Original Article:

Consistency of Fasting Blood Glucose & Oral Glucose Tolerance Test: A hospital based study in Bangladesh

M.S.H. Talukder[1], A.K.A. Khan[2], S.M.K. Ali[3], S. Vaaler[4], *A. Hussain[1]

Abstract:

Introduction: Data on the internal consistency of fasting blood glucose (FBG) and 2 hrs-oral glucose tolerance test (OGTT) are scarce despite of its importance both for research and treatment purposes. **Methods:** FBG and OGTT were performed on two consecutive days among the 218 (107 men and 111 women) newly diagnosed type 2 diabetes patients at BIRDEM (a diabetic hospital), Dhaka Bangladesh. Further, an interview with each subject was conducted and HbA1c, bio-physical and anthropometric examinations were performed. **Results:** The mean differences for the estimation of blood glucose values varied significantly among the female subjects from 1st to 2nd day following FBG procedures ($p < 0.01$, 95% CI -0.08 to -0.6). It appeared that there was a higher concordance between 1st and 2nd day at the lower level of FBG values, whereas OGTT showed improved concordance with higher blood glucose values. **Conclusions:** Further studies are needed to investigate the observed difference in FBG measures with specific attention to BMI and the fasting state. The observed variation for FBG and OGTT should be considered during diagnosis of diabetes or control of the condition.

Keywords: FBG, OGTT, Variability, Diagnosis, Diabetes

Introduction:

Different diagnostic criteria have been established to reduce the risks for the development of complications among the diabetic patients [1-4]. The most widely used diagnostic criteria for glucose intolerance was recommended by the World Health Organization (WHO) based on fasting plasma glucose (FPG) value and glucose value measured 2 hrs after a standard 75-g glucose load (OGTT) [5]. American Diabetes Association (ADA) has introduced a new diagnostic criteria for epidemiological studies, based on FPG or fasting blood glucose (FBG) to 7.0 or 6.1 mmol/l [6].

[1]University of Oslo, Norway

[2]Bangladesh Institute of Research on Diabetes, Endocrinology and Metabolism (BIRDEM)

[3]Institute of Nutrition and Food Sciences University of Dhaka, Bangladesh

[4]National Hospital, Oslo, Norway

***Corresponding Author:**

Prof. Akhtar Hussain

Department of International Health, Institute of General Practice and Community Medicine, University of Oslo, Norway
Email: akhtar.hussain@medisin.uio.no

The ADA published revised criteria for the diagnosis of diabetes that includes a FPG value, with a confirmatory test on a subsequent day [6]. In contrast to the recommendation of ADA, World Health Organization (WHO) recommends using the OGTT in clinical practice [5]. Although it was shown that FPG = 7.0 mmol/l and 2h-PG =11.1 mmol/l have similar predictive values for diabetes complications, these two criteria have shown poor concordance in identifying cases with Diabetes Mellitus (DM) [7 and 8]. Moreover, the DECODE study found that almost 30% of all patients with diabetes (based on fasting or 2hrs -PG following OGTT or both) would remain undetected [9]. This low agreement may raise concern for identification and treatment of people with diabetes. It was also recommended by ADA that the internal stability of the diagnostic procedures should be carefully considered when monitoring glycemic control for people with diabetes [10-13]. Data on the internal consistency of these two procedures is scarce especially from ethnic groups representing the highest increase of incidence in type 2 diabetes. Therefore the purpose of the study was to assess the day to day variability of FBG and OGTT in people with newly diagnosed type 2 diabetes in Bangladesh. In addition, both the diagnostic procedures were examined against glycosylated hemoglobin A1c in order to observe the strength of FBG and OGTT procedures.

Patients and Methods:

All people with type 2 diabetes who were diagnosed within 4 weeks prior to the scrutiny attending FBG test at outdoor facility of Bangladesh Institute of Research on Diabetes, Endocrinology and Metabolism (BIRDEM) hospital, Dhaka, Bangladesh were requested to participate in the study during the month of November, 2003. All subjects got screening results and confirmatory diagnostic test appointment within one month of scrutiny. We included subjects on the date of confirmatory diagnostic test. Women with gestational state, age = 20 years were not included in the study. A total of 218 subjects (107 males and 111 females) who participated in the two day procedure were included in the study after taking informed consent. Diagnosis of diabetes had been made according to 1999 WHO criteria [14].

