Research Article

Practices and insights for diabetes mellitus testing in Sri Lanka, Singapore and the Philippines

Indika Deepani Siriwardhana[*,1], Tan Jun Guan[2], Maria Ruth Pineda-Cortel[3], Samuel D. Vasikaran[4], Mithu Banerjee[5]

[1]*Department of Biochemistry and Clinical Chemistry, Faculty of Medicine, University of Moratuwa, Sri Lanka*
[2]*Department of Laboratory Medicine, Khoo Teck Puat Hospital, Singapore*
[3]*Department of Medical Technology, University of Santo Tomas, Manila, Philippines*
[4]*Department of Clinical Biochemistry, PathWest-Fiona Stanley Hospital, Murdoch, Australia*
[5]*Department of Biochemistry, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India*

Article Info

[*]***Author of correspondence:***
Indika Deepani Siriwardhana
E-mail: indikads@uom.lk
Address:
Department of Biochemistry and Clinical Chemistry, Faculty of Medicine, University of Moratuwa, Moratuwa, Sri Lanka

Keywords
Diabetes mellitus, Harmonization, HbA1c, Laboratory testing, Plasma glucose, Urine albumin

Abstract

Objectives: Considering The pivotal role of biochemical testing for the management of diabetes mellitus, we studied the current status of diabetes testing and reporting in three countries of the Asia-Pacific region.

Methods: A survey of 254 practicing pathology laboratories comprising of 40, 11 and 203 laboratories from Sri Lanka, Singapore and the Philippines was conducted under the auspices of the Asia-Pacific Federation for Clinical Biochemistry and Laboratory Medicine (APFCB) Working Group for Diabetes Testing Harmonization using Survey Monkey and Google Forms.

Results: The country response rate varied from 40% to 88%. A diagnostic threshold of 6.5% (48 mmol/mol) for HbA1c is reported by 51%, 22% and 90% of the participant laboratories in Sri Lanka, Singapore and the Philippines, respectively. All participants in Singapore and 86% of the laboratories in Philippines use NGSP-certified methods for HbA1c. Traceability to Certified Reference Materials for both glucose and HbA1c results was confirmed by 74% of Sri Lankan laboratories. For albuminuria testing, early morning spot urine albumin to creatinine ratio is recommended by 56%, 75% and 69% of the laboratories in Sri Lanka, Singapore and the Philippines, respectively, while 16%, 50% and 26% of the laboratories recommended 24-hour urine collection.

Conclusion: There is a lack of harmonization in diabetes testing and reporting practices both across and even within the three countries surveyed. Scientific bodies or professional associations have an important role in harmonization of laboratory testing and reporting of results for the diagnosis and management of diabetes mellitus.

Introduction

Biochemical testing for the diagnosis and management of diabetes mellitus (DM) is not standardized globally. The lack of standardization impacts the prevalence, as well as management strategies. The age-adjusted prevalence of DM from 2019 to 2030, is expected to increase from 11.4% (87 million) to 12.2% (115 million) for the South-East Asia region [1]. The proportion of undiagnosed diabetes in South-East Asia is 51.2% as against the worldwide figure of 44.7% [2].

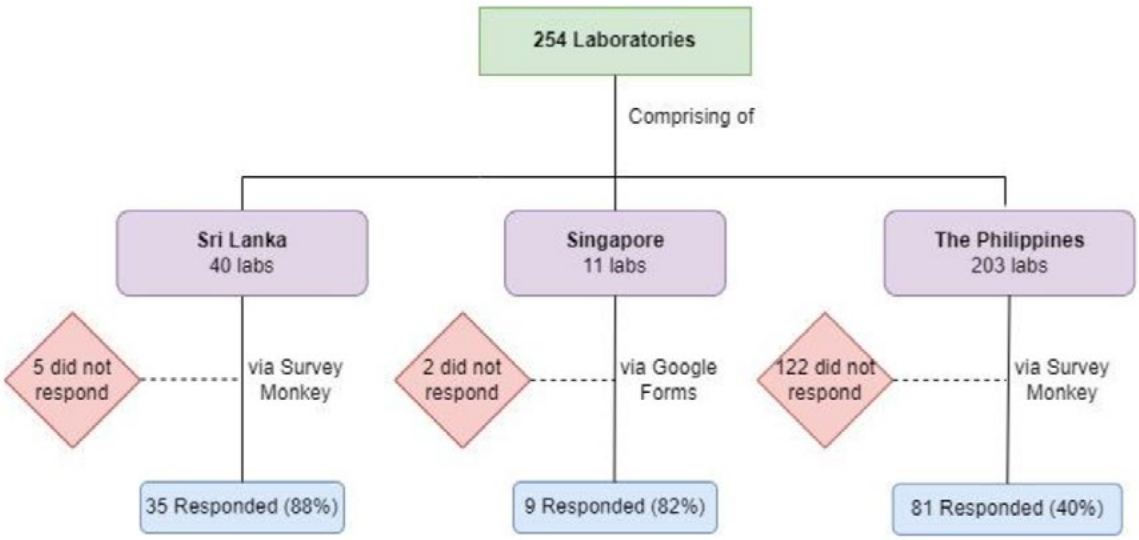
High proportion of undiagnosed diabetes represents a serious gap in healthcare. Type 2 diabetes mellitus (T2DM) has an asymptomatic stage of up to seven years [3], during which complications may develop. Hence, it is important to diagnose the disease early to enable early therapeutic and lifestyle interventions.

