Prevalence of Impaired Glucose Tolerance and Diabetes among patients with Impaired Fasting Blood Sugar in Seria Health Centre.

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ABSTRACT

Introduction: Fasting Plasma Glucose test is the mostly used screening test for Diabetes Mellitus in Brunei Darussalam. Oral Glucose Tolerance Test is recommended to determine exact glucose tolerance status if Fasting Plasma Glucose is impaired between 6.1 mmol/L and 6.9 mmol/L. It was assumed that there would be some undiagnosed Diabetes Mellitus and Impaired Glucose Tolerance among those with impaired Fasting Plasma Glucose but local data about their exact glucose tolerance status were not available. **Materials and Methods:** Oral Glucose Tolerance Test results of 59 patients with impaired Fasting Plasma Glucose in Seria Health Centre during three-year period (1st Nov 2012 - 31st Oct 2015) were reviewed to determine the proportion of undiagnosed Diabetes Mellitus, Impaired Glucose Tolerance, pure Impaired Fasting Glucose and to find the factors associated with different degree of glucose tolerance. **Results:** The finding revealed that 47.5 % (n=28) of sample were undiagnosed Diabetic, 22 % (n=13) with Impaired Glucose Tolerance, 6.8% (n=4) with pure Impaired Fasting Glucose and 23.7 % (n=14) were normoglycaemic. Among the undiagnosed diabetic patients (n=28), 2-hour Plasma Glucose test could detect 92.7 % (n=26) of them but Fasting Plasma Glucose test could detect only 42.9% (n=12) of them as Diabetics. More than half of these patients, 57.1% (n=16) would be misdiagnosed if Fasting Plasma Glucose test alone was repeated on their follow up. The sociodemographic factors and presence of risk factors for Diabetes showed no significant association with different degree of glucose tolerance. **Conclusion:** The study indicates that patients with impaired Fasting Plasma Glucose should be further tested with Oral Glucose Tolerance Test on follow up visits since repeating Fasting Plasma Glucose test alone could fail to detect Impaired Glucose Tolerance and 57% of Diabetes.

Keywords: Diabetes Mellitus, Oral Glucose Tolerance Test, Impaired Fasting Glucose, Impaired Glucose Tolerance.

INTRODUCTION

Diabetes Mellitus (DM) is the third leading cause of death in Brunei Darussalam for decades.[1;2] Prevalence of DM in Brunei was 12.4% and it was estimated that 44% of adult diabetes cases in the community were undiagnosed.[3]

It is important to diagnose DM in early stage and treat them aggressively and effectively because the longer a person lives with undiagnosed and untreated diabetes, the

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worse the health outcomes are.[4] Brunei Darussalam's BruMap-NCD targets to halt the rise in diabetes and Health Screening Services for Non-communicable Diseases (NCD) in Primary Health Centres were started in 2013.[5]

Diabetes can be diagnosed by measuring Fasting Plasma Glucose (FPG), 2-hour Oral Glucose Tolerance Test (OGTT) or glycated haemoglobin (HbA1c).[6;7] FPG is routinely used to screen for DM at Primary Health Centres in Brunei Darussalam. Those with FPG 7.0 mmol/ L and above are diagnosed with Diabetes.[4;7;8] FPG 6.0 mmol/L or less is considered normoglycaemia and FPG level between 6.1 mmol/L and 6.9 mmol/ L is considered as Impaired Fasting Glucose state (IFG).[7-12] Any abnormal FPG result needs further confirmation by one of the 3 tests mentioned previously.[13]

Two hour Plasma Glucose (2hPG) level 11.1 mmol/ L is diagnostic level for Diabetes while 2hPG between 7.8 mmol/L and 11.0 mmol/L is diagnosed as Impaired Glucose Tolerance (IGT) and 2hPG less than 7.8 mmol/L is considered normal.[7-12]

It is assumed that there would be some undiagnosed DM and IGT among those with impaired FPG level between 6.1 mmol/L and 6.9 mmol/ L, whose diagnosis could be confirmed by OGTT tests. OGTT test is recommended in Clinical Practice Guidelines of Brunei Darussalam to determine the exact glucose tolerance status if a person has impaired FPG.[7] However, data on the proportion of patients with IFG who subsequently undergo OGTT at Primary Health Centres, who are later diagnosed with DM, is not available. Hence it is commonly observed that despite recommendation to conduct OGTT in local Clinical Practice Guidelines, many patients with IFG are still tested with repeat FPG inappropriately.