Ethics

The ethical norms were followed in accordance with the Helsinki declaration. Subjects were assured that participation in the study will not have any impact on the treatment procedure at BIRDEM. The study was approved by both ethical committees in Norway and Bangladesh.

Survey Procedure:

1st day data collection- (FBG1 and OGTT1) – Screening subjects attending BIRDEM hospital for confirmatory test were informed about the procedures of the test previously at the time of collection screening test result. At that time participants were asked to undertake 12 hrs fast for confirmatory test, avoid any treatment for diabetes and physical activities during this one month. They were also rested for 30 minutes before the test was performed. The FBG test was performed in the morning from 8 am to 9 am. Capillary blood was collected by a needle through puncturing the tip of the middle finger of right hand. The third drop of blood was taken directly into the microcuvette. The correct volume was drawn into the cuvette by capillary action. The microcuvette was thus placed into the photometer.

Table 1: Characteristics of 218 newly diagnosed type 2 diabetes patients (Mean ± SD)

Mean ±SD	Male N=107	Female N=111	P for difference
Age(years)	46.9±10.8	43.9±11.4	.71
BMI (kg/m2)	22.65±2.8	25.15±4.0	.003
Waist heap ratio	.93±0.05	.87±0.06	.04
1st day fasting blood glucose	9.39±4.1	9.23±4.6	.20
2nd day fasting blood glucose	9.30±4.1	8.64±4.0	.90
1st day oral glucose tolerance test	16.14±4.9	15.00±5.3	.21
2nd day oral glucose tolerance test	16.00±5.1	15.30±5.2	.95
Systolic blood pressure (mmHg)	125.4±19.6	127.56±19.6	.65
Diastolic blood pressure (mmHg)	84.5±12.0	84.7±15.1	.89
HbA1c (%)	7.43±2.5	7.36±2.1	.64

Glucose values were then measured by HemoCue Blood-glucose analyzer, which can measure blood glucose at the upper level of 22 mmol/L. The subjects were then given 75 gm glucose drink immediately for OGTT. Subsequently, 2hrs after glucose drink, OGTT1 was performed following the same procedure. At the end of 2hrs blood glucose test, all subjects were interviewed to collect information regarding socio-economic, family history, treatment history and smoking habit etc. Then all subjects were informed about next day preparation for FBG and OGTT.

2nd day data collection- (FBG2 and OGTT2) - FBG and OGTT tests were repeated on all the subjects on the next day by ensuing the same procedure. A fasting sample of venous blood was also collected for HbA1c measurement on the second day by HPLC (ion exchange high-performance liquid chromatography) using a Modular Diabetes Monitoring System (BioRad, Variant, USA) method. A 17-gauge Luer-lock venflon was inserted in to both anticubital fossa and sample was taken for HbA1c. Anthropometrical data and blood pressure were measured in the same examination room to avoid any influence of physical activity between 2 hrs time of glucose drink and OGTT2. Participants were rested absolutely for a minimum of 30 minutes before the measurement was performed on the right arm with a random zero mercury sphygmomanometer using normal cuffs. Systolic blood pressure 140 and diastolic blood pressure 90 mm Hg were taken as systolic hypertension and diastolic hypertension, respectively. Height and weight of the subjects were measured with the subjects wearing light cloths and without shoes. Weight was taken to the nearest 0.1 kg by SALTER bathroom scale. Waist circumference was taken at the level of a mid-point between lower border of the 12th rib and the highest point of iliac crest on the mid axillary line at the end of normal inspiration. Hip circumference was taken at the level of pubic tubercle accepting the highest three measurements by a plastic measuring tape [15]. BMI was calculated as weight (kg) divided by height (meter) square. Waist-hip-ratio was determined as waist circumference divided by hip circumference in cm.

