Diabetes & Metabolic Syndrome: Clinical Research & Reviews 15 (2021) 221–227

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Blood glucose levels should be considered as a new vital sign indicative of prognosis during hospitalization

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ARTICLE INFO

Article history:
Received 14 December 2020
Received in revised form
17 December 2020
Accepted 17 December 2020

Keywords:
Blood glucose
Cardiovascular disease
Impaired glucose tolerance
Intensive insulin therapy
Hypoglycemia
Glycemic variability

ABSTRACT

Background and aims: The measurement of vital signs is an important part of clinical work up. Presently, measurement of blood glucose is a factor for concern mostly when treating individuals with diabetes. Significance of blood glucose measurement in prognosis of non-diabetic and hospitalized patients is not clear.

Methods: A systematic search of literature published in the Electronic databases, PubMed and Google Scholar was performed using following keywords; blood glucose, hospital admissions, critical illness, hospitalizations, cardiovascular disease (CVD), morbidity, and mortality. This literature search was largely restricted to non-diabetic individuals.

Results: Blood glucose level, even when in high normal range, or in slightly high range, is an important determinant of morbidity and mortality, especially in hospitalized patients. Further, even slight elevation of blood glucose may increase mortality in patients with COVID-19. Finally, blood glucose variability and hypoglycemia in critically ill individuals without diabetes causes excess in-hospital complications and mortality.

Conclusion: In view of these data, we emphasize the significance of blood glucose measurement in all patients admitted to the hospital regardless of presence of diabetes. We propose that blood glucose be included as the "fifth vital sign" for any hospitalized patient.

1. Introduction

Vital signs (temperature, pulse rate, blood pressure, and respiratory rate) represent objective measurements of the essential physiological functions of a human being [1]. For over 100 years, physicians and nurses have measured these vital signs, recognized changes in the clinical status, and reached important management decisions.

Assessment of vital signs of a patient is considered critical for clinical evaluation and forms the basis of management of patient care in triage, as it conveys to the physician the degree of derangements from the baseline parameters [2]. The extent of changes in vital signs also predicts severity of illness, long-term patient health outcomes, frequency of hospital readmissions, and prognosis [3]. Therefore, it is crucial for a health care professional to understand the various pathophysiological processes affecting the measurements of vital signs and their interpretation for timely clinical decision making.

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https://doi.org/10.1016/j.dsx.2020.12.032
1871-4021/

Blood glucose is a requisite for the body to maintain normal metabolic processes. Any deviation from the normal range of blood glucose may have adverse consequences and contributes to morbidity and mortality. Thus, blood glucose is one of the important parameters for the prognosis in any disease; signifying its documentation as an essential part of clinical monitoring.

In this review, we shall discuss the significance of blood glucose levels in the context of overall health, specifically in non-diabetic individuals. We present arguments that determination of blood glucose should be carried out in all hospitalized adults and screening in all patients visiting hospital. Finally, based on these data, we believe it is apt to consider "blood glucose" as the fifth vital sign.

2. Methods

The data were collected from studies published in the Electronic databases PubMed and Google Scholar on the various impacts of elevated blood glucose in hospitalized subjects without known diabetes, unrecognized diabetes, and prediabetes using the following keywords: Blood glucose, admissions, diabetes, critical illness, hospitalizations, cardiovascular disease (CVD), hyperglycemia, prediabetes, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), normal range of blood glucose, intensive insulin therapy, morbidity and mortality. Relevant studies were included to underline the consistent outcomes of blood glucose levels and to present arguments on the significance of considering blood glucose as parameter in clinical assessment along with other vital signs. The studies are presented based on the various health risks associated with blood glucose levels in upper normal range, mildly hyperglycemic range, hypoglycemic range and showing inordinate variations of blood glucose in non-diabetic individuals. Studies which revealed the importance of maintaining tight glycemic control in critical care settings were also included. These have been summarised in Table 1 and 2.

