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Biomarker Assessment of Dysglycemia Diagnosis: A Comparative Study

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Abstract **Original Research Article**

Background: Dysglycemia, a spectrum of glucose metabolism disorders, requires timely and accurate diagnosis to prevent complications like cardiovascular disease and diabetes progression. Biomarkers such as fasting plasma glucose, HbA1c, and oral glucose tolerance tests are widely used, offering distinct diagnostic advantages. This study aimed to assess and compare the effectiveness of various biomarkers in diagnosing dysglycemia. ***Methods:*** This cross-sectional study was conducted at the Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from March to 2019 to February 2020. A total of 1,165 individuals attending the Endocrinology Outpatient Department at BSMMU for dysglycemia screening, including prediabetes and diabetes, were enrolled using a non-probability sampling method. Data analysis was carried out using SPSS version 23.0. ***Results:*** In this study, diabetes prevalence was observed as 21.2% using 2hPG, 15.9% with FPG, and 23.3% through HbA1C, while prediabetes rates were 28.4% for FPG, 24.5% for 2hPG, and 37.8% for HbA1C. Although no significant difference was found between 2hPG and HbA1C, FPG tended to underestimate diabetes. The concordance among diagnostic tools was 12.4%, with the highest detection rate (25.6%) achieved using 2hPG and HbA1C. Age influenced diagnostic outcomes, and good agreement was noted among FPG, 2hPG, and HbA1C. FPG demonstrated lower sensitivity but comparable specificity to HbA1C. ***Conclusion:*** The study reveals that HbA1C has the highest diabetes detection rate, followed by 2hPG, while FPG underestimates diabetes. Combining 2hPG and HbA1C offers the most accurate diagnosis, with age-influencing outcomes and FPG showing lower sensitivity but similar specificity to HbA1C.

Keywords: Biomarker, Diabetes mellitus, Dysglycemia, Fasting plasma glucose, HbA1C, OGTT.

1. INTRODUCTION

Diabetes mellitus (DM) and its associated morbidity and mortality are increasingly becoming a serious burden for society in developed as well as developing countries. Approximately 451 million (8.8%) adults worldwide are expected to have diabetes, and the number is estimated to reach 693 million (9.9%) by the year 2045 [1]. The prevalence of diabetes has also been found high in Bangladesh. In 2010, the International Diabetes Federation estimated that 5.7million (6.1%) and 6.7 million (7.1%) people living in Bangladesh are suffering from diabetes and impaired glucose tolerance (IGT), respectively. By 2030, the number of diabetic populations is expected to rise to 11.1million in Bangladesh. Due to this explosion of diabetes prevalence. Dysglycemia includes diabetes and prediabetes and it is determined as hyperglycemia having the probability of future diabetic retinopathy as their specific complication and these hyperglycemic states are associated with cardiovascular diseases and metabolic syndromes [3]. Prediabetes includes individuals with impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) or elevated HbA1C [4]. According to previous studies; up to 70% of people with prediabetes

eventually develop overt diabetes during their lifetime. The annual incidence of progression from prediabetes to diabetes is around 5–10% depending on the population characteristics and the pattern of prediabetes [5]. 6–9% of isolated IFG, 4–6% of isolated IGT, 15-19% of IFG - IGT, and subjects with HbA1C levels from 5.7–6.4% have a 7.5-year predicted risk for incident of diabetes [5]. Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. With a better understanding of the pathophysiology and regulation of glucose metabolism, new classifications of diabetes based on etiologies (Box 1) and clinical staging have been recommended by the World Health Organization [6] and the American Diabetes Association [7]. In particular, the previous classification of insulin-dependent diabetes mellitus and non–insulin-dependent diabetes mellitus has now been replaced by type 1 and type 2 diabetes mellitus, respectively, because of the considerable overlap in the clinical stages between the two types of diabetes. HbA1C is formed by a post-translational, non-enzymatic, substrate concentration-dependent attachment of glucose to the N-terminal valine of the β chain of hemoglobin [8]. It is estimated that 1% reduction in HbA1C reduces the risk of Myocardial Infarction by 14% and microvascular complications by 37%. A1C within the target indicates that therapy is working appropriately to reduce the risk of microvascular long-term complications [9] In 2010, The American Diabetes Association recommended HbA1C as a diagnostic test for diabetes. A study done in China 2013 found that, individuals with diabetes and prediabetes diagnosed using HbA1C. Those who were diagnosed as diabetic on the basis of HbA1C levels had a relatively better metabolic condition than those diagnosed by 2hPG. This indicates that HbA1C test can detect metabolic disorders at an earlier time [10].