This study's primary objective is to evaluate the proportion of patients with pure IFG, IGT and undiagnosed DM among patients with initial impaired FPG. Secondary objective is to investigate the associations of sociodemographic factors and presence of risk factors for DM of the patients with different degree of glucose tolerance.

MATERIALS AND METHODS

This was a retrospective cross-sectional study of patients attending Seria Health Centre during a three-year period from 1st November 2012 to 31st October 2015. Seria Health Centre is in the District of Belait, which provide an outpatient service to the town of Seria and the surrounding area, with a recorded annual outpatient attendance of 20,678 in 2012. [2] Clinical data of patients with OGTT test performed during the study period were extracted from the phlebotomy registry and their blood results and clinical details were extracted from their medical records. Patients aged over 18 years with initial FPG between 6.1-6.9 mmol/L were included in the study. Pregnant mothers, previously diagnosed DM and patients who were follow up in other health facilities were excluded.

Those who met inclusion criteria were selected for the study and their medical records were reviewed. The data was collected by using the data collection form for each patient and transferred to a Microsoft Excel spreadsheet for analysis.

OGTT test procedures in Seria HC

Patients who need to check OGTT were referred to phlebotomist in Seria Health Centre for instructions and appointment. Patients were explained the procedure, instructed to take usual diet on prior days but to fast for 8 hours before appointment. The first blood sample was taken as baseline FPG. Patients were instructed to ingest 75 G of glucose provided in drinking water after taking first blood

Table 1: Socio-demographic and risk factors in relation with different degrees of Glucose Tolerance.

Socio-demographic factors	Degree of Glucose Tolerance				
	Normal N=14 (23.7%)	**IFG N=4 (6.8%)**	**IGT N=13 (22.0%)**	**DM N=28 (47.5%)**	**Total N=59 (100%)**
Age					
< 40 years	1 (7.1)	0 (0)	2(15.4)	2 (7.1)	5 (8.5)
40-59 years	7 (50.0)	3 (75.0)	4 (30.8)	12(42.9)	26 (44.0)
60 years and above	6 (42.9)	1 (25.0)	7 (53.8)	14 (50.0)	28 (47.5)
Gender					
Male	5 (35.7)	2 (50)	2 (15.4)	12(42.9)	21 (35.6)
Female	9 (64.3)	2 (50)	11(84.6)	16(57.1)	38 (64.4)
Co-morbidities/Risk Factors					
Family history of DM	2 (14.3)	2 (50)	1 (7.7)	4 (14.3)	9 (15.3)
Obese with sedentary life style (BMI > 25)	11(78.6)	4 (100)	10(76.9)	21 (75)	46 (78)
Hypertension	11(78.6)	3 (75)	11 (84.6)	25 (89.3)	50 (84.7)
Previous gestational diabetes mellitus	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Polycystic ovary syndrome with BMI> 30	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Triglyceride level >2.82 mmol/L	4 (28.6)	0 (0)	1 (7.7)	5 (17.9)	10 (16.9)
Status of body weight					
Normal	2 (14.3)	0 (0)	1 (7.7)	3 (10.7)	6 (10.2)
Over weight	7 (50)	1 (25)	9 (69.2)	16(57.1)	33 (55.9)
Obese	5 (35.7)	3 (75)	3 (23.1)	9 (32.1)	20 (33.9)
Cumulative Risk Factors					
0-1 Risk Factor	3 (21.4)	1 (25)	4 (30.7)	7 (24.9)	15 (25.5)
2 Risk factors	8 (57.1)	1 (25)	6 (46.2)	15(53.6)	30 (50.8)
>3 Risk Factors	3 (21.5)	2 (50)	3 (23.1)	6 (21.5)	14 (23.7)

sample. A second sample was taken as 2hPG, 2 hours after ingestion of the glucose solution. Specimen were sent to Raja Isteri Pengiran Anak Saleha (RIPAS) hospital Laboratory for analysis using glucose oxidase method. WHO's definition criteria which was adopt by Brunei Clinical Practice Guidelines was used to diagnose different level of glucose tolerance (Annex 1).[7;8]