2.1. Health risks associated with blood glucose in upper normal range or mild hyperglycemia in individuals without diabetes

There are a number of studies which show that blood glucose in 'upper normal range' or even mild increase in blood glucose could be harmful for health. The data have been summarised in Table 1. The association between fasting plasma glucose (FPG) in normoglycemic range and increased risk of CVD outcomes was evaluated in a prospective study in Israel. Individuals (n, 10,913 men and women) with fasting plasma glucose <100 mg/dL as well as 100–125 mg/dL and free of diagnosis of CVD were followed up for 4.3 years. The authors showed that subjects with fasting blood glucose levels in the high normal range of 95–99 mg/dL had an increased CVD risk (HR 1.53; CI 95% [1.22–1.91], P < 0.001), when compared to those having blood glucose levels <80 mg/dL [4]. In a study including 74,309 person-years of follow-up (from 1992 through 2004) among 13,163 subjects who had baseline fasting plasma glucose levels <100 mg/dL showed robust relationship between 'higher glucose in the normal range' and subsequent development of diabetes. Specifically, after adjustment for multiple factors (age, family history of diabetes, body mass index, physical-activity level, smoking status, and serum triglyceride levels), a progressively increased risk of type 2 diabetes was seen in men with fasting plasma glucose levels of 87mg/dL (4.83 mmol/L) or more, as compared with those whose levels were in the bottom quintile (less than 81 mg/dL [4.5 mmol/L], P for trend <0.001) [5]. Balkau *et al.* [6] in a systematic review analyzed the association between high blood glucose not in diagnostic range for diabetes (identified by their 2-h glucose levels following an oral glucose tolerance test and by the absence of a prior diagnosis of diabetes) and the risk of death from all causes, coronary heart disease (CHD), CVD, and neoplasms in non-diabetic cohorts of the Whitehall (n, 10,025), the Paris Prospective (n, 6629), and the Helsinki Policeman (n, 631) studies. Mortality analyzed according to the percentiles of the 2-h and fasting glucose distributions revealed that men in the upper 20% of the 2-h glucose distributions and those in the upper 2.5% for fasting blood glucose had a significantly higher risk of all-cause mortality in comparison with men in the lower 80% of these distributions. Interestingly, fasting plasma glucose ≥6.0 mmol/L or 106 mg/dL (OR 11.0; 95% confidence interval (CI) 2.1–77.3), in addition to age and BMI, were significant risk factor for post-operative complications after bariatric surgery [7]. In addition to these, a study among 5511 non-diabetic adults from the U.S showed association of insulin resistance (by homeostasis model assessment for insulin resistance (HOMA-IR)) with all-cause or disease-specific mortality among non-diabetic persons [8].

Subjects with prediabetes as compared to those without have higher chances of hyperglycemia during hospital admissions and are also prone to sepsis and infections [4,9–11]. In this context, it is important to note that high prevalence (14–29.5%) of prediabetes has been reported [12] from various regions of India [13] and conversion to diabetes from prediabetes is also rapid [14]. In a retrospective cohort of 260,487 Korean adults, association of changes in fasting blood glucose with incident CVD and all-cause mortality showed that when compared to individuals with persistent normal fasting glucose (NFG), individuals who shifted from NFG to diabetic fasting glucose (DFG) had an increased risk of stroke (HR [95% CI]: 1.19 [1.02–1.38]) and individuals who shifted from NFG to IFG or DFG had increased risks of all-cause mortality (HR [95% CI]: 1.08 [1.02–1.14] for NFG to IFG and 1.56 [1.39–1.75] for NFG to DFG). Further, when compared to individuals with persistent IFG, individuals who shifted from IFG to DFG had an increased risk of myocardial infarction and all-cause mortality (HR [95% CI]: 1.65 [1.20–2.27] and 1.16 [1.02–1.33]), respectively [15]. Data that show relationship of prediabetes with CVD have been consistently published. The Multi-Ethnic Study of Atherosclerosis (MESA) study revealed that prediabetes is associated with a nearly 3-folds higher prevalence of unrecognized myocardial infarction compared with NGT status [16]. A systematic review and meta-analysis of prospective studies also revealed that subjects with the highest post-challenge blood glucose level with a midpoint range of 150–194 mg/dL had a 27% greater risk for CVD compared with the group with the lowest level midpoint range of 69–107 mg/dL, (RR, 1.27 [95% CI, 1.09–1.48) [17]. A retrospective study in which the prevalence of new-onset prediabetes (with HbA1c levels of 5.7%–6.4%) in 362 hospitalized patients with acute ischemic stroke was examined, showed that prediabetes is highly prevalent in such patients [18]. These data indicate that blood glucose in upper normal range and in prediabetes range is associated with multiple adverse health outcomes.

