

# Non Diabetic and Stress Induced Hyperglycemia [SIH] in Orthopaedic Practice What do we know so Far?

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## ABSTRACT

Hyperglycemia is also seen amongst non-diabetics and can cause significant morbidity and mortality. SIH has been reported in literature and studied in relation to trauma and critically ill patients. However, literature specific to orthopaedics on this topic is very small. Further, management of hyperglycemia in such patients is still a matter of debate and no universal consensus exists regarding its management. Future studies are needed on this topic to provide appropriate management guidelines and optimal patient outcomes.

**Keywords:** Diabetes, Orthopaedic morbidity, Stress hyperglycemia

## INTRODUCTION

Diabetes Mellitus [DM] is synonym with hyperglycemia. However, not all patients with hyperglycemia are Diabetics. This is a very important consideration in surgical practice, especially orthopaedics. SIH is a form of hyperglycemia seen secondary to stress. Trauma of any kind causes a bodily response characterized by enhanced metabolism and hyperglycemia [1,2].

The bodily response involves endocrinal, immunological and hematological systems [3]. Increased pituitary hormone secretions and activation of sympathetic systems can lead to significant hyperglycemia [3]. Cortisol and catecholamine levels are said to correlate to type and severity of the injury [4]. Stress can result in up to 10 times greater adrenal cortical output causing SIH [5]. Neuroendocrine response to stress is characterized by excessive gluconeogenesis, glycogenolysis and insulin resistance. Stress hyperglycemia occurs as a result of increased hepatic output of glucose rather than impaired tissue glucose extraction [6].

Up to 30% of patients can have blood glucose levels greater than 200mg/dl after trauma and higher than normal values in majority of these patients can be seen [7]. Initially this hyperglycemia was felt to be just a response to stress and was considered at the most a transient phenomenon but over the years multiple studies have correlated the effects of hyperglycemia with various morbidities and increased incidences of mortality [5,6,8-10].

The problem comes when hyperglycemia control is discussed. Over the years literature has varied in its approach to manage hyperglycemia. Van den Bergh et al., have emphasized the role of Intensive Insulin Therapy [IIT] in management of hyperglycemia in surgical Intensive care unit (ICU) and Medial ICU patients [11,12]. They found a significant reduction in mortality of patients in surgical ICU with IIT and advised the same. Subsequent studies reported significant benefits of IIT and reinstated the previous existing guidelines [13-16]. However, this has been challenged by many studies conducted over the past few years which have found increased incidence of complications with IIT, especially hypoglycemic episodes and have recommended following a protocol base approach in glucose control after trauma and in critically ill patients to achieve optimal results, rather than IIT [17-21].

Orthopaedic literature on this topic is negligible and only a handful of studies have been done on this topic. The purpose of this article

was to analyze the impact of available information on this topic in orthopaedic practice and to summarize them for a better and concise understanding of the subject.

## ORTHOPAEDIC TRAUMA AND NON-DIABETIC HYPERGLYCEMIA

Karunakar et al., did a study to analyze the effect of stress hyperglycemia on infectious complications in orthopaedic trauma patients. They divided them into two subgroups based on mean serum glucose greater than 220 mg/dl (hyperglycemic index(HGI) 3.0 or greater) and concluded that mean perioperative glucose levels greater than 220 mg/dl (HGI > 3.0) were associated with a seven times higher risk of infection in orthopaedic trauma patients with no known history of diabetes mellitus [22].

Chen et al., carried out a prospective observational analysis of 1,257 consecutive patients with no history of diabetes who suffered hip fractures. They measured fasting blood glucose (FBG) and glycosylated hemoglobin. They divided all the patients into stress hyperglycemia and non-hyperglycemia groups according to their FBG, and recorded incidence of acute myocardial infarction (AMI). Among the patients enrolled, the frequency of stress hyperglycemia was 47.89% and that of AMI was 9.31% and the occurrence of AMI in the SIH group was higher than in the non-hyperglycemia group. The authors concluded that SIH after hip fracture increased the risk of AMI [10].

Richards et al., studied the relationship of SIH and surgical site infections(SSI). They studied 790 patients with orthopaedics injuries who required operative intervention. They found that hyperglycemia with blood glucose levels  $\geq$  200mg/dl and HGI  $\geq$  1.76 was an independent risk factor for 30 day surgical-site infection in orthopaedic trauma patients without a history of diabetes [23].

Another study evaluated SIH as a risk factor for surgical site infection in non-diabetic orthopaedic trauma patients. The authors concluded that SIH demonstrated a significant independent association with SSIs in nondiabetic orthopedic trauma patients who were admitted to the ICU [24].

A prospective observational cohort study was done at a single academic level 1 trauma center over nine months to see if SIH was associated with SSI. Twenty percent patients in their study were identified non-diabetic hyperglycemic and they concluded that SIH

Author	Year (of publication)	Category	Type	No. of patients	Parameter studied	Outcome
Karunakar et al.,	2010	Trauma	Retrospective study	110	Infectious complications	25% rate of infection
Chen et al.,	2013	Trauma	Prospective observational analysis	1257	Acute Myocardial Infarction	Increased risk of AMI with SIH
Richards et al.,	2012	Trauma	Prospective analysis	790	Surgical site infection	SIH as independent risk factor for 30 day SSI
Richards et al.,	2013	Trauma	Retrospective review	187	Surgical site infection in ICU patients	Significant association of SIH and SSI
Richards et al.,	2014	Trauma	Prospective observational cohort	171	Surgical site infection	Significant association of SIH and SSI
Olsen et al.,	2008	Spine	Retrospective case-control	2316	Surgical site infection	SIH as independent risk factor SSI
Mraovic et al.,	2011	Arthroplasty	Retrospective	1948	Post-operative infection	MPH predictor of PI
Reategui et al.,	2014	Arthroplasty	Prospective	833	Post-operative medical and infectious complication	Non-diabetic hyperglycemia caused post-operative medical and infectious complications

**[Table/Fig-1]:** Summary of studies relating to Non-Diabetic Hyperglycemia SIH – Stress Induced Hyperglycemia, AMI – acute Myocardial Infarction, SSI – Surgical Site Infection, MPH –Morning post-operative hyperglycemia, PI- Postoperative Infections

was associated with SSI in this prospective observational cohort of stable nondiabetic patients with orthopedic injuries [2].

