

# Chronic hyperglycemia in critically ill: Another piece in the glycemic control puzzle

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Diabetes has become a major healthcare problem in India. As per International Diabetes Federation, there were an estimated 40 million persons with diabetes in India in 2007 and this number is predicted to rise to almost 70 million people by 2025. It is estimated that every fifth diabetic patient in the world would be an Indian. Moreover for every known diabetic there is one unknown diabetic due to lack of universal screening. This immense public health problem will have a reflection on demographic of intensive care population. In a retrospective review 11% of all intensive care unit (ICU) admission in a general medical/surgical unit were diabetic. Diabetic status on admission is traditionally detected by history of previous diabetes and use of oral hypoglycemic agents or insulin, but this approach will miss patients with unknown diabetes or uncertain history. American Diabetes Association (ADA) has defined a glycosylated hemoglobin (HBA1c) cut-off of 6.5% for the diagnosis of diabetes. Thus it seems that admission HBA1c might be a better reflector of chronic hyperglycemia and will detect occult diabetes. In an observational study of trauma patients without a known history of diabetes, almost a quarter of patients had an elevated HBA1c reflecting high prevalence of occult diabetes in this population.<sup>[1]</sup>

A review of the literature on the effect of diabetes on the outcome in critically ill population need to differentiate the effects of pre-morbid diabetic status on the outcome of this patient population unrelated to the degree of hyperglycemia on admission and also consider effects of acute hyperglycemia in diabetics who become seriously ill.

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There are conflicting reports in the literature about the impact of pre-morbid diabetic status on the outcome of critically ill depending on the patient subset studied. Diabetics are shown to have an adverse outcome after surgery specifically coronary artery bypass surgery. On the contrary pre-morbid diabetic status was not shown to have an adverse prognosis in medically ill and septic patient.<sup>[2]</sup> In a large database of heterogeneous ICU population diabetic status had a protective effect on mortality, adjusted odds ratio for mortality 0.75 (0.74-0.76,  $P < 0.001$ ) compared to non-diabetics.<sup>[2]</sup> In an observational study diabetics with high HBA1c on admission fared worse when their sugars were intensively controlled during hospitalization than similar patients without sugar control. This was also reflected in an out-patient interventional study with type II diabetic.<sup>[3]</sup>

Acute hyperglycemia (stress induced), hypoglycemia and glycemic variability has been found to be poor prognostic factors in various subsets of critically ill patient including trauma patients. A large retrospective review of critically ill diabetic subsets, observed a decreased risk of mortality between blood sugars of 110 and 180 mg/dl in diabetics as compared to non-diabetics with similar blood sugar.<sup>[4]</sup> Hypoglycemia was an independent factor for mortality independent of diabetic status and glycemic variability was an independent risk factor for mortality only in patients

without diabetes. In another observational study non-diabetics with time weighted glucose concentration between 144 and 180 mg/dl were almost twice as likely to die in ICU than diabetics.<sup>[5]</sup> They were also three times more likely to die in ICU when compared to diabetics when the time weighted glucose concentration was between 180 and 198 mg/dl. In a multivariate logistic analysis hyperglycemia was strongly and significantly associated with worse outcome ( $P < 0.001$ ) in non-diabetics than in diabetic critically ill patient. Thus observational studies in a heterogeneous group of ICU patients clearly indicates that association of hyperglycemia and mortality is much stronger in non-diabetics than in diabetics and a premorbid state of diabetes may have a protective effect in these group of patients.

In this issue of the journal the authors have investigated outcome of the trauma patient with elevated HBA1c in a surgical ICU.<sup>[6]</sup> In their cohort of 120 consecutive trauma patients 17 patients had diabetes as per ADA criteria (HBA1c  $>6.5\%$ ) on admission. Of these six patients were not known to be diabetic. In a risk adjusted analysis patients with HBA1c of more than 6% were at 4.5 times more likely to have a poor outcome compared with those with HBA1c of  $<6$ . The investigators did not attempt to study the impact of glucose control on various outcomes in this subset or the effect of acute hyperglycemia on the outcome.

