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Possible Factors Affecting the Results of Blood Glucose Assay: A Survey in Central India

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Abstract: India harbors world's highest number of people with diabetes. Estimation of Blood Glucose, important in management of diabetes is done either in a clinical laboratory using wet chemistry kits or with SMBG device using dry-chemistry strips. To determine the possible factors affecting the results of blood glucose, a survey was undertaken in both segments. In the surveyed area, among lab participants, only 10% actually did calibration with calibrators. Half of the labs in the survey have performed IQC measures such as by using Internal Quality Control Materials (IQCM), but not with mandatory each batch of assay and among that, 20% used it on daily routine. Ouly 40% labs have verified the quality of standards provided with kits but none checked the manufacturers claim about its sensitivity, linearity, absorption wavelength, incubation intervals, color stability interval and the interferences. There are several studies demonstrating that diabetes can be controlled in a better way if patients have access to cost-free adequate supplies, especially of blood-glucose test strips along with a training class, consultations with dietitian and monthly support meetings. In the absence of such government-sponsored support systems for people with diabetes in India, we decided to undertake survey that would help us to understand the practices followed by the SMBG users and the level of understanding among them regarding their device and device strips. The survey brought out some important facts that would have a direct consequence on the management of diabetes. The users were not provided training about the use of the device and its strips, 55% had heard about the expiry date of the strips, but ouly 6% knew about Technical (desiccator's) Expiry of strips. Very few (~12%) had crosschecked their results from a clinical lab and this was when 25% of the users did not believe the results they got on their device. The results are presented here.

Key words: Diabetes mellitus, IDDM, NIDDM, SMBG

INTRODUCTION

According to the Diabetes Atlas, 2006, published by the International Diabetes Federation, the number of people with diabetes in India currently around 40.9 million is expected to rise to 69.9 million by 2025 unless urgent preventive steps are taken (Mohan *et al*., 2007). Diabetes is recognized as one of the most severe health problem in the world, attacking men, women, children and the elderly. It is a leading cause of kidney failure, (Anonymous, 2005), blindness in adults, nervous system damage and amputations. It has a major risk factor for heart disease, stroke and birth defects (Anonymous, 2004). SMBG device is considered an important component of preventive care in diabetes management

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(Clarke *et al*., 1987; Evans *et al*., 1999) and is strongly recommended to Type-1 diabetics (Anonymous, 2000, 2003). Also, if SMBG is not used properly or overused may lead to misleading results and increase in healthcare costs (Nichols *et al*., 2007). Two methods are available to both IDDM and NIDDM patients to monitor their blood glucose, one is by wet chemistry method in any clinical chemistry lab or by using SMBG device at home. Both methods need scrupulous adherence to quality assurance practices. Since at both the ends these practices are not mandatory in India, we wanted to find out the scenario by conducting two surveys to cover these two segments. The data is presented here.

MATERIALS AND METHODS

Two surveys were designed to understand the market trends, clinical/pathology lab practices and e ase and understanding of SMBG users about their devices (Table 1), during March 2006 to March 2007.

Survey-1

Survey on Practices Followed by Clinical Chemistry Labs

Survey-1, meant for clinical chemistry labs, was divided into three parts, (a) a feedback from the suppliers of diagnostic kits and IQC materials in the surveyed area, (b) a feedback from the quality control managers of participating labs on their analytical practices in the form of questionnaire and (c) enrollment of these labs in our External Quality Assessment Scheme (EQAS).

Survey-I

(a) Diagnostic kit dealers (Feedback on the demand of Quality Control Material)

To determine the market of internal quality control materials in Nagpur area (Vidarbha region, Maharashtra State, India), a short survey was done with five leading diagnostic dealers that cater to 95% of all operating clinical labs of the region. They were asked about their total number of clients, their sale of calibrators and control sera and its quantum (Table 2).