Data Analysis:

SPSS 11.0 software was used for data analysis. Descriptive analysis was performed to describe differences of variables stratified by sex. Statistical comparisons among sex, BMI, SBP and DBP were made by one sample t- test for continuous variables and chi-square tests for group comparisons. Variability of FBG was assessed by comparison of percentage differences (PD) =100 (FBG2 –FBG1)/FBG1, with averaged FBG (FBGaver =[FBG1 + FBG2]/2) [16]. Concurrently, variability of OGTT was also assessed by comparison of percentage differences (PDs) =100 (OGTT2 –OGTT1)/OGTT1, with averaged OGTT (OGTTaver = [OGTT1 + OGTT2]/2). Liner regression analysis was carried out to describe the relation between FBG, OGTT and HbA1c with PDs and averaged values of them. Scattered diagrams are also presented to indicate the correlation and inter-relationship of those values.

Results:

Female subjects had a significantly higher BMI compared to male participants (Table 1). No significant mean differences were observed between the OGTT1 and OGTT2 values, but a significant difference (p=.011, CI .077 to .604) was observed between FBG1 and FBG2 values.

The difference in FBG values were only observed in females p<0,05 (95% CI 0.23 – 0.94, n= 111) (Table 2). Differences in FBG values during two examination were also observed among normal group BMI (18.51 to 24.99) (p<0.05, 95% CI. 05-0,7, n = 134), sHTN (p <0.05, 95% CI .006 - 1.1, n = 73) and dHTN (p < 0.05, 95% CI .02 – 0.9, n = 88).

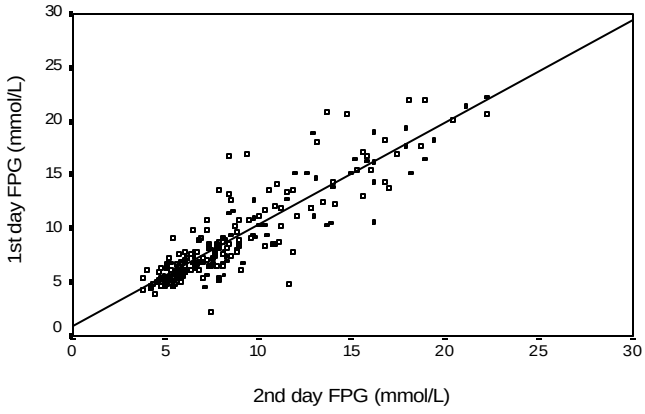
FBG and OGTT values for both days were illustrated (Fig -1) by a linear of regression. High correlations between 1st and 2nd day for FBG measures was observed as r=0.90, p<0.001, while this correlation for OGTT was found as r=0.89, p<0.001. The standardized b value for 1st day and 2nd day FBG and OGTT were .89 and .88 respectively. The absolute values of the differences were plotted against average values to assess the significance of FBG and OGTT. variance with increasing FBG values, while decreasing variance with increasing OGTT values (Figure 2).

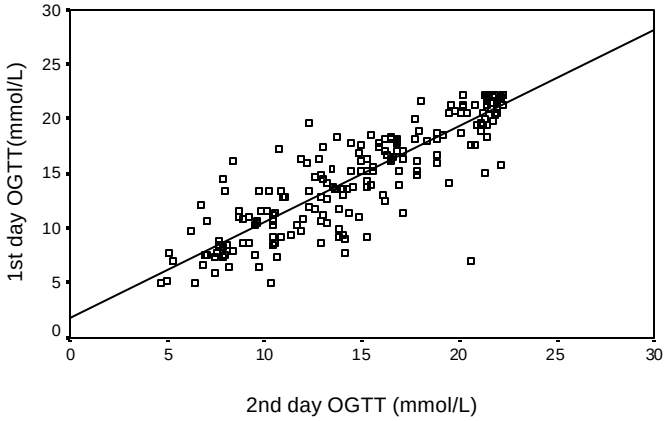
The slope of the regression line for FBG was positive (p<0.0001), but the line for OGTT was slightly negative (p<0.0001), indicating increasing