Statistical Analysis

The proportions of different degree of glucose tolerance were analysed by frequency distribution tables. The associations between their demographic factors, presence of risk factors for diabetes and different level of Glucose tolerance were further analysed by Chi-square test and Logistic Regression analysis, using IBM SPSS version 22 statistical package. The risk factors of diabetes described in Clinical Practice Guidelines of Brunei Darussalam were used for this analysis (Annex 2).[7]

RESULTS

A total of 59 patients met sampling criteria for study. Our results showed that for patients with initial impaired FPG, a subsequent OGTT according to the recommendation made by guidelines revealed that 47.5% (n=28) of them were confirmed to have undiagnosed DM, 22% (n=13) were categorised as IGT, 6.8 % (n=4) were diagnosed as pure IFG and 23.7 % (n=14) were normoglycaemic. The distribution of sociodemographic factors and risk factors of the patients in relation to different degree of glucose tolerance are demonstrated in Table 1.

Table 2: Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of FPG and 2hPG tests.

Validity	DM by FPG	DM by 2hPG
Sensitivity	42.86 %	92.86 %
Specificity	100 %	100 %
PPV	100 %	100 %
NPV	65.96 %	93.94 %

Table 3: Association between patient factors and different degree of glucose tolerance.

Risk Factors	OR	95% Confidence Interval	*p value*
< 40 yrs*			0.79
40-59 yrs	1.11	0.13-9.43	0.93
60 yrs and above	1.84	0.17-9.51	0.61
Male*			
Female	0.55	0.16-1.96	0.35
Malay*			0.41
Chinese	0.40	0.10-1.69	0.22
Others	0.83	0.16-4.19	0.82
No Family History of Diabetes*			
Family History of Diabetes	1.83	0.19-18.04	0.61
No Hypertension*			
Hypertension	2.78	0.31-24.52	0.36
Triglyceride level <2.82 mmol/L*			
Triglyceride level >2.82 mmol/L	1.25	0.16-9.94	0.83
Normal *			0.91
Over weight	1.63	0.14-19.13	0.70
Obese	1.37	0.11-16.76	0.81
Patients with 0-1 Risk Factors*			0.73
Patients with 2 Risk Factors	0.51	0.07-4.01	0.52
Patients with 3-4 Risk Factors	0.29	0.01-6.31	0.43

* Reference group

Of the 28 patients with undiagnosed diabetes based on OGTT, the 2hPG fraction of OGTT test could detect 92.7 % (n=26) of the undiagnosed diabetic patients but FPG test could only detect 42.9% (n=12). The validity of two fractions of OGTT test for Diabetes Mellitus are illustrated in Table 2. 2hPG showed higher sensitivity (92.9% vs 42.9%) and negative predictive value (93.9% vs 66%) compared to FPG.

The association of sociodemographic factors and presence of risk factors for DM of the patients with different degree of glucose tolerance were further analysed by multiple logistic regression analysis (Table 3). None of the patient factors showed significant association with different degree of glucose tolerance. The outcome of OGTT test among IFG patients was further grouped into two; diabetes and non-diabetes according to WHO diagnostic criteria (Annex 1) and was tested for any association with the presence of risk factors in the patients. No statistically significant association was found with Chi square analysis for diabetes and presence of multiple risk factors (Table 4).

DISCUSSION

The findings highlighted that almost half of sample population with FPG 6.1 - 6.9 mmol/L were undiagnosed diabetes based on OGTT testing. Repeating FPG test alone at their follow up clinic visits, which is currently being performed by some clinics, could miss their diagnosis and early intervention and treatment would not have been started. Our study showed that FPG testing has a low sensitivity compared to OGTT and this has been reported by other study to be between 40% and 65%.[13] FPG test also failed to diagnose IGT which were present in 22% of our study population.