Biochemical investigations are essential in the diagnosis of diabetes, monitoring treatment response, and assessment of diabetic complications such as nephropathy and cardiovascular diseases. Fasting plasma glucose and haemoglobin A1c are the important diagnostic tests for T2DM in adults whilst oral glucose tolerance test (OGTT) is essential for the diagnostic confirmation of gestational diabetes mellitus (GDM). Considering the significant economic burden of T2DM across low, middle and high- income countries [4], and the perspective that harmonization of practices worldwide may lead to better patient outcomes [5], we aimed to investigate the current status of laboratory testing practices related to T2DM in laboratories across Sri Lanka (South Asia), Singapore and Philippines (South-East Asia) by administering a survey. The survey has been conducted similar to a previous survey conducted in India [6], under the auspices of the Asia Pacific Federation of Clinical Biochemistry and Laboratory Medicine (APFCB) Working Group for Diabetes Testing Harmonization.

Materials and Methods

A web-based survey was circulated to 254 laboratories in year 2020-2021 comprising 40, 11 and 203 laboratories in Sri Lanka, Singapore and the Philippines, respectively (Figure 1). Survey Monkey was used by Sri Lanka, and Philippines while Singapore used Google Form. The College of Chemical Pathologists of Sri Lanka, and Singapore Association of Clinical Biochemists facilitated the distribution of the surveys to the laboratories in the respective countries while the country representative to APFCB Working Group for Diabetes Testing and Harmonization facilitated the survey in the Philippines.

Figure 1: Number of invited laboratories and participants.



The survey invitation was emailed to a point-of-contact for each laboratory which varied between a chemical pathologist, a laboratory manager or a senior scientist. A reminder was sent if there was no response within two months. The survey questions varied slightly among the three countries in keeping with the local practices. The medium of communication for the survey was English.

Results

A total of 125 laboratories responded. The response rate was 88%, 82% and 40% for Sri Lanka, Singapore and the Philippines respectively (Table 1).

Table 1: The response rates from laboratories in Sri Lanka, Singapore and the Philippines.

Questions		Sri Lanka	Singapore	Philippines
Response Rate (number of labs/total labs contacted*100%)		88% (35 out of 40)	82% (9 out of 11)	40% (81 out of 203)
1.	Units of Reporting Glucose	n=35	n=9	n=79 [2 labs did not respond to this question]
	mmol/L	8 (23%)	7 (78%)	42 (53%)
	mg/dL	22 (63%)	1 (11%)	32 (41%)
	both	5 (14%)	1 (11%)	5 (6%)
2.	Units of Reporting of HbA1c	n=32	n=9	This question was not included in the Philippines survey
	mmol/mol only	2 (6%)	0 (0%)	
	% only	19 (59%)	3 (33%)	
	both	11 (34%)	6 (67%)	
3.	Is HbA1c used for diagnosis in your lab?	This question was phrased differently in the Sri Lankan survey. [See 4]	n=9	n=79 [2 labs did not respond to this question]
	Yes		3 (33%)	70 (89%)
	No		6 (67%)	9 (11%)
4.	Diagnostic cut-offs for diabetes reported by the laboratory [labs may choose more than 1 answer]	n=34 [1 lab did not respond to this question]	n=9	n=77 [4 labs did not respond to this question]
	HbA1c≥6.5% (48 mmol/mol)	18 (53%)	2 (22%)	69 (90%)
	HbA1c≥7.0% (53 mmol/mol)		1 (11%)	
	Fasting plasma glucose≥ 7.0 mmol/L	20 (59%)	8 (89%)	48 (62%)
	Two-hour OGTT≥ 11.1 mmol/L	15 (44%)	8 (89%)	32 (42%)
	Symptoms of hyperglycaemia and random plasma glucose≥ 11.1 mmol/L	16 (47%)	3 (33%)	30 (39%)
5.	HbA1c cut-off recommended for monitoring control	This question was not included in Sri Lankan survey	n=9	n=64 [17 labs did not respond to this question]
	6.5%		1 (11%)	0 (0%)
	7%		3 (33%)	64 (100%)
	Not reported		5 (56%)	0 (0%)