Table 2. Mean differences for FBG & OGTT by sex, BMI, SBP and DBP with 95% CI

Variables	n	Mean Difference FPG	Sig	95% CI		Mean Difference OGTT	Sig	95% CI	
				Lower	Upper			Lower	Upper
SEX									
Total	218	.341	**.011**	-.077	.604	-.086	.607	-.418	.244
Male	107	*-.085*	*.666*	*-.307*	*.479*	*.136*	*.569*	*-.337*	*.610*
Female	111	*.587*	***.001***	*.235*	*.939*	*-.301*	*.204*	*-.769*	*.166*
BMI									
<18.50	17	*-.423*	*.16*	*-1.039*	*.192*	*-.070*	*.86*	*-.938*	*.797*
18.51-24.99	134	*.396*	***.02***	*.052*	*.740*	*.022*	*.91*	*-.396*	*.441*
25.00-29.99	52	*.250*	*.28*	*-.214*	*.714*	*-.084*	*.79*	*-.725*	*.556*
>30.00	15	*1.033*	*.19*	*-.607*	*2.674*	*-1.086*	*.29*	*-3.220*	*1.046*
Systolic Blood Pressure									
<140	145	*.249*	*.09*	*-.047*	*.545*	*-.226*	*.26*	*-.623*	*.171*
=>140	73	*.524*	***.05***	*-.006*	*1.055*	*.190*	*.53*	*-.415*	*.796*
Diastolic Blood Pressure									
<90	130	*.247*	*.12*	*-.073*	*.568*	*-.054*	*.79*	*-.467*	*.357*
=>90	88	*.479*	***.03***	*.024*	*.935*	*-.134*	*.63*	*-.695*	*.426*

Figure 1. FPG and OGTT values measured on consecutive days. The regression line are also shown





The associations between HbA1c and FBG was found to be 0.62 ($p<0.001$), while for OGTT this was 0.53 ($p<0.001$) (Figure 3). The percentage difference (PD) was assessed graphically, and no significant (0.7 for FBG and .08 for OGTT) departure from normality was observed. The mean PD's were -0.64 (-4.0 to 2.7) with SD ?25.17 % and 2.7 (-.4 to 5.9) with SD ?23.9 %, giving 95% limits of variability for FBG and OGTT respectively (Figure 4). The regression confidence interval is tight around the zero line, indicating constant variability for increasing FBG and decreasing OGTT. The 95% variability region (±41%) for FBG and (±46%) for OGTT are shown. No significant difference was found in PD by sex for OGTT (male, p=.76 and female, p=.06), but a significant difference was observed by sex for FBG (male, p=.74 and female, p=.01).

Figure 2. Regression of the absolute differences for FBG and OGTT against averaged FBG and OGTT with the 95% CI for the regression

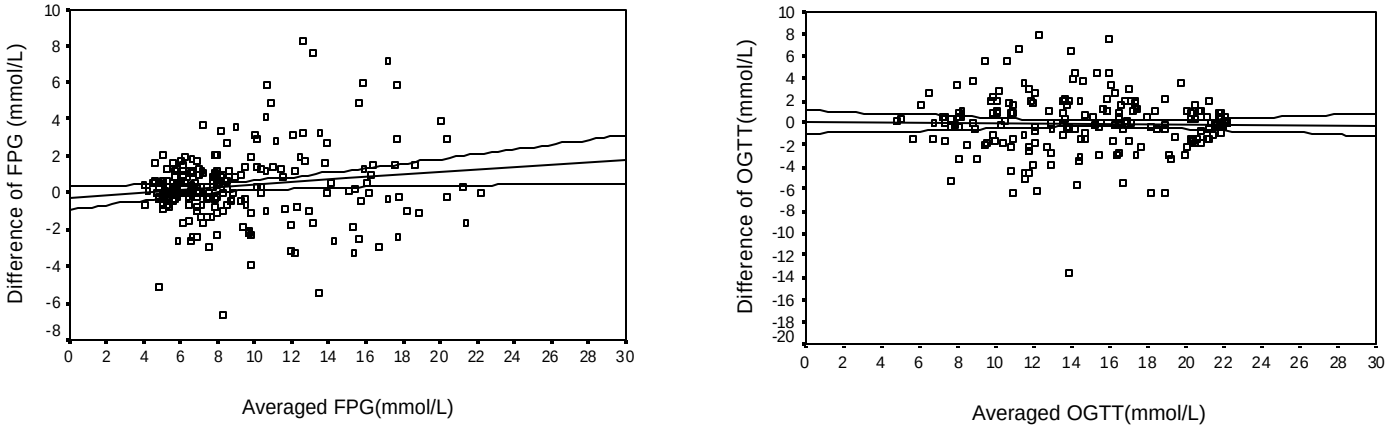


Figure 3. Association between FPG or OGTT and HbA1c.