2. METHODOLOGY

This comparative study was conducted in the Department of Biochemistry and Molecular Biology at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from March 2019 to February 2020. A total of 1,165 individuals attending the Endocrinology outpatient department for dysglycemia (prediabetes and diabetes) screening were included. Participants were selected using a non-probability sampling method. Ethical approval was obtained from the institutional review board. The study included patients aged 20–75 years of both genders suspected of having dysglycemia based on a history of polydipsia, polyuria, polyphagia, a family history of type 2 diabetes in first-degree relatives, gestational diabetes, obesity (BMI ≥ 30 kg/m²), polycystic ovary syndrome (in females), or sudden weight changes. Exclusion criteria encompassed diagnosed diabetes mellitus, elevated SGPT (hepatic impairment), high serum creatinine (renal impairment), thyroid, growth hormone, or adrenal disorders, anemia, hemoglobinopathies, BMI < 18.5 kg/m², pregnancy, malignancy, infections, and a history of gastric bypass surgery. Data were analyzed using MS Office and SPSS version 23.0.

3. RESULT

In this study, diabetes and prediabetes were defined per ADA criteria. The prevalence of diabetes was 21.2% by 2hPG, 15.9% by FPG, and 23.3% by HbA1C. Prediabetes prevalence was 28.4% by FPG, 24.5% by 2hPG, and 37.8% by HbA1C. The proportion test showed no significant difference between 2hPG and HbA1C in detecting diabetes, while FPG significantly underestimated the frequency of diabetes compared to 2hPG and HbA1C. Concordance among the three diagnostic tools for detecting diabetes mellitus was observed in only 12.4% of cases. The highest detection rate (25.6%) occurred with 2hPG combined with HbA1C. Adding FPG reduced the detection rate to 12.4%. The frequency of diabetes detected with all three tools significantly differed from that detected using any two combinations. HbA1C identified a higher percentage of diabetes cases in both sexes, while 2hPG identified fewer cases. The frequency of diabetes was similar between males and females. All three diagnostic tools identified a higher number of diabetic patients with increasing age, with a notable difference in diabetes prevalence between individuals below and above 40 years. The frequency of diabetes was similar across normal, overweight, and obese groups. Each tool consistently detected a higher prevalence of diabetes as age advanced, with a significant contrast between those below and above 40 years. Age was a significant independent variable influencing the diagnosis of diabetes mellitus by FPG, 2hPG (OGTT), and HbA1C. The Kappa test showed good agreement (Kappa value: 0.65) between HbA1C and 2hPG (OGTT), between FPG and 2hPG (OGTT) (Kappa value: 0.64), and between HbA1C and FPG for diagnosing diabetes mellitus, although the agreement was neither very good nor excellent. FPG demonstrated lower sensitivity than HbA1C, while their specificity and accuracy were approximately similar.