Questions		Sri Lanka	Singapore	Philippines
6A.	Is OGTT recommended for all pregnant mothers?	n=34 [One lab did not respond to this question]	A slightly different question was asked for Singapore Survey (See 6B)	n=79 [2 labs did not respond to this question]
	Yes	24 (71%)		67 (85%)
	No	10 (29%)		12 (15%)
6B.	Does your lab manual recommend OGTT at 24-28 weeks gestation for ALL women, and what is cut-off?	A slightly different question was asked for Sri Lankan Survey (See 6A)	n=5 [Four labs did not respond to this question]	A slightly different question was asked for Philippines (See 6A)
	Use IADPSG and recommend OGTT for all women at 24-28 weeks		2 (40%)	
	Use IADPSG but does not recommend OGTT for all women at 24-28 weeks		3 (60%)	
7.	Sample recommended for albuminuria testing	n=32 [3 labs did not respond to this question]	n=8 [One lab did not test urine albumin, for Singapore laboratories, percentage does not add to 100% as labs can choose more than 1 answer)	n=65 [16 labs did not respond to this question]
	Early morning spot urine	18 (56%)	6 (75%)	45 (69%)
	Twenty-four-hour urine	5 (16%)	4 (50%)	17 (26%)
	Timed overnight	0 (0%)	0 (0%)	3 (5%)
	Random spot urine	9 (28%)	1 (13%)	0 (0%)
8.	Reporting units for albuminuria	n=32 [3 labs did not respond to this question]	n=8 [One lab did not test urine albumin]	This question was not addressed in Philippines survey
	mg/L only	4 (13%)	0 (0%)	
	mg/mmol creatinine	13 (41%)	4 (50%)	
	mg/g creatinine	13 (41%)	1 (13%)	
	Both mg/mmol & mg/g creatinine	0 (0%)	3 (38%)	
	mg/day	0 (0%)	2 (25%)	
	µg/minute	1 (3%)	0 (0%)	
	mg/dL	1 (3%)	0 (0%)	
9.	What method does your lab use for HbA1c?	This question was not included in Sri Lankan survey	n=9	This question was not included in Philippines survey
	HPLC		2 (22%)	
	Immunoturbidimetry		5 (56%)	
	Capillary Electrophoresis		0 (0%)	
	Enzymatic		2 (22%)	

Questions		Sri Lanka	Singapore	Philippines
10A.	Traceability of glucose and HbA1c calibrators (labs may choose more than one answer)	n=34 [One lab did not respond to this question]	This question for Singapore and the Philippines was asked in a different format. (See 10B)	
	Only glucose calibrator is traceable to CRM/SRM	7 (21%)		
	Only HbA1c calibrator is traceable to CRM/SRM	2 (6%)		
	Both glucose and HbA1c calibrators are traceable to CRM/SRM	25 (74%)		
	Is the method IFCC standardized or NGSP certified or both	8 (24%)		
10B.	Is your laboratory HbA1c method NGSP certified?	This question for Sri Lanka was asked in a different format. (See 10A)	n=9	n=77 [4 labs did not respond to this question]
	Yes		9 (100%)	66 (86%)
	No		0 (0%)	11 (14%)
11A.	Participation in an EQA programme (labs may choose more than 1 answer)	n=34	n=9 [One lab did not do urine albumin]	This question for Philippines was asked in a different format. (See 11B)
	Plasma glucose	30 (88%)	9 (100%)	
	HbA1c	13 (38%)	9 (100%)	
	Urine albumin	7 (21%)	8 (89%)	
	Did not participate in EQA for all of the above analytes	3 (9%)	0 (0%)	
11B.	Is your lab participating in a PT program for Glucose and HbA1c?	This question for Sri Lanka and Singapore was asked in a different format. (See 11A)		n=76 [5 labs did not respond to this question]
	Glucose Only			33 (43%)
	HbA1c Only			2 (3%)
	Both			29 (38%)
	Neither			12 (16%)
12A.	Type of Laboratory	n=34 [One lab did not respond to this question]	See 12B	See 12C
	Teaching Hospital	7 (21%)		
	Provincial General Hospital	1 (3%)		
	District General Hospital	3 (9%)		
	Base Hospital	0 (0%)		
	Private Hospital	16 (47%)		
	Private Stand-Alone	4 (12%)		
	University	2 (6%)		
	Research	0 (0%)		
	Special Children Hospital	1 (3%)		

Questions		Sri Lanka	Singapore	Philippines
12B.	Type of Laboratory	See 12A	n=9	See 12C
	Private		2 (22%)	
	Public		7 (78%)	
12C.	Type of Laboratory	See 12A	See 12B	n=76 [5 labs did not respond to this question]
	Public Hospital			18 (24%)
	Private Hospital			33 (43%)
	Public Stand-Alone			5 (7%)
	Private Stand-Alone			15 (20%)
	University/Academic			4 (5%)
	Research			1 (1%)

Reporting units for HbA1c and glucose

For plasma glucose, 63% Sri Lankan laboratories reported in mg/dL while 78% laboratories in Singapore reported in mmol/L. In the Philippines, 53% of laboratories reported in mmol/L; 41% reported in mg/dL; and 6% reported in both units. Dual reporting of units is observed in Sri Lanka (5%) and Singapore (11%) as well.

For HbA1c, 59% of Sri Lankan laboratories reported solely in National Glycohemoglobin Standardisation Program (NGSP) units [%] compared to 33% in Singapore. Six percent of Sri Lankan laboratories but none of the Singapore laboratories reported solely in International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) unit [mmol/mol]. Dual reporting in NGSP and IFCC units is common in Singapore, where 67% of laboratories practise dual reporting as compared to 34% in Sri Lanka.