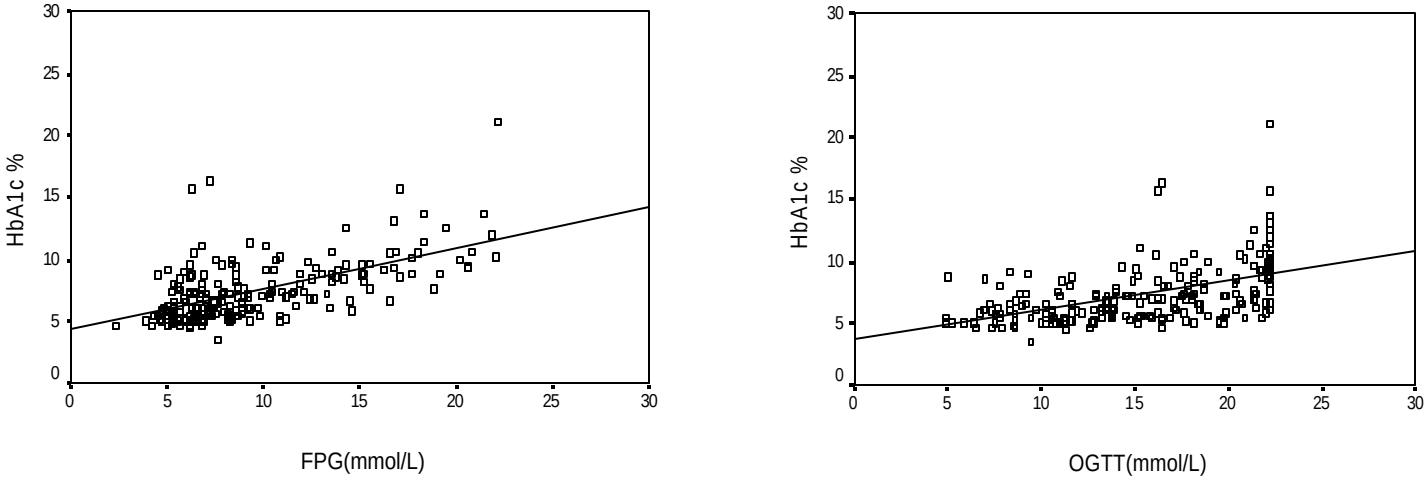
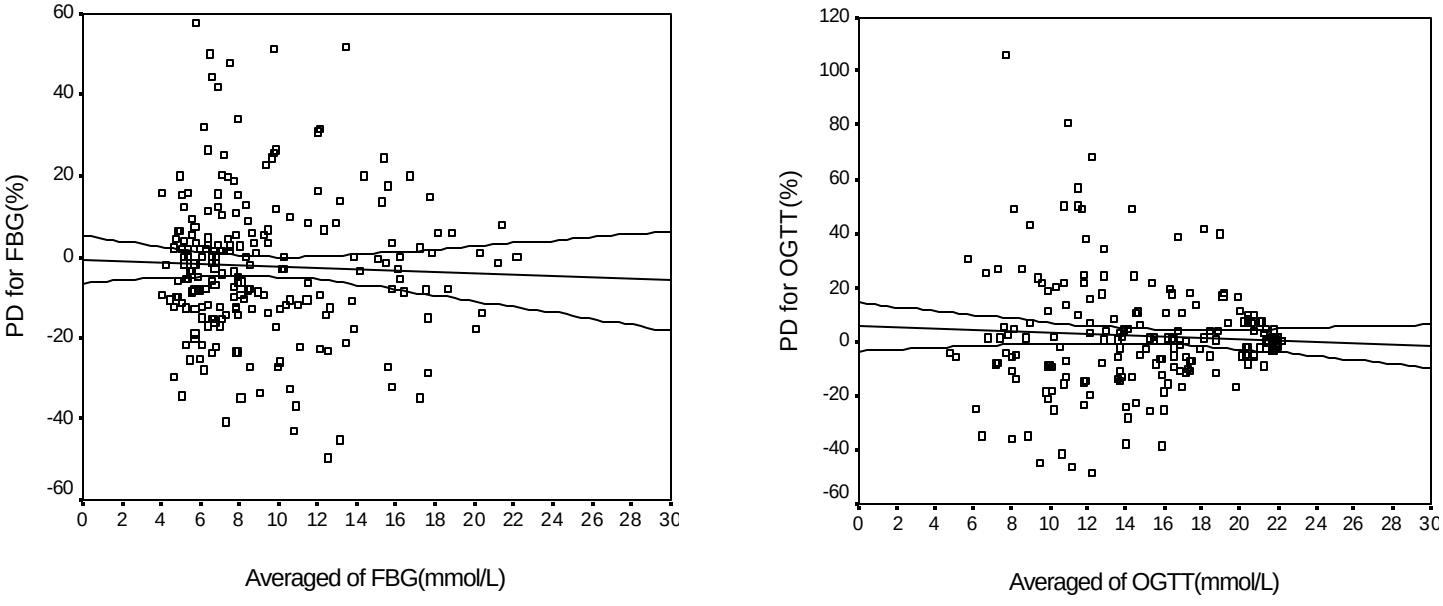