2.2. Hyperglycemia in apparently non-diabetic hospitalized patients and mortality

Several observational studies had shown that the prevalence of hyperglycemia in patients without diagnosis of diabetes or no history of diabetes at hospital admissions ranged from 32% to 38% in community hospitals [19–21], 44% in patients with heart failure [22], 41% in critically ill patients with acute coronary syndromes [22], and in 80% of patients after cardiac surgery [23,24]. In a heterogeneous population of critically ill patients in intensive care unit (ICU), about 31% of the population was shown to have at least one blood glucose reading of 200 mg/dL and nearly 100% of patients had a blood glucose value > 110 mg/dL [25].

Table 1
Studies detailing health risks associated with hyperglycemia in individuals with prediabetes and without diabetes.

S.No	Studies	Type of study	Glycemic variations and outcomes		
			Type of glycemic variation	Decision range/cut-off	Outcomes
1.	Wang *et al.* (2020) [30]	Retrospective	Fasting blood glucose (FBG)	FBG ≥ 126 mg/dL	Fasting blood glucose ≥ 126 mg/dL was associated with 28-day mortality risk in COVID-19 patients
2.	Li *et al.* (2020) [27]	Retrospective	Blood glucose within 24 h after ICU admission	Average, minimum, and maximum blood glucose levels within 24 h of hospital admission	Predicted lowest mortality risk and better prognosis for average and maximin blood glucose in the range of 110-140 mg/dL and for minimum blood glucose in the range of 80-110mg/dL within 24 hr after ICU admission
3.	Mcgrade *et al.* (2019) [26]	Retrospective	Elevated blood glucose during hospital admission	Blood glucose levels in quartiles; <55 mg/dL, 55 −140 mg/dL,140−200 mg/dL and >200 mg/dL	Highest mortality in quartiles with blood glucose levels <55 mg/dL and >200 mg/dL
4.	Lee *et al.* (2018) [15]	Retrospective	Normal fasting glucose (NFG): Impaired fasting plasma glucose (IFG)	NFG< 100 mg/dL: IFG:100.0 −125.9 mg/dL	Increased all-cause mortality in patients when status is shifted from NFG to IFG.
			Impaired fasting glucose (IFG): Diabetic fasting glucose (DFG)	IFG: 100.0−125.9 mg/dL: DFG≥ 126.0 mg/dL	Increased risk of stroke and all-cause mortality in patients when status is shifted from NFG to DFG
5.	Ausk *et al.* (2010) [8]	Prospective	Insulin resistance by homeostasis model assessment	Quartiles of HOMA-IR HOMA-IR < 1.4 HOMA-IR >1.4−2.0 HOMA-IR>2.0−2.8 HOMA-IR>2.8	Increased mortality risk in quartile with HOMA-IR>2.8 Increased cardiovascular mortality in quartiles with HOMA-IR >1.4−2.0 HOMA-IR>2.0−2.8 HOMA-IR>2.8
6.	Barsheshet *et al.* (2006) [28]	Prospective	Admission blood glucose levels	Admission blood glucose: First tertile: 84−97 mg/dL Second tertile: 108 −121 mg/dL Third tertile: 136−162 mg/dL	Increased in- hospital and 60-day mortality observed in third tertile with admission blood glucose levels are between is 136 −162 mg/dL Each 18 mg/dL rise in blood glucose was associated with 31% in-hospital mortality risk and 12% 60-day mortality
7.	Levintan *et al.* (2004) [17]	Meta-analysis of prospective studies	High post-challenge blood glucose	Post-challenge blood glucose Highest postchallenge glucose midpoint range :150-194 mg/dL Lowest postchallenge glucose midpoint range : 69-107 mg/dL	Increased risk of CVD in individuals with highest post-challenge blood glucose, midpoint range:150−194 mg/dL compared to individuals with lowest postchallenge glucose midpoint range.
8.	Balkau *et al.* (1998) [6]	Review on Whitehall, Paris Prospective & Helsinki Policeman studies	High but non-diabetic blood glucose levels	2 h blood glucose and fasting blood glucose	Increased risk of all-cause mortality observed for subjects in upper 20% of 2 h glucose & upper 2.5% of fasting blood in comparison with subjects in the lower 80% of these distributions