Diagnostic cut-off for diabetes

Overall, the majority of survey participants; 74% (89 out of 120) utilized the diagnostic cut-off of ≥ 6.5% (48 mmol/mol) for HbA1c. Of the laboratories surveyed, 53%, 22% and 90% participants indicated a diagnostic cut-off of 6.5% for Sri Lanka, Singapore and the Philippines respectively. Of note, one laboratory in Singapore reported a cut-off of ≥7.0% (53 mmol/mol].

Diagnostic threshold for fasting plasma glucose of ≥7.0 mmol/L (126 mg/dL) were reported by 59%, 89% and 62% of the laboratories in Sri Lanka, Singapore and the Philippines respectively.

The diagnostic cut-off of ≥11.1 mmol/L (200 mg/dL) for post two-hour plasma glucose in an OGTT was reported by 44%, 89% and 42% of the laboratories in Sri Lanka, Singapore and Philippines respectively.

What is considered as adequate control of diabetes?

All participants in Philippines reported HbA1c of <7% [53 mmol/mol] as adequate control. This contrasts with Singapore where only 33% reported <7% as adequate control; while one laboratory reported <6.5% [48 mmol/mol]. More than half of the laboratories in Singapore (56%) did not report HbA1c targets recommended for monitoring of DM. HbA1c targets for control was not assessed in the Sri Lankan survey.

Diabetes screening in pregnancy

Since, not all laboratories provide obstetrics services, only 34, 5 and 79 laboratories responded in Sri Lanka, Singapore and the Philippines respectively. Of the participant laboratories that responded, 71%, 40% and 85% stated that an OGTT is recommended for all pregnant women for Sri Lanka, Singapore and the Philippines respectively.

Urine albumin testing

Fifty six percent, 75% and 69% laboratories recommended early morning spot urine in Sri Lanka, Singapore and the Philippines respectively. Random spot urine is recommended by 28%, and 13% of the laboratories in Sri Lanka and Singapore. The laboratories in the Philippines did not recommend random spot urine. Of the participants, 16%, 50% and 26% laboratories also recommended 24-hour urine albumin measurement in Sri Lanka, Singapore and the Philippines respectively.

For reporting units of spot albumin to creatinine ratio (ACR), it was equally divided between mg/mmol and mg/g, 41% each in Sri Lanka. Fifty percent laboratories in Singapore reported ACR in mg/mmol, 13% reported in mg/g; 38% practise dual reporting. This question was not addressed in the Philippines survey.

Methods for HbA1c and glucose

Traceability to certified reference materials in HbA1c was confirmed by 79% of Sri Lankan laboratories. All laboratories in Singapore and 86% of laboratories in the Philippines use NGSP certified methods. Among the participants in Sri Lanka, 94% declared traceability for the glucose assay. This was not checked in the surveys of the other two countries.

For the assay methodology of HbA1c, 56% of Singapore laboratories use immunoturbidimetry; 22% use enzymatic methods and 22% use high performance liquid chromatography (HPLC). Analytical methodology for HbA1c was not surveyed in the Philippines and Sri Lanka.

EQA Participation for HbA1c and glucose

Thirty eight percent, 100% and 41% of laboratories in Sri Lanka, Singapore and the Philippines respectively, participated in an External Quality Assurance (EQA) programme for HbA1c. The EQA participation rates for HbA1c is lower than that for plasma glucose, for which 88%, 100% and 82% of laboratories in Sri Lanka, Singapore and the Philippines participated respectively.

Types of laboratories

A diverse group of laboratories responded in Sri Lanka, comprising of teaching hospitals (21%), provincial general hospital (3%), district general hospitals (9%), private hospitals (47%), private stand-alone (12%), university (6%) and special children's hospital (3%). One participant did not indicate the type of laboratory.

In Singapore, 78% public laboratories and 22% private laboratories responded.

For the Philippines, the participant laboratories comprised of public hospitals (24%), private hospitals (43%), public stand-alone (7%), private stand-alone (20%), university (5%) and research (1%) respectively. Five respondents from Philippines did not indicate the type of laboratory.

Discussion

Both conventional (mg/dL) and SI units (mmol/L) are used for reporting of glucose results. American journals express glucose in mg/dL while European journals express in mmol/L, reflecting the practice in the respective country and the region. We do not expect confusion over the use of mg/dL or mmol/L as the conversion factor [18 mg/dL = 1 mmol/L] is easily done by a phone calculator. However harmonized reporting in SI Units by all laboratories would make it easier for results interpretation for the end user. A system of dual reporting for a specified period of time, prior to full transition will facilitate this process.

While Europe and New Zealand have adopted sole reporting of HbA1c in mmol/mol, only 6% of laboratories in Sri Lanka, and none of the laboratories in Singapore reported solely in mmol/mol. Thirty four and 67% of laboratories in Sri Lanka and Singapore respectively reported both NGSP% and IFCC mmol/mol, in keeping with the 2007 Consensus statement endorsed by American Diabetes Association (ADA), European Association for Study of Diabetes (EASD), IFCC and International Diabetes Federation (IDF) that results be reported in both IFCC and NGSP units [7].