Table 1: Distribution of prediabetes and DM determined by three diagnostic tests

Test	Diabetic		Prediabetic		Non-diabetic		Total
	n	%	n	%	n	%	
FPG (mmol/L)	185	15.90%	331	28.40%	649	55.70%	1165
2 hPG (mmol/L)	247	21.20%	286	24.50%	632	54.20%	
HbA1C	271	23.30%	440	37.80%	454	39%	

FPG: Fasting Plasma Glucose, 2hPG: Two-hour plasma glucose after oral glucose load, HbA1C: Hemoglobin A1C

Table 2: Comparison of the frequency of DM determined by three diagnostic tools

Diagnostic tools	P Value
FPG (15.9%) vs 2hPG (21.2%)	<0.05
2hPG (21.2%) vs HbA1C (23.3%)	>0.05
FPG (15.9%) vs HbA1C (23.3%)	<0.05

Table 3: Concordance and discordance of three diagnostic tools in the diagnosis of DM

Tools	Concordance		Discordance	
	n	%	n	%
FPG (≥7.0mmol/l) +2hPG (≥11.1mmol/l) +HbA1C (≥6.5%)	144	12.40%	1021	87.60%

Table 4: Comparison between concordance and discordance of three diagnostic tools in the diagnosis of DM

Different combinations of tools	n	%
FPG (≥7.0mmol/l) +2hPG (≥11.1mmol/l) +HbA1C (≥6.5%)	144	12.40%
FPG (≥7.0mmol/l) +2hPG (≥11.1mmol/l)	212	18.20%
2hPG (≥11.1mmol/l) +HbA1C (≥6.5%)	298	25.60%
FPG (≥7.0mmol/l) +HbA1C (≥6.5%)	236	20.30%

Table 5: Comparison of the frequency of DM determined by different combinations of three diagnostic tools

Different combinations of 3 diagnostic tools	P Value
FPG+2hPG+HbA1C (12.4%) vs FPG+2hPG (18.2%)	<0.05
FPG+2hPG+HbA1C (12.4%) vs 2hrPG+ HbA1C (25.6%)	<0.05
FPG+2hPG+HbA1C (12.4%) vs FPG+HbA1C (20.3%)	<0.05
2hPG+ HbA1C (25.6%) vs FPG+HbA1C (20.3%)	<0.05
2hPG+ HbA1C (25.6%) vs FPG+2hrPG (18.2%)	<0.05
2hPG+ FPG (18.2%) vs FPG+HbA1C (20.3%)	>0.05

Table 6: Frequency of DM determined by three diagnostic tools in male and female

Test	Male (n=420)		Female (n=745)	
	n	%	n	%
FPG (mmol/L)	126	30.00%	205	27.50%
2 hPG (mmol/L)	101	24.00%	193	25.90%
HbA1C (%)	150	35.70%	290	38.90%

Table 7: Frequency of DM determined by three diagnostic tools in different age groups

Test	Different age group							
	<30 years (n=320)		30-40 years (n=384)		40-50 years (n=270)		>50 years (n=191)	
	n	%	n	%	n	%	n	%
FPG	22	6.90%	51	13.30%	61	22.60%	51	26.70%
2hPG	29	9.10%	74	19.30%	81	30%	63	33.00%
HbA1C	27	8.40%	86	22.40%	93	34.40%	65	34.00%

Table 8: Frequency of DM determined by three diagnostic tests in different BMI groups

Test	Different BMI Group					
	Normal<23.0kg/m^2 (n=148)		Overweight 23.0-24.99 kg/m^2 (n=205)		Obese ≥25.0 kg/m^2 (n=812)	
	n	%	n	%	n	%
FPG	19	12.80%	31	15.10%	135	16.60%
2hPG	27	18.20%	43	21%	177	21.80%
HbA1C	28	18.90%	46	22.40%	197	24.30%

Table 9: Binary logistic regression of predictors influencing diagnosis of DM by fasting plasma glucose

Variables	P Value	Exp (B)	95% CI
Age	<0.05	1.658	1.417-1.942
Sex	>0.05	0.75	0.539-1.044
BMI	>0.05	1.191	0.936-1.515

Table 10: Binary logistic regression of predictors influencing diagnosis of DM by 2hPG

Variables	P Value	Exp (B)	95% CI
Age	<0.05	1.651	1.434-1.902
Sex	>0.05	0.825	0.612-1.111
BMI	>0.05	1.128	0.913-1.393