Table 1: Fact file of clinical lab tests and SMBG

Factors	Clinical lab testing	SMBG Device
Users	Skilled and trained professionals	Unskilled amateur
Minimum qualification	Post graduates	None
Portable system	No	Yes
Self monitoring	Not Possible	Routine
Blood specimen	Venous	Capillary, Venous
Specimen quantity	1000-2000 µL	3 to 20 µL
Time interval for estimation	20 minutes or more	3 to 50 seconds
Odd hour testing for patients	Difficult	Routine
Internal QCM available	Yes	Rarely
External quality control program available	Yes	None
Reagent kits	Wet-chemistry	Dry-chemistry
Close system for consumables	No	Yes
Repeat assay for crosschecking specimen	Possible	Impossible
Repeat assay comparison with other labs	Possible	Impossible
Humidity factor for assay	No	Yes
Temperature control for assay	Yes	Difficult
Hematocrit volume interference in assay	No	Yes
Calibration of pipetting volume	Possible	Impossible
Cost of setup	High	Very low
Cost of reagent	Less	High
Specimen required	Plasma, sernm	Whole blood
Skill of blood withdrawal	High	Low
Verification of stability of reagents	Routine	Difficult

Table 2: Feedback survey from local diagnostic dealers

	Participant dealers				
Questions	I	II	III	IV	V
With approximately how many laboratories do you deal?	400	200	220	120	190
Do you sell calibrators?	No	No	No	No	Yes
Do you sell quality control sera (Material)?	Yes	No	Yes	No	Yes
How many laboratories buy calibrators?	None	None	None	None	0 to 1
How many different brands of QC material do you deal?	2 to 3	0	1	0	1
How many laboratories buy quality control Sera (Material)?	20	None	12	None	4

Table 3: The feedback from the participating clinical lab practitioners

Questions	Yes (%)
Do you participate in EQAS?	70
Do you participate in at least one EQAS Program?	70
Do you know the importance of calibrators?	40
Have you calibrate your system with a calibrator?	10
Did you perform IQCM Test ever?	50
Do you do IQCM testing with each batch?	0
Do you do IQCM testing daily?	20
Do you do IQCM testing continuously?	20
Do you think there is any need to use IQCM daily?	20
Have you ever checked the calibration of your pipettes?	20
Have you ever checked the calibration of your standards?	40
Have you ever checked the linearity and sensitivity of your reagent kit?	0
Have you ever checked the wavelength study of your reagent kit?	0
Have you ever checked the incubation and color stability study on reagent kit?	0
Have your lab derived your own reference intervals for any analyte?	0
Have you ever verified internal and external interference claims of kit's manf.?	0
Do you verify all results with high abnormality constituents on dilution?	80
Do you think it will be helpful to have compulsory IQCM+EQAS participation?	10
Do you think a regularity authority like FDA, India for Blood Banks, should help?	0
Do you think attending regular scientific updates should be made compulsory?	70

(b) Clinical/Pathology Laboratory (Feedback from Quality Managers)

In the second part of Survey-1, a total of 44 request letters were sent to small-scale clinical laboratories to participate in a survey. The participating labs were asked to answer a questionnaire about their quality control practices (Table 3) and to report assayed values of requested analytes in the two unknown specimens.

(c) External Quality Assessment Program (Two Specimens)

These labs were then recruited in the third part of the survey-I. All participating labs were sent bovine-sera in ethanadiol stabilizing agent as specimens. This sera was received nnder the ACBI/CMC-EQAS. ACBI/CMC conducts External Quality Assurance program for all voluntarily participating clinical chemistry labs in India http://www.acbiindia.org). This sera was used as a specimen as it could be refrigerated many times and was stable at room temperature for one day http://www.cmcvellore.ac.in). As previously informed, on a given day two unknown specimens were dispatched in sterile single use container to each lab for analyzing Glucose by GOD-POD. Each specimen was carefully sealed and delivered within 1 h to city labs and within a day to outstation labs.