One advantage of IFCC over NGSP units is that numerical changes of IFCC units appear greater compared to the equivalent NGSP units. For example, a diabetic patient whose HbA1c is improved by NGSP 1% (e.g. from 8% to 7%) may perceive it as insignificant. However, in reality, each 1% HbA1c improvement is associated in relative risk reduction of 14% and 37% for myocardial infarction and microvascular complications respectively as reported in the UKPDS Study [8], and 26% relative reduction in major adverse cardiovascular events in a meta-regression of 18 randomized controlled trials [9]. Conversely, that same diabetic patient whose HbA1c is reported by a laboratory using IFCC unit would have seen the result reduced from 64 mmol/mol to 53 mmol/mol. The reduction in mmol/mol may be perceived to be more significant, may provide motivation for continued medication compliance and sustained lifestyle changes. Secondly, numerical values for NGSP units are similar to values of plasma glucose concentration when expressed in mmol/L which may lead to confusion for some patients. Thirdly, IFCC units are scientifically valid, traceable to SI units and accurately indicate the amount of HbA1c. NGSP units are directly related to clinical outcomes in DCCT and UKPDS trials [10]. To mitigate the confusion, and provide time for adjustment, some countries offered dual reporting for a transitional period of two years before implementing the sole IFCC units [11].

One-third of laboratories in Singapore, and 89% in Philippines offer HbA1c as a diagnostic test. In Singapore, only 33% of laboratories following a diagnostic cut-off for HbA1c could be explained by the relatively late official adoption of HbA1c for diagnosis in 2019 [12]. The late adoption in Singapore was due to the concerns over high prevalence of beta-thalassemia trait and haemoglobin E variant in the local population [13]. The Singapore Ministry of Health (MOH) Circular 08/2019, [12] recommended a HbA1c diagnostic cut-off of ≥7% (53 mmol/mol), based on a local study [14] while patients with HbA1c of 6.1- 6.9% (43 – 52 mmol/mol) shall proceed to test for fasting glucose or 75 g OGTT.

In 2010, the ADA adopted the diagnostic cut-off of HbA1c ≥ 6.5% (48 mmol/mol). Although ADA acknowledges that HbA1c cut-off of ≥6.5% may identify one-third fewer cases of undiagnosed diabetes than a fasting glucose cut-off of ≥ 7.0 mmol/l (126 mg/dL) based on USA National Health and Nutrition Examination Survey (NHANES) data, it notes that a wider application of a more convenient test (HbA1c) will actually increase the number of diagnoses made [15]. In 2011, the World Health Organisation (WHO) also adopted HbA1c of ≥6.5% as the recommended cut-off for diagnosing diabetes [16]. In this regard, Philippines laboratories with 90% of the laboratories indicating the use of HbA1c, demonstrate concordance with international guidelines. There is significant difference in cost per test for plasma glucose and HbA1c, with the former being more cost effective. This may explain the reason for only 50% of laboratories offering HbA1c as a diagnostic test in Sri Lanka.

For monitoring of diabetes, 56% laboratories in Singapore did not report a recommended target, while 100% laboratories in the Philippines recommended a monitoring target of 7%. This may be attributed to the differences in demographics between Singapore and Philippines. In 2022, 15% and 5% of the population is older

than 65 years in Singapore and Philippines respectively [17, 18]. While the HbA1c monitoring target for non-pregnant adults is ≥7%, older adults may benefit from less intensive glycaemic control [19]. The Action to Control Cardiovascular Risk in Diabetes Study Group (ACCORD) randomized 10,251 patients with mean age of 62.2, and showed that intensive glycaemic control does not significantly reduce major cardiovascular events and may increase mortality [20]. ADA recommends an individualised target of 7.5% to 8.5% (58 to 69 mmol/mol) for older adult based on functional status, cognitive impairment and comorbidities taking into account the risk of hypoglycaemia, fall risk and treatment burden [21]. The need for individualised target for elderly patients may dissuade Singaporean laboratories from following a HbA1c monitoring target.