Table 11: Binary Logistic Regression of predictors influencing diagnosis of DM by HbA1C

Variables	P Value	Exp (B)	95% CI
Age	<0.05	1.68	1.464-1.928
Sex	>0.05	0.784	0.587-1.048
BMI	>0.05	1.191	0.967-1.467

Table 12: Agreement between FPG and 2hPG (OGTT) in diagnosis of DM

FPG	Glycemic status (2hPG)		Total	Kappa value
	Diabetic	Non-diabetic		
Diabetic	152 (a)	33(b)	185	0.64
Non-diabetic	95 (c)	885(d)	980	
Total	247	918	1165	

Table 13: Agreement between HbA1C and 2hPG (OGTT) in the diagnosis of DM

HbA1c	Glycemic status (2 hPG)		Total	Kappa value
	Diabetic	Non-diabetic		
Diabetic	192 (a)	79(b)	271	0.65
Non-diabetic	55(c)	839(d)	894	
Total	247	918	1165	

Table 14: Agreement between HbA1C and FPG in the diagnosis of DM

HbA1c	Glycemic status (FPG)		Total	Kappa value
	Diabetic	Non-diabetic		
Diabetic	164 (a)	107(b)	271	0.65
Non-diabetic	21(c)	873(d)	894	
Total	185	980	1165	

Table 15: Performance of FPG for diagnosis of DM, where 2hPG is considered as the gold standard

FPG	Gold Standard (2 hPG)		Total
	Diabetic	Non-diabetic	
Diabetic	152	33	185
Non-diabetic	95	885	980
Total	247	918	1165

Table 16: Performance of HbA1C for diagnosis of DM, where 2hPG is considered as the gold standard

HbA1c	Gold Standard (2hPG)		Total
	Diabetic	Non-diabetic	
Diabetic	192	79	271
Non-diabetic	55	839	894
Total	247	918	1165

Table 17: Comparison of performance between FPG & HbA1C for diagnosis of DM compared to 2hPG

Test	sensitivity	specificity	accuracy	PPV	NPV	LR+	LR-
FPG	61.54%	96.41%	89.01%	82.16%	90.31%	17.12%	0.40%
HbA1C	77.70%	91.90%	88.40%	70.80%	93.80%	9.00%	0.24%

Table 18: Receiver operating characteristic curve shows performance of fasting plasma glucose for diagnosis of DM