Survey-II: Survey of SMBG Use

Survey-II was primarily designed to survey the level of operational and extra-operational knowledge of users about SMBG device and to determine their routine practices in using them. In survey-II, a total of 250 diabetic patients using SMBG device from 6 months to 8 years participated verbally by answering 25 questions. Participants were informed about the objective of this survey and were asked questions in the language of their choice. The participants, 131 Males and 119 Females were from a cross-section of society with differing socio-economic backgronnd (Table 6).

RESULTS AND DISCUSSION

Two methods are available to both IDDM and NIDDM patients to monitor their blood glucose, one is by wet chemistry method in any clinical chemistry lab or by using SMBG device at home (Table 1).

Survey-I

The outcome of the first part of Survey I is shown in Table 4 and 5. All the five participating dealers in the survey have a clientele ranging from 120 to 400 labs with a sum of 1130 labs. Considering common clients for more than one dealer and from inputs of dealers, it was estimated that the total number of labs in the region is around 500 (Table 4 and 5).

The survey revealed that about 36 labs ask for QCM from their dealers and on taking the details of each, many names were in duplicate that brought down the actual buyers of IQCM to 16. There was one dealer who dealt in calibrators and sold it to only one buyer. Three dealers were dealing in 2 to 3 different brands of internal qnality control material and selling it to all prospective buyers. Accreditation guidelines of NABL do not mention mandatory use of calibrators on routine, as long as the results of IQCM fall within acceptable range, whereas, the application of multilevel IQCM in each batch of assay is mandatory (ISO 15197). The results of the survey reveal the alarmingly low number of labs using calibrators and control.

In a questiounaire sent to participating private laboratories (Table 3), 50% labs informed performing IQC (Internal Quality Control) measures and 70% labs participated in ouly one EQAS (External Quality Assessment Scheme) in clinical chemistry. Among participants, 40% knew the importance of using calibrator for calibrating clinical assays but ouly 10% actually performed it. Half of the labs in the survey have performed IQC measures such as using internal qnality control materials (IQCM), but not routinely used it along with each batch of assay, whereas, 20% participants used it daily. Moreover, only 40% labs have verified the quality of standards provided with the reagent kits but none of the participants have ever checked the manufacturers claim about its sensitivity, linearity, absorption wavelength, incubation intervals, color stability interval and the interferences. A good 80% labs acknowledged verifying all grossly abnormal values by suitable means, but only 20% of these labs checked the calibration status of their pipettes. On questioning participants whether it should be made compulsory 'to attend regular scientific updates,' 70% said yes, but all the participants rejected the idea of compulsory involvement in internal quality control measures and participation in external quality control schemes. Moreover, none of the participants endorsed the need to have a body for regulating practices of clinical laboratories in India. All the participating labs preferred to use reference intervals for all biochemical analytes from the standard textbooks, rather than generating their own reference intervals. Among the participants the best score of a lab was 65% and the worst was Zero. In the third part of Survey I, initially only four out of 44 labs consented to the request to participate in the survey; showing their reluctance to participate in such EQAP. Similar reluctance was also observed from the fact that 1587 labs participated in CMC/ACBI-EQAS program in 2004. That number rose to 1775 in the year 2005, although there are at least 50,000 Labs operating in India (Francis, 2002).

Two specimens were sent to participating labs for glucose assay. The average difference from the mean value is 11 and 10.3 mg dL^{-1} for specimen 1 and 2, respectively, with a highest difference of 25.1 mg dL^{-1} (16.7%). The average SDs for all participating labs is 1.409 and 1.716 for specimen 1 and 2, respectively and 60% labs obtained 2SD. The 30% of the participating labs that received specimen-1 and 20% of the participating labs that received specimen-2 obtained the results between 2 and 3 SD. Ten percent participants for specimen1 and 20% participants of specimen-2 obtained results beyond

Table 4: Survey report on glucose (specimen-1)