Seventy one percent laboratories in Sri Lanka and 85% in Philippines recommend OGTT for pregnant women. This contrasts with Singapore, where only 40% of laboratories that served obstetrics patients recommend testing at 24 -28 weeks of gestation, despite all of them using International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria for diagnosis of GDM. Variation in practice of GDM screening is not unexpected. For example, United Kingdom National Institute of Clinical Care Excellence (NICE) does not recommend antenatal screening in the absence of risk factors, such as BMI above 30 kg/m2, previous macrosomic baby weighing 4.5 kg or more, and family history of diabetes with or without an ethnicity with a high prevalence of diabetes [22]. Globally the most popular diagnostic criteria are the IADPSG criteria, with cut-offs after a 75 g OGTT of ≥5.1, ≥10.0 and ≥8.5 mmol/L (≥92, ≥180, ≥153 mg/dL) at 0, 1 and 2 hours respectively. These cut-offs were derived from the Hyperglycaemia and Adverse Pregnancy Outcome Study (HAPO) and represent the glucose values at which the odds for birth weight > 90th percentile, cord C-peptide > 90th percentile, and neonatal percent body fat >90th percentile reached 1.75 times the odds of these outcomes at the mean glucose values, based on a fully adjusted logistic regression [23]. IADPSG criteria was noted to increase prevalence of gestational diabetes [24], but may present opportunities for intensive treatment. A Clinical Practice Guideline jointly issued by the Ceylon College of Physicians and Sri Lanka College of Endocrinologists in 2018 endorses universal screening for gestational diabetes at the booking visit based on the IADPSG criteria [25]. In 2022, the Singapore Ministry of Health Agency of Care Effectiveness updated a care guide recommending universal screening at 24 to 28 weeks of gestation using the IADPSG criteria [26]. This updated care guide was timely as only 40% of the Singapore laboratories that served obstetrics patients recommended universal screening prior to the update. In the Philippines, there is no consensus related to the interpretation of results; in addition to the cut-offs recommended by the Philippine Obstetrical and Gynaecological Society, WHO, IADPSG and ADA criteria are also being utilized for interpretation [27]. In view of the wide variation in practice, we recommend professional societies such as IFCC and APFCB to formulate uniform guidelines in consultation with the professional colleges of obstetrics and gynaecology to unify screening strategies for GDM.

Majority of the laboratories in all three countries recommend early morning spot urine or random spot urine for albuminuria, concordant with major professional guidelines [28,29]. The convenience of morning/random spot sampling will enable more patients to be tested, resulting in a higher detection rate. Since effective treatment for albuminuria exists [Angiotensin Converting Enzymes (ACE) inhibitors, Angiotensin Receptor Blocker (ARB) or sodium-glucose cotransporter 2 (SGLT2) inhibitors], early detection and initiation of these drugs will improve renal outcomes [30,31,32].

We note that 78% of laboratories in Singapore currently use immunoturbidimetric assay or enzymatic method for glycated haemoglobin. Only 22% laboratories use HPLC. By automating HbA1c immunoassay or enzymatic method, the requirement to operate a separate instrument is obviated which reduces the manpower requirements and enhances round the clock reporting [33]. Non-HPLC or non-capillary electrophoresis methods (E.g. Immunoassay, enzymatic,) may limit the ability of the laboratory to discern haemoglobin variants [34]. However, HPLC and other chromatographic techniques are also often susceptible to interferences [35,36,37].

While EQA participation rate is high for all participants for glucose, only 38% and 41% of laboratories in Sri Lanka, and the Philippines respectively participated in EQA for HbA1c which may be attributed to high cost and scarce availability of HbA1c EQA programmes.

Our study has several limitations. It has a relatively low response rate of 40% for the Philippines. However, the absolute number of 80, should be representative of the laboratories in Philippines. Validity of our study is contingent on the accuracy of response by the participant laboratories. We did not verify the accuracy of the participant response independently.

The literature reveals wide variation in the cut-offs used for the interpretation of the OGTT in diagnosing GDM in the Philippines [27]. However, we did not verify this observation by a pertinent question related to plasma glucose thresholds in the Philippines survey, which is a limitation.

While we surveyed the reporting units of albuminuria, we did not collate information on the criteria laboratories used to assign albuminuria to different categories. There are various criteria for albuminuria/microalbuminuria. For example, KDIGO guidelines classify spot albuminuria stages into A1 (<30 mg/g or 3 mg/mmol), A2 (30-300 mg/g or 3-30 mg/mmol), and A3 (>300 mg/g or >30 mg/mmol) [38]. In the literature, other guidelines define microalbuminuria as an albumin: creatinine ratio of 2.5 - 25 mg/mmol for men and 3.5 – 35 mg/mmol for women [39]. While we explored the reporting units for albuminuria in question 8, we did not however specify the criteria to assign microalbuminuria.

Our strength includes a diverse group of laboratories (private, public and university) being surveyed in each country, providing a unique perspective of three tropical island-nations in Asia.

Conclusion

Based on the above survey, there are differences in practice across laboratories in the three countries, Sri Lanka, Singapore and the Philippines. Lack of harmonization is evident in reporting units, diabetes monitoring targets, gestational diabetes screening, albuminuria testing and EQA participation. The widespread adoption of SI unit as the sole reporting unit, especially the use of IFCC unit mmol/mol for HbA1c remains difficult for Sri Lanka and Singapore. Scientific bodies and professional associations have an important role in harmonization of laboratory testing related to diabetes. They need to encourage all laboratories to include the use of spot urine albumin to creatinine ratio for albuminuria testing given the convenience, improved access, and actionable renal outcomes through the use of ACE inhibitor, ARB and SGLT2 inhibitor drugs. Overall, the rates for EQA participation for glucose is commendable but can be improved for HbA1c.

Conflicts of interest

Authors have no conflicts of interest to declare.