Mcgrade *et al.* [26] investigated the effect of elevated blood glucose levels at the time of admission with in-hospital mortality and length of hospital stay in 18,478 adults admitted to a University Medical Centre in US. These authors classified blood glucose (mg/dL) levels in the following quartiles of mg/dL; <55, 55−140, 140−200 and > 200. The data showed an increase in mortality in each glucose quartile; highest in patients admitted with a glucose value of <55 mg/dL or >200 mg/dL. Association between blood glucose within 24 h after ICU admission and prognosis was evaluated in a retrospective cohort study in non-diabetic Chinese patients (n, 14,237). The authors showed that after adjusted for confounders including age, sex, disease severity scores and comorbidities, an average blood glucose ranged 110−140 mg/dL, a minimum blood glucose ranged 80−110 mg/dL, and a maximum blood glucose ranged 110−140 mg/dL was associated with the lowest risk of hospital mortality and better prognosis in patients

Table 2
Studies detailing health risks associated with blood glucose in hypoglycemic range in individuals without diabetes.

S.No	Studies	Type of study	Glycemic variations and outcomes		
			Type of glycemic variation	Decision range	Outcomes
1.	Mcgrade *et al.* (2019) [26]	Retrospective	Blood glucose levels during hospital admissions	Blood glucose <55 mg/dL	Increased in-hospital mortality in patients with blood glucose levels <55 mg/dL.
2.	Tsujimotto *et al.* (2015) [37]	Retrospective	Hypoglycemia during hospital emergency room visits	Blood glucose <40 mg/dL	Increased mortality risk is associated with blood glucose <40 mg/dL
3.	Egi *et al.* (2010) [39]	Retrospective	Blood glucose level in critically ill patients	Blood glucose <81 mg/dL	Increased mortality in critically ill patients with blood glucose <81 mg/dL
4.	Preiser *et al.* (2009) (GLUCONTROL study) [40]	Prospective	Blood glucose	Target blood glucose in intensive insulin therapy (IIT) arm: 80–110 mg/dL	No significant reduction in mortality in IIT arm *vs.* conventional insulin therapy arm. Trial halted prematurely because of an increased incidence of hypoglycemia in the intensive insulin therapy arm
5.	Mendoza *et al.* (2005) [38]	Retrospective	Blood glucose levels during hospital admissions	Blood glucose≤50 mg/dL	Increased mortality risk in patients with hypoglycemia

without diabetes [27]. Association between admission glucose levels and mortality outcome was robustly shown in a cohort of 4102 hospitalized non-diabetic Israeli patients with heart failure. Specifically, these authors showed that each 18 mg/dL increase in blood glucose level was associated with a 31% increased risk of in-hospital mortality (adjusted odds ratio, 1.31; 95% confidence interval, 1.10–1.57; P = 0.003) and a 12% increase in 60-day mortality (adjusted odds ratio, 1.12; 95% confidence interval, 1.01–1.25; P = 0.04) but no increase in 6 month and 12 month mortality [28].