	Acceptable range (mg dL^{-1})					
Lab No.	Low	High	Target	Lab result (mg dL^{-1})	Difference (mg dL^{-1})	LAB-SD
1	128.7	175.5	152.1	160.0	7.9	1.010
2	128.7	175.5	152.1	145.0	-7.1	-0.910
3	128.7	175.5	152.1	152.0	-0.1	-0.010
4	128.7	175.5	152.1	127.0	-25.1	-3.220
5	128.7	175.5	152.1	171.0	18.9	2.420
6	128.7	175.5	152.1	144.0	-8.1	-1.040
7	128.7	175.5	152.1	155.0	2.9	0.370
8	128.7	175.5	152.1	173.0	20.9	2.680
9	128.7	175.5	152.1	165.0	12.9	1.650
10	128.7	175.5	152.1	146.0	-6.1	-0.780
Average	128.7	175.5	152.1	152.1	11.0	1.409
Research lab	128.7	175.5	152.1	150.0	-2.1	-0.270

Table 5: Survey report on glucose (specimen-2)

	Acceptable range (mg dL^{-1})					
Lab No.	Low	High	Target	Lab result (mg dL^{-1})	Difference (mg dL^{-1})	LAB-SD
1	99.1	135.1	117.1	123.0	5.9	0.980
2	99.1	135.1	117.1	109.0	-8.1	-1.350
3	99.1	135.1	117.1	115.0	-2.1	-0.350
4	99.1	135.1	117.1	98.0	-19.1	-3.180
5	99.1	135.1	117.1	136.0	18.9	3.150
6	99.1	135.1	117.1	109.0	-8.1	-1.350
7	99.1	135.1	117.1	121.0	3.9	0.650
8	99.1	135.1	117.1	134.0	16.9	2.820
9	99.1	135.1	117.1	132.0	14.9	2.480
10	99.1	135.1	117.1	112.0	-5.1	-0.850
Average	99.1	135.1	117.1	117.1	10.3	1.716
Research lab	99.1	135.1	117.1	118.0	0.9	0.150

Table 6: Questionnaire for SMBG users practices and knowledge

Questions to smbg users	(%)
Can you read and nnderstand English?	56
Have you read your SMBG user manual?	29
Have you read your SMBG Strips user manual?	08
Did any responsible person train you about using SMBG and its strips?	32
Do you know that you should consume strips within expiry date of bottle?	55
Are you aware that your SMBG strips have technical expiry date?	06
Do you consume strips within Expiry date of bottle?	36
Would you consume strips pack within technical expiry date (~ 60-90 days)?	34
Do you regularly check your SMBG with electronic strips?	10
Have you ever checked your SMBG with Quality Control Solutions (QCS)?	00
Do you have the knowledge about quality control solutions?	15
Have you ever verified your SMBG results with clinical lab results?	12
Are you aware of latest SMBG's giving lab equivalent results and not higher?	00
Have you ever noticed your diabetologist doing device checks with QCS?	00
Do you know retesting on device to confirm its accuracy is not much useful?	05
Have you purchased SMBG for cutting the cost on lab testing?	32
Do you close the cap of strip bottle immediately and not after the test are done?	26
Do you believe in accuracy of your SMBG results?	30
Have you regularly used SMBG during nighttime and at odd hours?	36
Have you been taught to self re-adjusting your anti-diabetic doses?	17
Are you achieving better glycemic control after SMBG use?	34
Are you willing to perform SMBG test, as per norms of >4 times per week?	06
If user manuals of SMBG and its strips are in local languages, will you read?	40
Do you think that prior to using SMBG, knowledge is required for its use?	90
If QCS costs less than in Rs.100/-, will you buy them every month?	06

3SD. As per accreditation norms of NABL, all results should be within 2SD for IQCM and within 3SD for EQAS. A corrective action is advised for results beyond 3SD or for results continuously beyond 2SD parameter.