Test	Gold Standard	AUC
FPG	2 h PG after oral glucose load	0.92

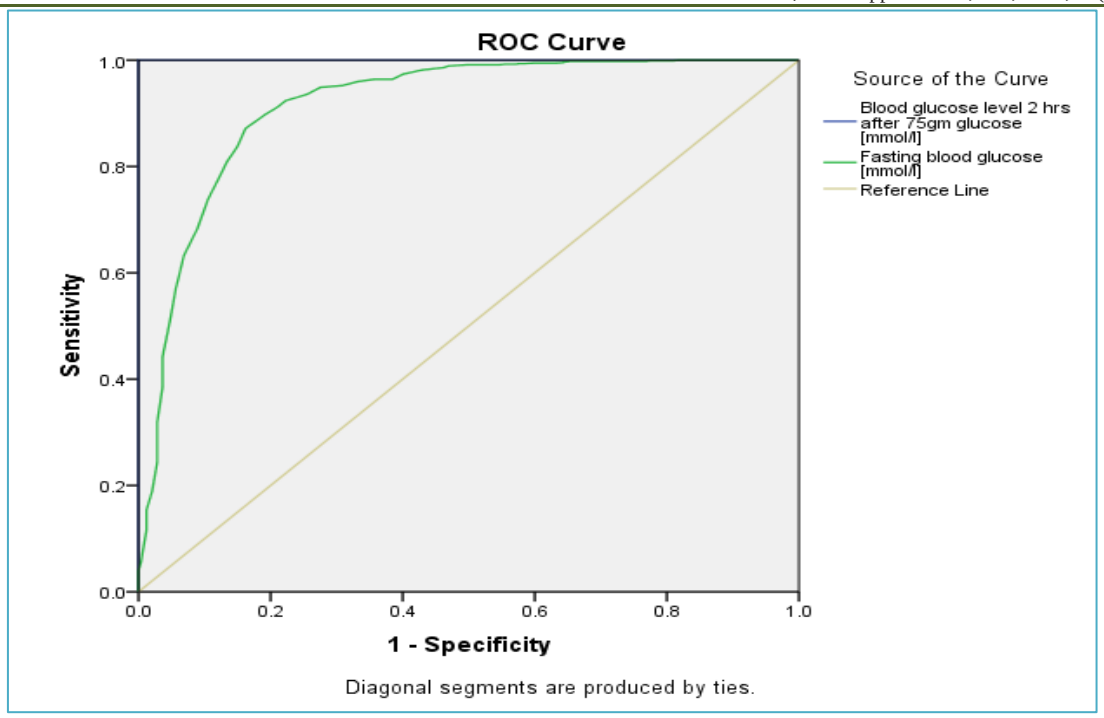

Figure 1: Receiver operating characteristic curve shows performance of fasting plasma glucose for diagnosis of DM

Table 19: Receiver operating characteristic curve shows performance of HbA1C for diagnosis of DM

Test	Gold standard	AUC
HbA1C	2 h PG after oral glucose load	0.92

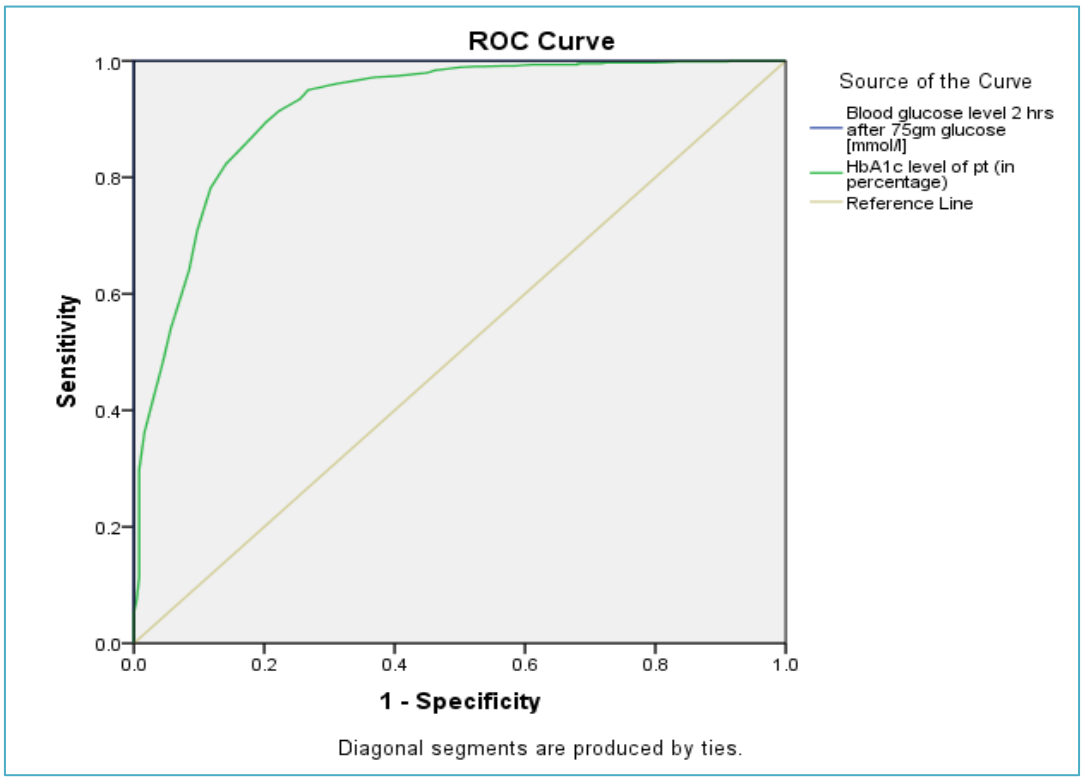

Figure 2: Receiver operating characteristic curve shows performance of HbA1C for diagnosis of DM