Figure 4. Percentage differences between the two FBG and OGTT values versus averaged FBG and OGTT.



Discussion:

Consistency of the diagnostic procedures FBG or OGTT for the diagnosis of diabetes mellitus appeared to be reasonably reliable on two consecutive days. However, it was observed that PD was normally distributed and that a total of 95% of the FBG and OGTT values varied respectively within approximately ± 25 % and ± 24% on a day to day basis. Compared to the Ollertron study our subject's day to day changeability measures were higher following PD assessments [17]. The Ollertron study [17] found that FBG varied up to ?14.8%, in 95% among the newly diagnosed, Caucasian type 2 subjects. Another study by Mooy et al [18] assessed the intra-individual variation of glucose specific insulin, and proinsulin by two OGTTs given at an interval ranging from two to six weeks. The study revealed that among the normal subjects and subjects with impaired glucose tolerance, the PD of FBG varied respectively 14% and 16%. The PD variability for newly diagnosed type 2 diabetic subjects was approximately 20%. She also found significant difference for FBG values in the total subjects, but no significant for newly diagnosed subjects. OGTT was found to be insignificant on both categories. The observed higher PDs difference might be due to ethnic difference or unusual food habit of the subjects during fasting month.

Our data showed a relatively stable reproducibility of both test results. Nevertheless, significant differences for FBG values were observed. The inconsistency of the test results was largely influenced by female subjects following FBG procedure. The females had significantly higher BMI compared to male subjects. Moreover, the increased variability was also stratified by hypertension, which may raise attention for diagnosis of hypertensive subjects. Therefore, elevated variability of the test results among women and hypertensive subjects by FBG procedure deserves attention for future studies with a focus on obese status.

Relatively stronger consistency over the repeated tests was observed among lower level of FBG values, while this was true for higher OGTT values. This may suggest that either FBG or OGTT may not identify all true cases. HbA1c appeared to have improved associations with FBG measures contrasting against OGTT values. Moreover, both FBG and OGTT values appeared to have no significant deviation from normality as assessed by the PD. However, the deviation was higher compared to the other referred studies. This may have been true for the newly diagnosed cases as was observed in other studies [18].

More investigations are needed to reduce the ambiguity of the test results by including some control subjects, preferably in the hospital and rather than fasting time to reduce the confusion, and to observe the creditability of the fasting state as assessed by interviews. [19] Diagnosis of diabetes deserve further attention as a combination of both tests may give rise to false negatives, while recruiting patients by either test may result in false positives. The upper limit of blood glucose measurement by HemoCue Blood-glucose analyzer and sample size may also be a concern for further investigation. Either setting will likely have implications in the epidemiology, treatment and control of the state of diabetes.