Further, ICU mortality was observed to be more than doubled in patients with new onset hyperglycemia (NOH) as compared to known patients with diabetes (25.3% ± 3.3% *vs* 12.8% ± 2.6%, p < 0.05) despite having similar blood glucose concentrations. These authors opined that "having hyperglycemia without a history of previous diabetes mellitus is a major independent risk factor for ICU and hospital mortality" [29]. Interestingly, in a recent study the relationship between fasting blood glucose (FBG) and 28-day mortality in patients with SARS-CoV-2 infection(COVID-19) without previous diagnosis of diabetes was investigated. The results showed that FBG ≥126 mg/dL at admission was an independent predictor for 28-day mortality [30]. Further, in a recent modeling study from Kuwait, level of FBG and risk of ICU admission in patients with COVID-19 were analyzed. These authors proposed that the optimal level at which intensive glucose control should be initiated cannot be determined using conventional modeling of FBG. They emphasized that even a small incremental increase within the normal range of blood glucose is associated with a substantial increase in risk of ICU admissions [31]. It has been argued that hyperglycemia is likely to be a marker of illness, rather than a direct mediator [32]. Nonetheless, clinicians should understand this exponential risk especially in countries where prediabetes and undiagnosed diabetes are prevalent, e.g., Kuwait, India etc.

Relationship of blood glucose levels and malignancies continues to be explored. In a meta-analysis of eight studies in non-diabetic patients, authors analyzed the effect of hyperglycemia on overall survival, disease-free survival (DFS) and progression-free survival. They showed that hyperglycemia was associated with adverse DFS and overall survival [33]. Further, the correlation between increased random blood glucose (RBG) in non-diabetic breast cancer patients with their overall survival (OS) and time to tumor recurrence (TTR) showed that patients with elevated RBG levels had shorter overall survival (HR 3.01; 95% CI [1.70–5.33]; p < 0.001) and time to TTR (HR, 2.08; CI [1.04–4.16]; p = 0.04) when compared to patients with non-elevated RBG levels after controlling for tumor grade, tumor stage, race and BMI (HR, 3.50; CI [1.87–6.54]; p < 0.001) [34].

2.3. Health risks of hypoglycemia or inordinate variations in blood glucose levels (glycemic variability) in hospitalised patients with and without diabetes

2.3.1. Hypoglycemia

Even though hypoglycemia is not common in non-diabetic individuals but may occur in sepsis, severe liver disease, malnutrition, alcohol abuse, malignancies, post-gastrectomy syndrome, post bariatric surgery dumping syndromes, Addison's disease etc. [35,36]. It is becoming clearer that hypoglycemia in critically ill patients without diabetes is associated with poor clinical outcomes. Data from various studies have been summarised in Table 2. In a total of 59,602 consecutive cases that visited the emergency room in a Japanese hospital, 530 patients with severe hypoglycemia (patients with and without diabetes) were identified. Interestingly, the data showed that mortality within 90 days after severe hypoglycemia was significantly higher in patients without diabetes than in patients with diabetes [20.3 *vs.* 1.6% (P < 0.001)]. Importantly, authors stated that a blood glucose level of <40 mg/dL was a strong predictor of death in the non-diabetic people [37]. In a retrospective review of medical records [38], 88 patients without diabetes but having other disease conditions (chronic renal failure, alcohol intoxication, liver failure, sepsis, cancer, etc.) who presented with a blood glucose level of ≤50 mg/dL at the time of hospital admission were shown to have a high mortality rate. A study from Australia in critically ill patients who had at least one episode of hypoglycemia (blood glucose level, <81 mg/dL) showed the association between mild or moderate hypoglycemia and increased risk of mortality [hypoglycemic group, 36.6% *vs.*19.7% in non-hypoglycemic control group (P < 0.001)] [39]. As discussed previously, Mcgrade *et al.* [26] showed that low blood glucose level (<55 mg/dL) is significantly associated with in-hospital mortality. The GLUCONTROL study in which effects of intensive insulin therapy (IIT) was compared with an intermediate glucose control in ICU patients also demonstrated an increased incidence of hypoglycemia in the IIT arm. No significant reduction in mortality was observed in the IIT arm in comparison with the conventional insulin therapy arm (17.2% in IIT arm *vs.* 15.3% in conventional insulin therapy arm). The trial was halted prematurely [40].