References

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas. Diabetes Res Clin Pract. 2019; 157:107843. doi: 10.1016/j.diabres.2019.107843.
2. Ogurtsova K, Guariguata L, Barengo NC, Ruiz PL, Sacre JW, Karuranga S, et al. IDF diabetes Atlas: Global estimates of undiagnosed diabetes in adults for 2021. Diabetes Res Clin Pract. 2022;183:109118. doi: 10.1016/j.diabres.2021.109118.
3. Harris MI, Klein R, Welborn TA, Knuiman MW. Onset of NIDDM occurs at least 4–7 years before clinical diagnosis. Diabetes care. 1992;15(7):815-819. doi:10.2337/diacare.15.7.815
4. Afroz A, Alramadan MJ, Hossain MN, Romero L, Alam K, Magliano DJ et al. Cost-of- illness of type 2 diabetes mellitus in low and lower-middle income countries: a systematic review. BMC Health Serv Res. 2018;18(1):972. doi:/10.1186/s12913-018-3772-8
5. Tate JR, Myers GL. Harmonization of clinical laboratory test results. EJIFCC. 2016; 27(1):5-14.
6. Banerjee M, Vasikaran S. Trends in laboratory testing practice for diabetes mellitus. EJIFCC. 2020;31(3):231-241.
7. American Diabetes Association; European Association for the Study of Diabetes; International Federation of Clinical Chemistry and Laboratory Medicine; International Diabetes Federation. Consensus statement on the worldwide standardisation of the HbA1c measurement. Diabetologia. 2007;50(10):2042-2043. doi: 10.1007/s00125-007-0789-7.
8. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000;321(7258):405-412. doi: 10.1136/bmj.321.7258.405.
9. Maiorino MI, Longo M, Scappaticcio L, Bellastella G, Chiodini P, Esposito K, et al. Improvement of glycemic control and reduction of major cardiovascular events in 18 cardiovascular outcome trials: an updated meta-regression. Cardiovasc Diabetol. 2021;20(1):210. doi: 10.1186/s12933-021-01401-8.
10. Florkowski C, Crooke M, Reed M. Implementation of the HbA1c IFCC unit --from the laboratory to the consumer: The New Zealand experience. Clin Chim Acta. 2014; 432:157-161. doi: 10.1016/j.cca.2013.10.009.
11. Jones GR, Barker G, Goodall I, Schneider HG, Shephard MD, Twigg SM. Change of HbA1c reporting to the new SI units. Med J Aust. 2011;195(1):45-46. doi: 10.5694/j.1326-5377.2011.tb03190.x.
12. Ministry of Health Singapore. Release of new screening test review committee guidelines, including changes to diabetes mellitus, lipid disorders, and cervical cancer screening. MOH Circular No. 08/2019. 6 March 2019. (Accessed 10/04/2024). Available at https://www.diabetes.org.sg/wp-content/uploads/2021/11/MOH-Circular-New-Screenting-Test.pdf.
13. Tan ES, Koh C, Law HY, Tan GP, Lai AH, Ng IS. Haemoglobin E-beta Thalassaemia in Singapore. Ann Acad Med Singap. 2014 ;43(6):331-333.
14. Lim WY, Ma S, Heng D, Tai ES, Khoo CM, Loh TP. Screening for diabetes with HbA1c: Test performance of HbA1c compared to fasting plasma glucose among Chinese, Malay and Indian community residents in Singapore. Sci Rep. 2018;8(1):12419. doi: 10.1038/s41598- 018-29998-z.
15. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33 (Suppl 1): S62-69. doi: 10.2337/dc10-S062.
16. World Health Organisation. Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus. Abbreviated Report of a WHO Consultation 2011. (Accessed 10/04/2024). Available at https://iris.who.int/bitstream/handle/10665/70523/WHO_NMH_CHP_CPM_11.1_eng.pdf.
17. The World Bank. Population ages 65 and above (% of total population) - Singapore. United Nations Population Division's World Population Prospects: 2022 Revision. (Accessed 10/04/ 2024). Available at https://data.worldbank.org/indicator/SP.POP.65UP.TO.ZS?locations=SG.
18. The World Bank. Population ages 65 and above (% of total population) - Philippines.United Nations Population Division's World Population Prospects: 2022 Revision. (Accessed 10/04/ 2024).Available at https://data.worldbank.org/indicator/SP.POP.65UP.TO.ZS?locations=PH,
19. Moghissi E. Management of type 2 diabetes mellitus in older patients: current and emerging treatment options.