Similar to the medical/surgical critically ill patient, observational studies have confirmed that acute glucose elevation is predictive of adverse outcome in critically injured trauma patient. In observational studies in trauma population admission blood sugar of  $>200$  mg/dl was associated with worse outcome and increased infectious morbidity.<sup>[7,8]</sup> There is a 1.5 fold increased mortality in diabetic patients with isolated traumatic brain injury when compared to non-diabetics. In a study analyzing National Trauma Bank data to assess the impact of diabetic status on the outcome of the trauma patient it was found on multivariate analysis, insulin-dependent diabetes was an independent weak predictor of infectious morbidity and ICU length of stay.<sup>[9]</sup> However, diabetes was not associated with mortality or hospital length of stay. In a large observational study on tight glycemic control in a mixed medical surgical ICU, subset of the trauma patient failed to show better outcome.<sup>[10]</sup> In this study, non-diabetics benefitted more with tight glycemic control than diabetics.

The biological plausibility of diabetics behaving differently than non-diabetics in critically ill patient in

general and trauma population in particular is still not clear. Adaptive mechanisms to chronic hyperglycemia might make this population less vulnerable to toxic effects of stress induced acute hyperglycemia and they might be more tolerant to fluctuations of blood sugar. On the other hand patients with uncontrolled diabetes may fare worse due to metabolic derangements associated with poor diabetes control and other associated comorbidities.

The authors have addressed the need of utilizing a robust marker of chronic hyperglycemia to study outcome of critically ill diabetic patient which probably will be the standard in future studies. They have also selected a group of trauma cohort in whom this problem has not been much explored. Larger studies of similar kind need to be done to address definitively the issues of effect of premorbid diabetic status as assessed by HBA1c in trauma patients. Studies are need to assess their effects on mortality and clinically relevant morbidity parameters and organ specific dysfunction, with correlation with the degree of raised HBA1c on admission to outcomes, effect of acute stress induced hyperglycemia in diabetic patients, effect of intensive glucose control in diabetic subset of the trauma patient, effect of type of diabetes and the desirable range of blood sugar in diabetics to achieve optimal outcome.

Finally, given the seemingly paradoxical and contradictory observations in various studies of subset analysis, the logic of categorization of critically ill patient in various categories of trauma, sepsis, burn etc., need to be reconsidered. The internal homeostasis may be deranged by external or internal injury factors which leads to a similar cascade of response irrespective of the type of initial insult. Thus it is conceivable that the differences in the outcome of various categories of critically ill patient observed in subset analyses are artefactual and may disappear if large enough studies with enough power are carried out in these population.

## References

1. Kopelman TR, O'Neill PJ, Kanneganti SR, Davis KM, Drachman DA. The relationship of plasma glucose and glycosylated hemoglobin A1C levels among nondiabetic trauma patients. *J Trauma* 2008;64:303.
2. Graham BB, Keniston A, Gajic O, Trillo Alvarez CA, Medvedev S, Douglas IS. Diabetes mellitus does not adversely affect outcomes from a critical illness. *Crit Care Med* 2010;38:16-24.
3. The Action to Control Cardiovascular Risk in Diabetes Study Group Effects of Intensive Glucose Lowering in Type 2 Diabetes *N Engl J Med* 2008; 358:2545-2559.
4. Krinsley JS, Meyfroidt G, van den Berghe G, Egi M, Bellomo R. The impact of premorbid diabetic status on the relationship between the three domains of glycemic control and mortality in critically ill patients. *Curr Opin Clin Nutr Metab Care* 2012;15:151-60.
5. Egi M, Bellomo R, Stachowski E, French CJ, Hart GK, Taori G, . The

- interaction of chronic and acute glycaemia with mortality in critically ill patients with diabetes. *Crit Care Med.* 2011 Jan;39(1):105-11.
6. Karen RL, Jacob J, Nagamani S. Glycated hemoglobin A: A predictor of outcome in trauma admissions to intensive care unit 2014. *Indian J Crit Care Med*; 18:20-24.
  7. Bochiechio GV, Sung J, Joshi M, Bochiechio K, Johnson SB, Meyer W, *et al.* Persistent hyperglycemia is predictive of outcome in critically ill trauma patients. *J Trauma* 2005;58:921-4.
  8. Bochiechio GV, Bochiechio KM, Joshi M, Ilahi O, Scalea TM. Acute glucose elevation is highly predictive of infection and outcome in critically injured trauma patients. *Ann Surg* 2007;246:605-10.5.
  9. Kao LS, Todd SR, Moore FA. The impact of diabetes on outcome in traumatically injured patients: an analysis of the National Trauma DataBank. *Am J Surg.* 2006 Dec;192(6):710-4
  10. Finfer S, Chittock DR, Su SY, Blair D, Foster D, Dhingra V, Intensive versus conventional glucose control in critically ill patients. *N Engl J Med.* 2009 Mar 26;360(13):1283-97

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