2.3.2. Glycemic variability

Glycemic variability, recently an area of intense research in patients with diabetes, may also pose health risk in individuals without diabetes. In a heterogeneous population of 3252 critically ill adult patients, the effect of glycemic variability (assessed by the standard deviation of each patient's mean glucose level), on mortality was investigated using the Acute Physiology and Chronic Health Evaluation II score (APACHE II, standard point score method mortality rates) among the study cohort. This score was 12.1% with the lowest quartile of glycemic variability (least glycemic variability), 19.9% in the second quartile, 27.7% in the third and 37.8% in the fourth quartile (highest glycemic variability). In addition, ICU stay was shortest in those with lowest quartile of glycemic variability [41]. A retrospective review of a large cohort of prospectively collected database in setting of medical and surgical ICUs in 2208 patients with a total of 11,335 blood glucose values was carried out in India. Glycemic variability measured by the standard deviation (SD) of mean blood glucose and glycemic lability index, were significantly associated with medical and surgical ICU mortality. Patients with blood glucose values in the euglycemic range but highest glycemic variability had higher mortality (54%) compared to mortality (24%) in patients above the euglycemic range [42]. Bancks *et al.* [43] in their study that included non-diabetic participants of the Coronary Artery Risk Development in Young Adults (CARDIA) Study showed that higher intra-individual fasting plasma glucose variability during young adulthood before the onset of diabetes was associated with incident diabetes, macrovascular events and mortality. A study by Yu *et al.* [44] among Korean population showed that long-term fasting plasma glucose variability was independently associated with myocardial infarction and stroke in a general population without diabetes.

2.4. Impact of maintaining blood glucose in tight range in critical care settings

Benefits of maintenance of blood glucose levels within a tight range in critically ill patients have been subject of studies and debate. Moreover, cut-off of good control of blood glucose in ICU has been a moving target. Two decades ago, Van den Berghe *et al.* [24] were first to demonstrate benefits of aggressive glycemic control in critical care setting. These investigators performed proof of concept single centre randomized controlled trials in surgical, medical, and pediatric ICUs. Patients admitted to ICUs were randomized to receive either IIT (target blood glucose range 80–110 mg/dL) or conventional blood glucose range (180–200 mg/dL). The study including 1548 patients of which 86% has hyperglycemia but were not known to have diabetes and approximately 60% had cardiac ailments (either underwent a coronary bypass surgery or valve replacement or a combined procedure) [24,45]. The authors reported that subjects receiving IIT had reduced ICU mortality by 42% (4.6% in the intensive-treatment group *vs.* 8.0% in the conventional-treatment group). The authors further showed a reduction in overall in-hospital mortality by 34%, bloodstream infections by 46%, acute renal failure requiring dialysis or hemofiltration by 41%, the median number of red-cell transfusions by 50%, and critical-illness polyneuropathy by 44% with intensive blood glucose control *vs.* conventional treatment group. Importantly, patients receiving IIT were less likely to require prolonged mechanical ventilation and intensive care [24]. Overall, beneficial response of IIT which could control blood glucose within age-adjusted narrow limits (80–110 mg/dL in adults, 70–100 mg/dL in children, and 50–80 mg/dL in infants) was clearly shown by these authors. Significant results among the critically ill surgical patients, along with remarkable mortality benefits from the use of IIT targeting normoglycemia created a strong interest in intensive glycemic management in the ICU. In another study, the use of Intensive Insulin Protocol (IIP) was shown to be beneficial in reducing incidence of deep sternal wound infections and risk of death in patients undergoing open heart surgery when target level of blood glucose were 150–200 mg/dL *vs.* > 200 mg/dL [46].