Diabetes Ther. 2013;4(2):239-256. doi: 10.1007/s13300-013-0039-6.
20. Action to Control Cardiovascular Risk in Diabetes Study Group; Gerstein HC, Miller ME, Byington RP, Goff DC Jr, Bigger JT, Buse JB, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008;358(24):2545-2559. doi: 10.1056/NEJMoa0802743.
21. American Diabetes Association. 11. Older Adults: Standards of Medical Care in Diabetes- 2018. Diabetes Care. 2018 ;41(Suppl 1):S119-125. doi: 10.2337/dc18-S011.
22. National Institute for Health and Care Excellence 2015. Diabetes in pregnancy: management from preconception to the postnatal period (NG3). Last updated: 16 December 2020. (Accessed 11/07/2024) Available at https://www.nice.org.uk/guidance/ng3
23. Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33(3):676-682. doi: 10.2337/dc09-1848.
24. Visser GH, de Valk HW. Is the evidence strong enough to change the diagnostic criteria for gestational diabetes now? Am J Obstet Gynecol. 2013;208(4):260-264. doi: 10.1016/j.ajog.2012.10.881.
25. Ceylon College of Physicians and Sri Lanka College of Endocrinologist. Diabetes Mellitus Management Guideline 2018. (Accessed on 10/04/2024) Available at https://edu.ccp.lk/mod/resource/
26. MOH Agency for Care Effectiveness (ACE). Gestational diabetes mellitus. An Update on screening, diagnosis and follow-up. 22 August 2022. (Accessed 10/04/2024). Available at https://www.ace-hta.gov.sg/docs/default-source/acgs/gdm-an-update-on- screening-diagnosis-and-follow-up-(updated-on-22-august-2022).
27. Pineda-Cortel MR, Suratos T, Mamerto TP. Cut-off points of 75-gram oral glucose tolerance test as a diagnostic test for gestational diabetes mellitus in pregnant Filipino population. J Lab Precis Med. 2022;7:22-26 doi: 10.21037/jlpm-22-26
28. American Diabetes Association. 11. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes-2021. Diabetes Care. 2021;44(Suppl 1):S151-167. doi: 10.2337/dc21-S011.
29. National Institute for Health and Care Excellence 2021. Chronic kidney disease: assessment and management (NG203). Last updated: 24 November 2021 (Accessed 10/04/2024). Available at https://www.nice.org.uk/guidance/ng203
30. Xie X, Liu Y, Perkovic V, Li X, Ninomiya T, Hou W, et al. Renin-Angiotensin System Inhibitors and Kidney and Cardiovascular Outcomes in Patients With CKD: A Bayesian Network Meta-analysis of Randomized Clinical Trials. Am J Kidney Dis. 2016; 67(5):728-741. doi: 10.1053/j.ajkd.2015.10.011.
31. Jongs N, Greene T, Chertow GM, McMurray JJV, Langkilde AM, Correa-Rotter R, et al. DAPA-CKD Trial Committees and Investigators. Effect of dapagliflozin on urinary albumin excretion in patients with chronic kidney disease with and without type 2 diabetes: a prespecified analysis from the DAPA-CKD trial. Lancet Diabetes Endocrinol. 2021;9(11):755-766. doi: 10.1016/S2213-8587(21)00243-6.
32. Cherney DZI, Zinman B, Inzucchi SE, Koitka-Weber A, Mattheus M, von Eynatten M, et al.Effects of empagliflozin on the urinary albumin-to-creatinine ratio in patients with type 2 diabetes and established cardiovascular disease: an exploratory analysis from the EMPA- REG OUTCOME randomised, placebo-controlled trial. Lancet Diabetes Endocrinol. 2017;5(8):610-621. doi: 10.1016/S2213-8587(17)30182-1.
33. Yeo CP, Ng WY. Automation and productivity in the clinical laboratory: experience of a tertiary healthcare facility. Singapore Med J 2018;59(11):597-601. doi: 10.11622/smedj.2018136.
34. Rhea JM, Molinaro R. Pathology consultation on HbA1c methods and interferences. Am J Clin Pathol 2014 ;141(1):5-16. doi: 10.1309/AJCPQ23GTTMLAEVL.
35. Lorenzo-Medina M, De-La-Iglesia S, Ropero P, Nogueira-Salgueiro P, González-Fernández FA. Interference of hemoglobin (Hb) hope on measurement of HbA1c using an HPLC method. J Diabetes Sci Technol 2021;15(4):974-975. doi: 10.1177/19322968211008521.
36. Wan Nik WNFH, Shafii N, Che Soh NAA, Bahar R. Significantly High HbA1c in Diabetic Patient with Hb J: Case Report. Oman Med J. 2022;37(4): e393. doi: 10.5001/omj.2022.14.
37. Chen CF, Tai YK. A rare haemoglobin variant (Hb Phnom Penh) manifesting as a falsely high haemoglobin A1c value on ion-exchange chromatography. Singapore Med J. 2014;55(8):e126-128 doi: 10.11622/smedj.2014108.
38. Rossing P, Caramori ML, Chan JC, Heerspink HJ, Hurst C, Khunti K, Liew A, Michos ED, Navaneethan SD, Olowu WA, Sadusky T. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. Kidney international. 2022 ;102(5):S1-27. https://doi.org/10.1016/j.kint.2022.06.008
39. Johnson DW, Jones GR, Mathew TH, Ludlow MJ, Chadban SJ, Usherwood T, Polkinghorne K, Colagiuri S, Jerums G, MacIsaac R, Martin H. Chronic kidney disease and measurement of albuminuria or proteinuria: a position statement. Medical Journal of Australia. 2012 ;197(4):224-225. https://doi.org/10.5694/mja11.11468