Acknowledgements:

We sincerely thank the team at BIRDEM hospital for their cooperation and the subjects for their participation. We extend our thanks to Medical Statistician Geir Aamodt at the Department of Medical Statistics, University of Oslo for his assistance in analyzing the data.

References:

1. DR McCance, RL Hanson, M-A Charles, LTH Jacobsson, DJ Pettitt, PH Bennet et al. Comparison of tests for glycated haemoglobin and fasting and two hour plasma glucose concentrations as diagnostic methods for diabetes. BMJ 308 (1994), pp. 1323 – 1328.

2. MA Charles, B Balkau, F Vauzelle-Kervroe-Den, N Thibult, E Eschwege. Revision of Diagnostic criteria for diabetes (Letter). Lancet 348 (1996), pp. 1657 – 1658.

3. MM Engelgau, TJ Thompson, WH Herman, JP Boule, RE Aubert, SJ Kenny et al. Comparison of fasting And 2-hour glucose and HBA1c levels for Diagnosing diabetes: diagnostic criteria and Performance revisited. Diabetes Care 20 (1997), pp. 785 – 791.

4. World Health Organization. Diabetes Mellitus: Report of a WHO Study Group Geneva, World Health Org. (1985), (Tech. Rep. Ser.,No. 727).

5. KGMM Alberti & PZ Zimmet. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional Report of WHO Consultation. Diabet Med 15 (1998), pp. 539-553.

6. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus Diabetes Care 20 (1997), pp. 1183 – 1197.

7. AL Drash. Is the oral glucose tolerance test obsolete? Diabetes Care 18 (1995), 1072 – 1073.

8. M Davies. New diagnostic criteria for diabetes--are they doing what they should? Lancet 354 (1999), pp. 610-611.

9. The DECODE Study Group on behalf of the European Diabetes Epidemiology Group: Is fasting glucose sufficient to define diabetes? Epidemiological data from 20 European studies. Diabetologia 42 (1999), pp. 647-654.

10. DR McCance, RL Hanson, MA Charles, LT Jacobsson, DJ Pettitt, PH Bennett et al. Which test for diagnosing diabetes? Diabetes Care 18 (1995), pp. 1042-1044.

11. DE Goldstein. Isn't time to retire the oral Glucose tolerance test for diabetes screening and diagnosis? (Editorial). Diabetes Care 21 (1998), pp. 1215 – 1216.

12. MI Harris, RC Eastman, CC Cowie, KM Flegal, MS Eberhardt. Comparision of Diabetes diagnostic categories in the U.S. population according to 1997 American Diabetes Association and 1980 – 1985 World Health Organization diagnostic criteria. Diabetes Care 20 (1997), pp. 1859 – 1862.

13. B Balku, E Eschwege. Repeatability of the oral glucose tolerance test for the diagnosis impaired glucose tolerance and diabetes? Diabetes Care 18 (1991), pp. 104– 1044.

14. Definition, diagnosis and classification of diabetes mellitus and its complications. Report of a WHO Consultation, Part 1: Diagnosis and classification of Diabetes Mellitus, Geneva 1999, Worl Health Organization.

15. P Bjorntrop. Measurment of regional distribution of adipose tissue. In, Rossner S (eds) Obesity in Europe 1. London: John Library 1998: 351– 359.

16. MJ Bland, DG Altman. Comparing methods of mesurment: why plotting difference against standard method is misleading. Lancent 346 (1995), pp. 1085-1087.

17. RL Ollerton, FD Dunstan. Day-to-day variability of fasting plasma in newly diagnosed type 2 diabetic subjects, Diabetes Care 22 (1999), pp. 394-398.

18. JM Mooy JM, PA Grootenhuis, H de Vries, PJ Kostense, C Popp-Snijders, LM Bouter et al. Intra-individual variation of glucose, specific insulin and proinsulin concentrations measured by two oral glucose tolerance tests in general population: the Hoorn Study. Diabetologia 39 (1996), pp. 298-305.

19. The DECODA study group on behalf of the Intentional Diabetes Epidemiology Group (2000). Comparison of the fasting and the 2-hour glucose criteria for diabetes in different Asian cohorts. Diabetologia 43 (2000), pp. 1470-1475.