4. DISCUSSION

This study examined the prevalence of diabetes and prediabetes using three widely accepted diagnostic tools: Fasting Plasma Glucose (FPG), 2-hour postprandial glucose (2hPG), and Hemoglobin A1C (HbA1C), in line with the American Diabetes Association (ADA) criteria. The results indicated varying prevalence rates, with diabetes diagnosed in 21.2% of cases by 2hPG, 15.9% by FPG, and 23.3% by HbA1C. Prediabetes prevalence was higher in HbA1C (37.8%) compared to 2hPG (24.5%) and FPG (28.4%). These discrepancies are in agreement with previous studies that have shown variability in the diagnostic ability of these tools, with HbA1C and 2hPG generally identifying a higher number of cases [11,12]. The study also found that FPG significantly underestimated the frequency of diabetes compared to both 2hPG and HbA1C. This is consistent with findings in other research, which have demonstrated that FPG alone may fail to capture individuals with impaired glucose tolerance, who may still be at risk for diabetes but are classified as normal based on FPG alone [13]. Moreover, the concordance between all three diagnostic tools was low (12.4%), suggesting that relying on a single diagnostic method may not be sufficient to identify all individuals with dysglycemia, which is supported by studies advocating for a more comprehensive approach to diagnosing diabetes and prediabetes [14]. Interestingly, the combination of 2hPG and HbA1C yielded the highest detection rate (25.6%), whereas adding FPG reduced this rate significantly. This finding aligns with recent studies suggesting that combining 2hPG and HbA1C may offer better diagnostic sensitivity and a more accurate representation of the diabetes burden in a population [15]. The significant difference in diabetes detection when all three diagnostic tools were used compared to any two combinations further underscores the importance of using multiple diagnostic criteria for a more robust assessment of diabetes status. The study also found that age played a significant role in diabetes diagnosis. All three diagnostic tools identified a higher number of diabetic patients with increasing age, particularly after 40 years. This trend is consistent with the well-established relationship between aging and the increased risk of developing diabetes [16]. The finding that the frequency of diabetes was similar across normal, overweight, and obese groups could suggest that factors other than weight, such as genetic predisposition and lifestyle, may also contribute to the development of diabetes. This observation warrants further investigation into the non-obesity-related pathways that contribute to diabetes onset in the general population [17]. The Kappa test demonstrated good agreement among FPG, 2hPG, and HbA1C, with Kappa values ranging from 0.64 to 0.65, suggesting good agreement. These findings are similar to those from other studies that reported moderate-to-good agreement among these tools, though they fell short of excellent agreement [18]. FPG exhibited lower sensitivity compared to HbA1C, while their specificity and accuracy were comparable. This suggests that while FPG is a commonly used tool for diabetes diagnosis, it may miss some cases, especially in individuals with impaired glucose tolerance who may be classified as having normal glucose levels based on FPG alone [19]. Overall, this study emphasizes the need for multiple diagnostic tools when assessing dysglycemia to ensure accurate diagnosis and early intervention, particularly in populations with advancing age.

5. CONCLUSION & RECOMMENDATION

This study underscores the variability in the diagnostic performance of different biomarkers for dysglycemia. The prevalence of diabetes was highest when assessed by HbA1C, followed by 2hPG, with FPG showing the lowest detection rate. Prediabetes was most frequently identified through HbA1C, while FPG appeared to underestimate the presence of diabetes compared to the other biomarkers. Despite good agreement among the diagnostic methods, combining 2hPG and HbA1C provided the most accurate detection. Age played a role in influencing diagnostic outcomes, with FPG demonstrating lower sensitivity but similar specificity to HbA1C. These findings suggest that using a combination of biomarkers provides a more comprehensive approach to diagnosing dysglycemia.