Contrary to these remarkably positive results, subsequent studies which replicated the above protocol showed increased mortality risk with intensive glycemic control. These trials included prospective randomized multi-centre controlled trial on tight glucose control by intensive insulin therapy in heterogenous patients in adult intensive care units (GLUCONTROL), Normoglycemia in Intensive Care Evaluation and Surviving Using Glucose Algorithm Regulation (NICE-SUGAR), and Efficacy of Volume Substitution and Insulin Therapy in Severe Sepsis (VISEP). The GLUCONTROL, a prospective, randomized, controlled, multi-centric study was conducted in a heterogeneous population of 3500 critically ill patients aged 18 years and older at the time of admission. The participants were randomized to two groups: group 1 with target blood glucose 140–180 mg/dL as the conventional insulin therapy arm or to group 2 with target blood glucose 80–110 mg/dL as the IIT arm. However, the study failed to show any clinical benefit of IIT on ICU mortality. In addition, higher rate of hypoglycemia was observed in group 2 (8.7%) than in group 1 (2.7%, $p < 0.0001$) [40]. The NICE-SUGAR study, a multi-centered, multinational trial involving 42 hospitals in Australia, New Zealand, Canada, and the United States included 6100 medical and surgical patients admitted to the ICUs. The investigators showed that, compared with conventional therapy (maintaining the glucose concentration at <180 mg/dL), IIT (target blood glucose 81–108 mg/dL) was associated with an increased mortality 90 days after randomization. Further, severe hypoglycemia was observed [blood glucose level, ≤40 mg/dL], in 6.8% patients in the intensive-control group and 0.5% in the conventional-control group ($P < 0.001$)] [47]. Similarly, the VISEP trial on ICU patients with severe sepsis or septic shock also failed to reproduce the mortality benefits of IIT as observed in the Van den Berghe trial [48]. In this context, it is important to note that increased cardiovascular risk with intensive blood glucose control has been shown in several trials in patients with type 2 diabetes [49–51]. It is possible that the higher mortality in intensively blood glucose control group as compared to conventional group could be due to reasons beyond hypoglycemia such as changes in drug regimens, unidentified interaction of prescribed combination of drugs, and risk factors for hypoglycemia [40,47,48]. Importantly, as discussed previously, an unrecognized factor could be occurrence of glycemic variability [52]. Furthermore, the success of Van den Berghe protocol can be viewed based on the selected factors and the criteria and other confounding factors [53].

3. Conclusion

Studies till date indicate that blood glucose, in the upper normal, mildly hyperglycemic, or hypoglycemic ranges adversely influences hospital outcomes in those not known to have diabetes previously. This may be particularly important in developing countries where considerable number of individuals is at risk for developing hyperglycemia [54]. We suggest that blood glucose be measured in all hospitalized patients and should be considered as fifth vital sign. Further, variability of blood glucose must be taken in consideration of treatment protocol in an effort to decrease mortality in individuals without diabetes. Further research in this area is now possible with the widespread availability of low cost glucose meters and advanced technologies for continuous glucose monitoring [55].

Authorship contrbution statement

Jothydev Kesavadev: Conceptualization, Methodology, Writing, Reviewing, Editing, Finalisation. Anoop Misra Conceptualization, Methodology, Writing, Reviewing, Editing, Finalisation. Banshi Saboo: Conceptualization, Methodology, Reviewing, Editing. Aravind SR: Conceptualization, Methodology, Reviewing, Editing. Akhtar Hussain: Reviewing, Editing. Leszek Czupryniak: Reviewing, Editing. Itamar Raz: Reviewing, Editing.

Acknowledgements

We are thankful to Sreelakshmi R and Gopika Krishnan for writing, editing, and finalising this paper.

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