Our results add further support to the Clinical Practice Guidelines of Brunei Darussalam to recommend an OGTT to determine the exact glucose tolerance status if a patient

Table 4: Association of multiple risk factors with final diagnosis in patients with IFG.

Cumulative Risk Factors	Final Diagnosis			Chi sq value	df	*p value*
	No DM N=31(%)	DM N=28(%)	Total N=59 (%)			
0-1 Risk Factor	8 (25.8)	7 (25)	15 (25.4)	0.20	2	*0.905*
2 Risk Factors	15 (48.4)	15 (53.6)	30 (50.8)			
3-4 Risk Factors	8 (25.8)	6 (21.4)	14 (23.7)			

is noted to have impaired FPG.[7] Thus all patients with FPG 6.1 - 6.9mmol/L should be tested with OGTT to determine their exact glucose tolerance level to ensure not to miss the diagnosis of diabetes in early stage since those with IGT which is also highly associated with increased risk of cardiovascular disease, including heart disease, stroke and peripheral vascular disease.[13]

Recently, many studies have proved that HbA1c test also can be used as screening and diagnostic test for diabetes. However, HbA1c may be affected by a variety of genetic, haematological and illness-related factors.[11] Diagnostic cut off level of HbA1c also varies in different centres. American Diabetes Association and WHO set the diagnostic level of HbA1c at 6.5% but Clinical Practice Guidelines in Brunei accepted the diagnostic level at 7%.[7;11;14] It is important to consider that a value of less than 6.5% does not exclude diabetes diagnosed using glucose tests if HbA1c test is used as confirmatory test to diagnose DM.[11] As a result, replacing OGTT test with HbA1c as confirmatory test is still controvesial. Combination of FPG and OGTT test is still considered as gold standard in defining prediabetes and DM.[15;16]

Limitations

This study was conducted as a pilot survey in a single Healthcare in the Belait district, which accounts for the small sample size, a major limitation to the study design. This may have resulted in a non-significant finding on multiple logistic regression analysis of the associated risk factors. However, our results is valid in that performing a repeat FPG alone is not clinically appropriate since more than half of the test sample will miss out on a diagnosis of diabetes if present. The further follow up study to the patients with IFG and IGT may be beneficial to understand the progression towards diabetes and to explore modifiable risk factors among these patients.

CONCLUSION

Based on an OGTT, nearly half (47.5%) of patients attending Seria Health Centre, whose initial FPG showed an IFG picture with glucose levels between 6.1 mmol/L and 6.9 mmol/L were confirmed as undiagnosed DM. If only a repeat FPG was carried out as a confirmatory test, instead of an OGTT, more than half (57.1%) of these patients with undiagnosed DM would be misdiagnosed as not diabetic. The study highlighted that all patients with IFG should be further tested with OGTT as recommended by the Clinical Practice Guidelines in Brunei Darussalam, to detect undiagnosed DM and IGT. Further study at multiple health centres with larger sample size may be required to validate these findings and explore the associated risk factors for different level of glucose tolerance.

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Annex 1. Definition and diagnosis of Diabetes Mellitus and intermediate hyperglycaemia by WHO. [8]

Test	Impaired Fasting Glucose (IFG)	Impaired Glucose Tolerance (IGT)	Diabetes Mellitus (DM)
Fasting Plasma Glucose (FPG)	6.1 -6.9 mmol/L	6.1 -6.9 mmol/L	7.0 mmol/L or more
2 –h Plasma Glucose (2hPG)	Less than 7.8 mmol/L	7.8 to 11.0 mmol/L	11.1 mmol/L or more

Annex 2. Risk factors for Diabetes[7]

- Family history of diabetes in first degree relatives
- Obese with sedentary life style (BMI $\geq$ 25)
- Ischemic heart disease, cerebrovascular disease, peripheral vascular disease
- Hypertension
- Previous gestational diabetes mellitus
- Polycystic ovary syndrome with BMI$\geq$ 30
- Triglyceride level >2.82 mmol/L