## SPINAL SURGERIES AND NON-DIABETIC HYPERGLYCEMIA

Olsen et al., studied various risk factors related to spinal surgical site infection. They reported serum glucose levels, preoperatively and within five days after the operation, to be significantly higher in patients in whom surgical site infection developed than in uninfected control patients. They concluded that elevated preoperative or postoperative serum glucose level was independently associated with an increased risk of surgical site infection and recommended that the role of hyperglycemia as a risk factor for surgical site infection in patients not previously diagnosed with diabetes should be investigated further [25].

## ARTHROPLASTY AND NON-DIABETIC HYPERGLYCEMIA

Role of non-diabetic hyperglycemia has also been studied in joint replacement surgeries. Mraovic et al., reviewed elective primary total hip and knee arthroplasty from 2000 to 2008. They found that Non-DM patients were 3 times more likely to develop the infection if their morning BG was >140 mg/dl on post-operative day and gave their concluding remarks that even patients without a diagnosis of DM who developed postoperative hyperglycemia had a significantly increased risk for the infection [26].

Reategui et al., found increased incidence of medical and infectious complications with hyperglycemia in total knee arthroplasty patients who did not have DM and emphasized the need of glucose control in non-diabetic hyperglycemic patients [1].

[Table/Fig-1] provides a summary of all the studies related to non –diabetic hyperglycemia in orthopaedic patients.

## SUMMARY AND CONCLUSION

Orthopaedic conditions are prone to complications resulting from non-diabetic hyperglycemia and significant morbidity and mortality can result if appropriate steps are not taken at adequate time to prevent these complications. Evidence based medicine is the need of the hour and we hope with time more studies will analyze and further delineate these findings and suggest possible measures.

## REFERENCES

- Reategui D, Sanchez-Etayo G, Nunez E, Tio M, Popescu D, Nunez M, et al. Perioperative hyperglycaemia and incidence of post-operative complications in patients undergoing total knee arthroplasty. *Knee surgery, sports traumatology, arthroscopy : Official Journal of the ESSKA*. 2014.
- Richards JE, Hutchinson J, Mukherjee K, Jahangir AA, Mir HR, Evans JM, et al. Stress hyperglycemia and surgical site infection in stable nondiabetic adults with orthopedic injuries. *The journal of trauma and acute care surgery*. 2014;76(4):1070-75.

- Desborough JP. The stress response to trauma and surgery. *British journal of anaesthesia*. 2000;85(1):109-17.
- Marik PE. Critical illness-related corticosteroid insufficiency. *Chest*. 2009;135(1):181-93.
- Marik PE, Bellomo R. Stress hyperglycemia: an essential survival response! *Critical care medicine*. 2013;41(6):e93-94.
- Dungan KM, Braithwaite SS, Preiser JC. Stress hyperglycaemia. *Lancet*. 2009;373(9677):1798-807.
- Laird AM, Miller PR, Kilgo PD, Meredith JW, Chang MC. Relationship of early hyperglycemia to mortality in trauma patients. *The Journal of Trauma*. 2004;56(5):1058-62.
- Kerby JD, Griffin RL, MacLennan P, Rue LW, 3<sup>rd</sup>. Stress-induced hyperglycemia, not diabetic hyperglycemia, is associated with higher mortality in trauma. *Annals of surgery*. 2012;256(3):446-52.
- Bosarge PL, Kerby JD. Stress-induced hyperglycemia: is it harmful following trauma? *Advances in surgery*. 2013;47:287-97.
- Chen Y, Yang X, Meng K, Zeng Z, Ma B, Liu X, et al. Stress-induced hyperglycemia after hip fracture and the increased risk of acute myocardial infarction in nondiabetic patients. *Diabetes care*. 2013;36(10):3328-32.
- Van den Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters PJ, Milants I, et al. Intensive insulin therapy in the medical ICU. *The New England journal of medicine*. 2006;354(5):449-61.
- van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, et al. Intensive insulin therapy in critically ill patients. *The New England journal of medicine*. 2001;345(19):1359-67.
- Li J, Li L, Ma B, Yang KH. (The influence of intensive insulin therapy on the mortality of critically ill patients in intensive care unit: a meta-analysis). *Zhongguo wei zhong bing ji jiu yi xue = Chinese critical care medicine = Zhongguo weizhongbing jijiuyixue*. 2009;21(6):349-52.
- Raurell Torreda M, del Llano Serrano C, Almira Solsona D, Catalan Ibars RM, Nicolas Arfelis JM. [The optimal blood glucose target in critically ill patient: comparison of two intensive insulin therapy protocols]. *Medicina clinica*. 2014;142(5):192-99.
- Scalea TM, Bochicchio GV, Bochicchio KM, Johnson SB, Joshi M, Pyle A. Tight glycemic control in critically injured trauma patients. *Annals of surgery*. 2007;246(4):605-10; discussion 10-2.
- Thorell A, Rooyackers O, Myrenfors P, Soop M, Nygren J, Ljungqvist OH. Intensive insulin treatment in critically ill trauma patients normalizes glucose by reducing endogenous glucose production. *The Journal of clinical endocrinology and metabolism*. 2004;89(11):5382-86.
- