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Original Article

Paediatrics Section

The Role of Point-of-care Glucose Monitoring Devices in Initiating Treatment for Neonatal Hypoglycaemia: A Cross-sectional Study

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ABSTRACT

Introduction: Detection and prompt management of hypoglycaemia among at-risk and symptomatic neonates is crucial to prevent neurodevelopmental morbidity. Laboratory-based Formal Random Blood Sugar (FRBS) is the gold standard for estimating Blood Glucose (BG) levels. Point-of-care Glucose Monitoring Devices (POCGMD)/glucometers that provide immediate results are used as surrogates. Glucometers provide widely variable and overestimated values of BG. Therefore, when using glucometers, a higher cut-off value for glucose may have to be considered as the operational threshold for hypoglycaemia.

Aim: To evaluate the adequacy of POCGMD for detecting the threshold levels for treating neonatal hypoglycaemia by assessing the agreement with FRBS values.

Materials and Methods: This cross-sectional study was conducted in the Neonatal Intensive Care Unit (NICU), Malankara Orthodox Syrian Church Medical College, Kerala, India, from July 2022 to October 2022. A total of 258 infants at risk for and with hypoglycaemia were selected through convenience sampling. BG was estimated simultaneously in the laboratory and with a POCGMD. Three different types of POCGMDs were consecutively used in the unit during the study period. FRBS and POCGMD values were evaluated using Spearman's rank correlation coefficient. The agreement between the gold standard FRBS and POCGMD values was ascertained through Bland-Altman plots. Receiver Operating Characteristic (ROC) curves identified the higher cut-off levels for each of the brands of POCGMDs at which intervention for hypoglycaemia should be initiated.

Results: The present study showed a strong positive correlation between the standard laboratory FRBS and POCGMD measurements. However, there was no agreement between FRBS and POCGMD values according to Bland-Altman graphs. The mean bias values for BG were higher for glucometers. The ROC curves identified 62 mg/dL for Accu-Check, 59 mg/dL for Contour, and 53 mg/dL for AccuSure as the optimum cut-off corresponding to the operational threshold of FRBS of 45 mg/dL.

Conclusion: Glucometers overestimate BG values and miss the biochemical thresholds for treating neonatal hypoglycaemia. When POCGMDs are used, a higher cut-off value may have to be considered as the operational threshold for initiating treatment for hypoglycaemia.

Keywords: Agreement, Blood glucose, Glucometers, Newborns

INTRODUCTION

Blood sugar monitoring is one of the most common investigations undertaken during neonatal care. Infants who are premature, of low birth weight, growth-retarded, born to diabetic mothers, or have had perinatal hypoxia-ischaemia are at risk for hypoglycaemia [1,2]. The incidence of hypoglycaemia was, as high as, 51% in these at-risk infants [3]. Studies from India have reported an incidence ranging from 15.3% to 33.3% [4,5].

Hypoglycaemia was defined as a BG concentration of less than 45 mg/dL [2]. Immediate therapy needs to be initiated at the operational threshold of blood sugar levels [6,7]. This is to prevent the adverse neurological effects of hypoglycaemia, such as acute cerebral dysfunction (seizures and coma) associated with long-term neurodevelopmental impairment [8]. While laboratory-based FRBS estimation continues to be the gold standard for BG estimation, values obtained by POCGMD or glucometers are accepted surrogates for initiating treatment [9].

The advantage of immediate availability of results, a small volume of blood sample, ease of utilisation and cost-effectiveness has made the POCGMD an inseparable part of newborn care. The present study was undertaken to evaluate the adequacy of POCGMD for detecting the threshold levels for treating neonatal hypoglycaemia by assessing the agreement of FRBS values with three different types of glucometers.

MATERIALS AND METHODS

The present cross-sectional study was undertaken in the NICU, Malankara Orthodox Syrian Church Medical College, Kerala, India, over a period of 4 months from July 2022 to October 2022. Institutional ethics committee clearance (MOSC/IEC/632/2022) was obtained before commencing the study.

Inclusion criteria: Infants at risk of neonatal hypoglycaemia, such as Infant of Diabetic Mother (IDM), Large for Gestational Age (LGA) (birth weight >90th centile), Small for Gestational Age (SGA) (birth weight <10th centile), Low Birth Weight (LBW) (birth weight <2.5 kg), and preterm infants (<37 weeks gestation), were included in the study.

Exclusion criteria: Infants who did not warrant glucose monitoring were excluded from the study.

Sample size: A total of 432 samples were evaluated from 258 infants who were enrolled in the study by convenience sampling.

Study Procedure

Parents were informed of their infant's risk for hypoglycaemia and consent for monitoring of BG was obtained. From all the neonates 0.5 mL of blood was collected in fluoride tubes at the time of venous cannulation and FRBS estimated by the glucose oxidase method was considered the gold standard. POC glucose measurement was simultaneously done from the same venipuncture.

Three different types of devices namely Accu-Chek Aviva Plus (Roche), Contour Next (Bayer) and AccuSure Pro (Taldoc Technology Corporation) were used consecutively in the unit during the study period for POC assessment of glucose. (Contour Next was sourced from overseas for the present study and only 56 strips were available).

STATISTICAL ANALYSIS

The relationship between laboratory FRBS and POCGMD values was evaluated using Spearman's rank correlation coefficient. Bland-Altman plots were plotted for agreement between the FRBS value and the values obtained by the glucometers. ROC curves were generated to detect the optimal cut-off glucometer values for FRBS of 45 mg/dL. R (EZR) software was used for statistical analysis.

RESULTS

A total of 258 infants were enrolled in the study. Of these, 143 (55.4%) infants were males and 115 (44.6%) were females. Among them, 168 (65.1%) were term infants and 90 (34.9%) were preterm infants. Additionally, 57 (22.1%) infants were small for gestational age while 10 (3.9%) were large for gestational age. Fifty-nine (22.9%) infants were born to mothers with gestational diabetes. The mean birth weight was 2.63±0.7 kg (Range: 0.78-4.78 kg) [Table/Fig-1].

Characteristics	n (%)
Gender	
Male	143 (55.4)
Female	115 (44.6)
Gestation	
Term	168 (65.1)
Preterm	90 (34.9)
Birth weight, Kg	
(Mean±SD)	2.63±0.70
Range	0.78-4.78
Small for Gestational Age (SGA)	57 (22.1)
Large for Gestational Age (LGA)	10 (3.9)
Infant of Diabetic Mother (IDM)	59 (22.9)
Formal Random Blood Sugar (FRBS) (Mean±SD)	45.97±24.92

[Table/Fig-1]: Demographic characteristics of study cohort (N=258).

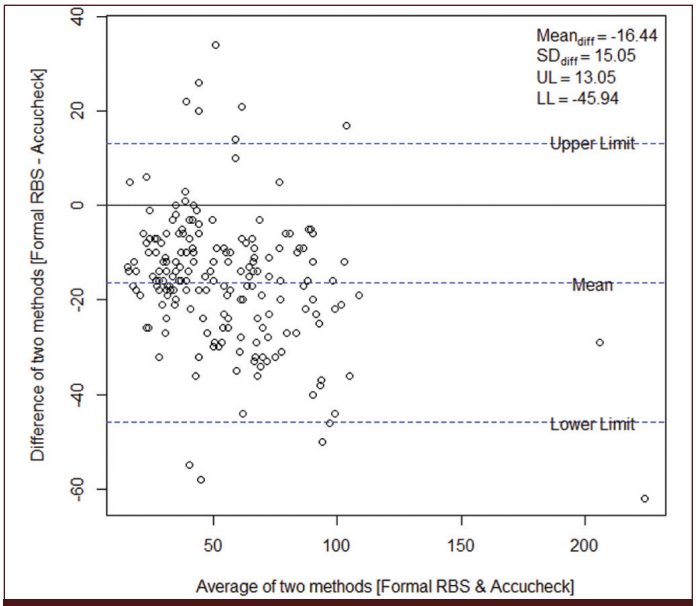
Of the 432 samples, 196 were evaluated with Accu-Chek, 180 with AccuSure, according to the availability of the glucometer in the unit, and 56 with Contour.

Correlation coefficients showed a strong positive correlation between FRBS and each of the three POCGMD values. For Accu-Chek r-value=0.849 (p-value <0.001), for Contour r-value=0.88 (p-value <0.001) and for AccuSure r-value=0.87 (p-value <0.001) [Table/Fig-2].

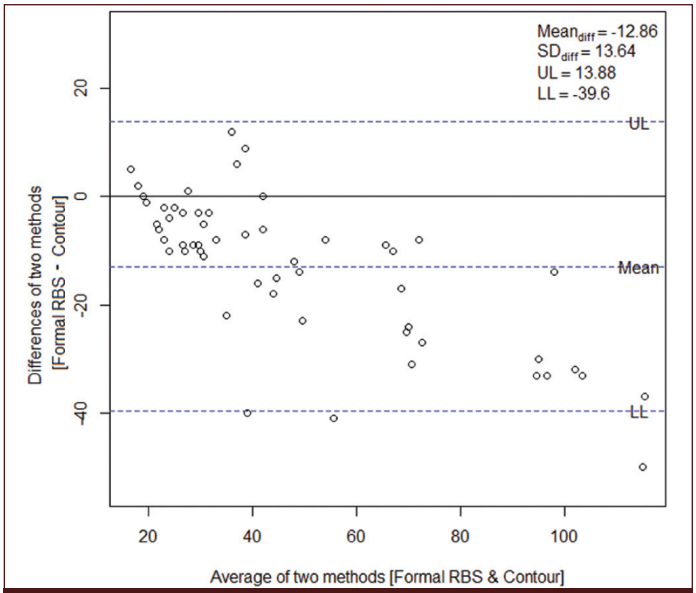
Device	Mean±SD		n	r-value	p-value
	POCGMD	FRBS			
Accu-Check	63.12±32.12	46.71±26.80	196	0.849	**<0.001**
Contour	54.28±32.94	41.58±22.65	56	0.880	**<0.001**
AccuSure	51.19±23.53	46.5±23.40	180	0.870	**<0.001**

[Table/Fig-2]: Correlation between POCGMD and FRBS.

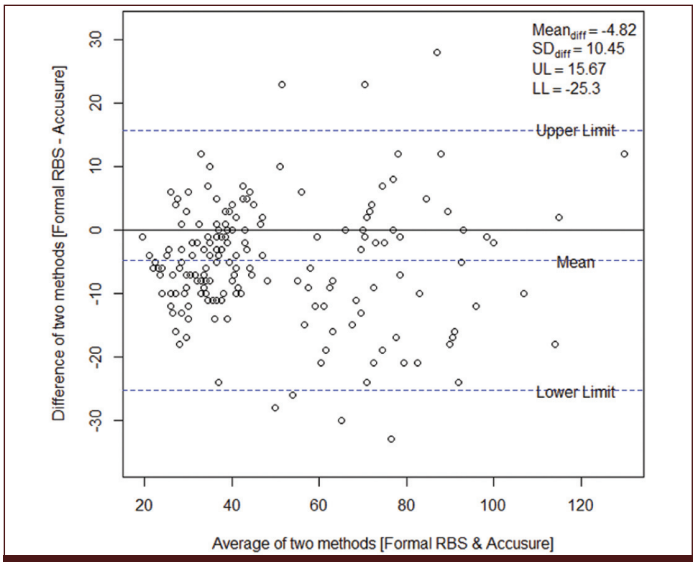
Bland-Altman graphs were generated to find the agreement of POCGMD readings with FRBS values. The mean bias values for BG measured by the glucometers were higher than the formal glucose levels, with the lowest bias of -4.8±10.45 for AccuSure compared to -16.44±15.05 for Accu-Chek and -12.86±13.64 for Contour. There was no significant agreement between FRBS and the values of any of the three glucometers. Values obtained by AccuSure were closer to formal blood sugar [Table/Fig-3a-c].



[Table/Fig-3a]: Bland-Altman graph for Agreement-Accu-Chek and FRBS (n=196).

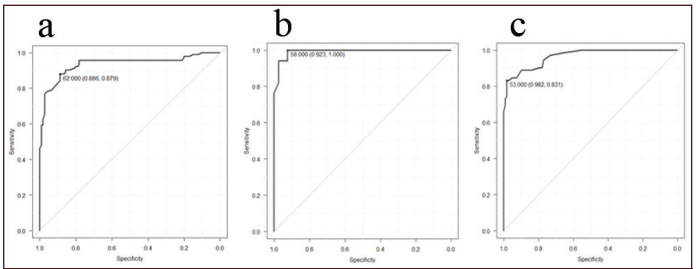


[Table/Fig-3b]: Bland-Altman graph Agreement-Contour and RBS (n=56).



[Table/Fig-3c]: Bland-Altman graph Agreement-AccuSure and RBS (n=180).

The ROC curves identified 62 mg/dL for Accu-Chek, 59 mg/dL for Contour and 53 mg/dL for AccuSure as the optimum cut-off for FRBS of 45 mg/dL [Table/Fig-4].



[Table/Fig-4]: ROC to detect FRBS=45 mg/dL: a) for Accu-Chek; b) for Contour; c) for AccuSure.

Using Accu-Chek, a cut-off value of <62 mg/dL had 88% sensitivity, 89% specificity, 87% Positive Predictive Value (PPV) and 89% Negative Predictive Value (NPV) for predicting hypoglycaemia as defined by formal BG of <45 mg/dL. With Contour, a cut-off value of <59 mg/dL had 92% sensitivity, 100% specificity, 100% PPV, and 85% NPV. A value of <53 mg/dL on AccuSure had 83% sensitivity, 98% specificity, 96% PPV and 89% NPV for predicting hypoglycaemia [Table/Fig-5].

Variables	Accu-Chek (n=196)	Countor (n=56)	AccuSure (n=180)
Optimum cut-off	62	59	53
Sensitivity	0.88	0.92	0.83
Specificity	0.89	1.00	0.98
PPV	0.87	1.00	0.96
NPV	0.89	0.85	0.89

[Table/Fig-5]: Sensitivity and specificity of POCGMD in relation to Formal Random Blood Sugar (FRBS) cut-off of 45 mg/dL.

DISCUSSION

Neonates are vulnerable to disturbances in glucose metabolism, particularly hypoglycaemia. Both preterm and term neonates are at risk for adverse neurodevelopmental outcomes with prolonged hypoglycaemia. Hence, accurate and rapid determination of hypoglycaemia and its prompt treatment is of utmost importance to decrease potential morbidity.

Enzyme-based (glucose oxidase/hexokinase) auto analysers are routinely used in laboratories for measuring plasma/BG levels and have been found to be reliable, irrespective of the enzymatic methodology used [10]. Factors like haematocrit levels and interference by metabolites do not significantly affect these values. Blood glucose measured by laboratory methods has always been the gold standard to confirm the glycaemic status of an individual. However, the longer time to obtain results and the requirement of a greater volume of blood make laboratory-based "formal blood sugar" assessment suboptimal for immediate intervention at operational thresholds of neonatal hypoglycaemia.

Glucometers like AccuSure and Contour use flavin adenine dinucleotide-glucose dehydrogenase and Accu-Chek Aviva by Roche uses Quinoprotein glucose dehydrogenase enzyme test strip technology. The enzymes in the strip convert glucose to byproducts, which generate a direct current that the meter interprets as BG [9,11].

Caution about interpreting "finger stick" glucose values has been mentioned in earlier studies [12]. Elaborate evaluation using different types of POCGMD highlighted that the greatest accuracy was within physiological limits of glucose levels and became less reliable at higher and lower levels. Most POCGMDs were more unreliable at lower levels of glucose [9].

Various studies have compared results between glucometers of different manufacturers with variable results in neonatal units and commented on the sensitivity and specificity of glucometer values [13,14]. The present study has shown a strong positive correlation between laboratory FRBS and POCGMD values, similar to studies that have used the coefficient of correlation [15-17]. However, when Bland-Altman analysis was used, there was no agreement between the laboratory and POC device measurements.

A good correlation is often, albeit erroneously, considered adequate for a good surrogate test [13]. As is often the case, these studies are done with adult diabetics in mind. It is felt by the authors that "Agreement" and "Correlation" should never be considered synonymous. A good correlation with poor agreement would be even more dangerous in matters of neonatal hypoglycaemia, where the decision for treatment is based on very narrow variations in BG values. Therefore, the agreement between the glucometer values and the formal blood sugar values is of importance, especially at lower glucose levels.

A difference of 15 mg/dL between POCGMDs and reference measurements was considered acceptable for values less than or equal to 75 mg/dL by the International Organisation for Standardisation (ISO) and Food and Drug Administration (FDA) [18,19]. However, this would not be considered acceptable in neonates, where a difference of 15 mg/dL would affect the interventional threshold for hypoglycaemia. While a BG value of 50 mg/dL would be considered normal in first 48 hours of life, a value of 35 would warrant therapy. This was highlighted by the absence of agreement observed in the present study of different types of glucometers.

It must be recognised that while screening at-risk infants, the glucometer is expected to forewarn the clinical team about impending hypoglycaemia rather than inform when the formal glucose values are indeed well below the accepted operational threshold. The present study has shown that higher glucometer values would have to be considered as operational thresholds for managing neonatal hypoglycaemia. Therefore, it would be prudent for every neonatal unit to have specific POCGMD-based cut-off levels determined by the brand of glucometer in use for initiating intervention for hypoglycaemia.

Limitation(s)

Parameters like haematocrit, temperature, hypoxia, etc., that could alter or affect the glucometer readings were not evaluated in the present study. Other glucometers available in the market were not used for the study.

CONCLUSION(S)

The POCGMDs could overestimate the blood sugar values and miss the biochemical thresholds for treating neonatal hypoglycaemia. When glucometers are used, a higher cut-off value for glucose may have to be considered as the operational threshold for initiating management for hypoglycaemia. Neonatal units should ascertain this threshold cut-off value for the brand of POCGMD being used. It is recommended that future studies be undertaken with different types of glucometers to realise their advantages and limitations.

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