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REFERENCES

1. Cho, N. H., Shaw, J. E., Karuranga, S., Huang, Y., da Rocha Fernandes, J. D., Ohlrogge, A. W., & Malanda, B. I. D. F. (2018). IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes research and clinical practice*, *138*, 271-281.
2. Shaw, J. E., Sicree, R. A., & Zimmet, P. Z. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes research and clinical practice*, *87*(1), 4-14.
3. American Diabetes Association (ADA). (2018) Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes. Diabetes Care. *41*(1), S13-27.
4. Mirasol, R., Thai, A. C., Salahuddin, A. A., Tan, K., Deerochanawong, C., Mohamed, M., ... & Uddin, F. (2017). A consensus of key opinion leaders on the management of pre-diabetes in the Asia-Pacific region. *Journal of the ASEAN Federation of Endocrine Societies*, *32*(1), 6.
5. Buysschaert, M., Medina, J. L., Bergman, M., Shah, A., & Lonier, J. (2015). Prediabetes and associated disorders. *Endocrine*, *48*, 371-393.
6. World Health Organization. (2011) Use of glycated hemoglobin (HbA1c) in the diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. Geneva: WHO Press.

7. American Diabetes Association (ADA). (2017) Classification and Diagnosis of Diabetes. Diabetes Care. 40(1), S11-24.
8. Burtis, C.A., Ashwood, E.R. & Bruns, D.E. (2012). Tietz Textbook of Clinical and Molecular Diagnostics. London, Elsevier.
9. Saudek, C. D., & Brick, J. C. (2009). The clinical use of hemoglobin A1c. *Journal of diabetes science and technology*, *3*(4), 629-634.
10. Wu, S., Yi, F., Zhou, C., Zhang, M., Zhu, Y., Tuniyazi, Y., ... & Ning, G. (2013). HbA1c and the diagnosis of diabetes and prediabetes in a middle-aged and elderly H an population from northwest C hina (HbA1c 与中国西北部地区中老年汉族人群糖尿病和糖尿病前期的诊断). *Journal of diabetes*, *5*(3), 282-290.
11. Carson, A. P., Reynolds, K., Fonseca, V. A., & Muntner, P. (2010). Comparison of A1C and fasting glucose criteria to diagnose diabetes among US adults. *Diabetes care*, *33*(1), 95-97.
12. American Diabetes Association. "2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2020." Diabetes care 43. Supplement_1 (2020): S14-S31.
13. Nathan, David, M., & DCCT/Edic Research Group. (2014). "The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview." Diabetes care 37.1. 9-16.
14. Rani, P. Reddi, & Jasmina, Begum. (2016). "Screening and diagnosis of gestational diabetes mellitus, where do we stand." Journal of clinical and diagnostic research: JCDR 10.4, QE01.
15. Ergul, A. (2011). Endothelin-1 and diabetic complications: focus on the vasculature. *Pharmacological Research*, *63*(6), 477-482.
16. Lee, Y. S., Komar, J., & Chia, M. Y. H. (2021). Physical activity measurement methodologies: A systematic review in the association of South East Asian Nations (ASEAN). *Sports*, *9*(5), 69.
17. Kahn, R., & Davidson, M. B. (2014). The reality of type 2 diabetes prevention. *Diabetes care*, *37*(4), 943-949.
18. Guan, X., Zheng, L., Sun, G., Guo, X., Li, Y., Song, H., ... & Sun, Y. (2016). The changing relationship between HbA1c and FPG according to different FPG ranges. *Journal of Endocrinological Investigation*, *39*, 523-528.
19. Leonetti, D., Soleti, R., Clere, N., Vergori, L., Jacques, C., Duluc, L., ... & Andriantsitohaina, R. (2018). Extract enriched in flavan-3-ols and mainly procyanidin dimers improves metabolic alterations in a mouse model of obesity-related disorders partially via estrogen receptor alpha. *Frontiers in Pharmacology*, *9*, 406.