The analytical evaluation study for blood glucose with 10 participant labs under the survey did not show any blunder in the results, although a few of them showed more inaccuracy than others. Survey-2: This survey brought out some glaring facts, such as:

- Manufacturers and suppliers did not arrange training for SMBG buyers. They are only interested in the sale.
- Users are not interested in reading elaborate user mannals.
- Users have low dependability on their SMBG results.
- Many users are ignorant about technical expiry of strips and even after awareness, cost burden pushes them to intentionally ignore.
- None of the IDDM participants have ever monitored their blood glucose, 4 times a day as per ADA guidelines.
- The quality control solutions are not included in the SMBG kit by most of the manufacturers, moreover they are also not available off the counter and all such reasons make its users unaware about its usefulness.

Survey-II

In India, there are many more challenges for a proper usage of SMBG devices by its users especially due to socio-economic conditions (Table 6). Moreover, all such devices marketed and available in India have their user mannals and strip literatures either in English or in other foreign languages. This is very important since ouly 34% population of India understands English Language, although, English is Indian's second language but only after Hindi (Anonymous, 2005) and almost negligible number of people understand other foreign languages. Also, it is important to mention that these instructions are often exhaustive (one of them has 133 pages for devices), elaborate, scientific and hardly readable (with a very small font size). It is worth a mention that these non-analytical parameters are very important for an overall performance of device and its strips (Anonymous, 1990). The survey showed that although 56% of the users could read and understand English, less than a third number (29%) of participants had read the device user manual and mere 08% had read SMBG device strips user instructions. A good 90% participants accepted that prior knowledge of working of device is necessary but only 32% actually received any training by a responsible person (not compulsorily a diabetic trainer and includes SMBG-retailers). This is on the backdrop that 55% were aware of the concept of expiry and 36% agreed that they do use strips before the expiry date on the bottle, However, the most startling revelation was the lack of awareness with participants since only 06% were aware of technical (desiccator's) expiry of strips, since, on making them aware of technical expiry (often within 2 to 3 months), about 34% showed willinguess to use the strips within technical expiry. Some of the participants accepted to have used 50 strips in a bottle for up to one year; this is almost 4 to 6 times of permissible duration. None of the participants had any idea about the quality control solutions and its usefulness in crosschecking the results. Probably this is the reason why ouly 30% participants believed in their SMBG results. Among participants ouly 6% (IDDM or NIDDM) of them were performing tests more than 4 times a week on their SMBG as advised by ADA (Anonymous, 1995). The 94% participants did not show any willingness to buy quality control solutions even when made available at low price. The SMBG is not been used by the participants for what it is developed for, testing glucose at odd hours and at bedtime. The survey also highlighted the

improper storage of strips, since only 26% participants closed the cap of the strip container immediately after taking out the strips. This also suggests fast `aging of the strips', which may further affect the sensitivity of strips (Frishman *et al*., 1992). We are fully aware that the cost of regular utilization of SMBG strips is a costly proposition for majority of people (Bowker *et al*., 2004), more so, for Indians in view of the poor economic scene. It was also found that SMBG devices are more popular in medium to higher income groups of the Indian society. But cutting across various strata of the society, none of the IDDM patients of the surveyed group acknowledged testing blood glucose at least 4 times a day and only 6% of patients (IDDM or NIDDM) acknowledged going by a plan of testing at least 4 times a week (Evan Benjamin, 2002).

CONCLUSIONS

Authors acknowledge that the sample size in this study was small and a more in depth and extended approach is needed to draw any conclusive decisions. The results obtained here may not be extrapolated to visualize a global scenario even in the Indian context, but will certaiuly help to visualize a situation in small towns and cities of India and other equivalently placed countries.

ABBREVIATIONS

SMBG	:	Self Monitoring Blood Glucose
IQCM	:	Internal Qnality Control Material
EQAS	:	External Qnality Assessment Scheme
QCM	:	Quality Control Material
ACBI/CMC	:	Association of Clinical Biochemists of India/Christian Medical College, Vellore, India
NABL	:	National Accreditation Board for Testing and Calibrating Laboratories (India)
ADA	:	American Diabetes Association

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