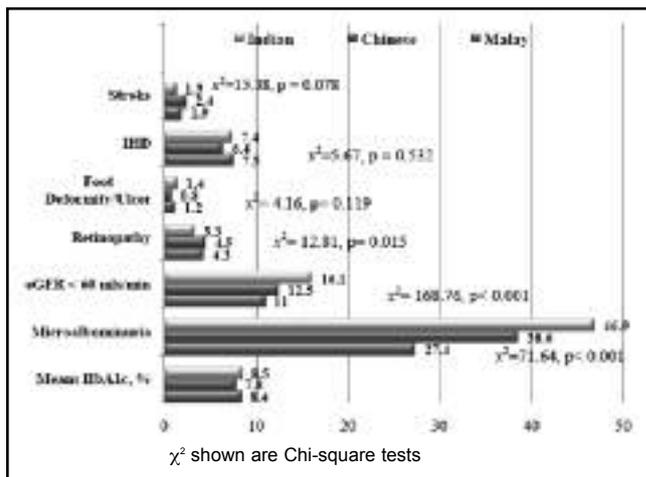found to have higher insulin resistance than Chinese and Malays15 and high insulin resistance may cause more difficulties in glycaemic control. Another Singaporean study reported that Asian Indians had poorer glycaemic control when compared to the Chinese but were less prone to having either microalbuminuria or macroalbuminuria [30] though they had a higher risk of IHD when compared to other ethnic groups, according to another study also done in Singapore [16]. Wong TY *et. al.* reported from a multi-ethnic cohort in the United States that the ethnic factor was found not to be an independent predictor for both diabetic retinopathy and macular oedema as analyses accounted for other concrete predictors such as longer duration of diabetes, higher fasting serum glucose, use of diabetic oral medication or insulin, and greater waist-hip ratio [31]. On the contrary however, this study showed that Indians were the most affected ethnic group from complications such namely nephropathy and diabetic foot problems, a finding somewhat corroborated by NHMS III's conclusions that Indians in this country had the highest rate of lower limb amputations compared to other ethnic groups.

Besides this, the rates of other diabetic complications were not significantly different amongst the ethnic groups despite different levels of glycaemic control. A study conducted by Geirgeo L. Burke *et al* in the United States noted that the Chinese American, despite having lower rates of obesity and overweight (higher of these were shown to be associated with hypertension, hyperlipidaemia and dysglycaemia) but showed similar relationship between greater body size and cardiovascular diseases as in other ethnic groups [32]. The reason for this similar observation of the better glycaemic control but not better complication profiles among the Chinese could not be alluded to our study with explanation given below. We believe this may reflect the under-reporting of complications as a whole but more so for renal complications' status as about 60% of patients had 'unknown' status when being assessed for urine protein in the study.

The other possible reasons that can explain this phenomenon were the confounding effect of concurrent hypertension and/or dyslipidaemia [33,34]. A better control of blood pressure (a

10/5-mmHg difference) appeared to confer more benefits than those resulting from the intensified glycaemic control strategy for both the macrovascular and microvascular endpoints [35]. The increased risks of death and cardiovascular events in Framingham subjects were reported to be attributed much by the coexistent hypertension (44% and 41% respectively) in comparison to that attributable to diabetes (7% and 9%) [36].

LIMITATION

Further interpretation of the relationship between ethnicity and other available socio-clinical parameters (such as waist circumference, body mass index, blood pressure control and lipid profiles) as well as the depth of their influence upon glycaemic control and diabetic complications was limited by absence of more advanced statistical analyses. We believe there could be significant ethnic differences in terms of the proportion of each ethnic group in achieving target waist circumference, body mass index, and blood pressure and lipid profiles. There are other possible clinical variables that might contribute to the current complications profile of the three ethnic groups but were not captured by this study such as are socio-economic status, education level, occupation, frequency of exercise, smoking status, rural or urban area of residence and depression [37].

However, it was felt that it was adequate at this juncture for the registry, being in its infancy at the time, to document these ethnic differences in glycaemic control and counter-check the validity of these findings with other similar studies done locally and in the region.

Findings from the registry at that stage in 2008 was expected to, and as a matter of fact, did draw the attention of the nation's stake-holders as to the seriousness of diabetic epidemic, and encouraged more eager participation of SDP as well as serving to kindle the diabetes research at the primary care level. As the registry continues to grow, there is a need to improve the CRF so as to include more clinically relevant variables to further explore in depth the complex correlation between various predictors in determining glycaemic control and onset of complications.

Multiple data transfer before and during data entry into the online system carries with it many pitfalls and the risk of increasing biases. For instance, in some cases latest HbA1c results were not captured due to missing documentation or filing; some complications were not noted because of poor communication or consultation between the patients and health care providers. This was compounded by illegible hand-writing and multiple patient charts present currently in practice which often made accuracy of identifying variables and data entry difficult at the early stage. Nevertheless, with improved training and teamwork we believe these issues were ameliorated and have become minimal at present.

CONCLUSION

The relationships between diabetic control and complications are not as straight forward as expected. There must be other possible socio-genetic factors underpinning the development of diabetes as evidenced by Chinese diabetics suffering from as many complications despite better disease control compared to other ethnic groups. Other comorbids of diabetes mellitus such as hypertension and/or dyslipidaemia may pose larger effect on diabetes-related complication than glycaemic control. Hence, future studies in this aspect would need to cover more clinical and psychosocial variables in order to discover the possible causes of ethnic differences in diabetic complications beside glycaemic control.

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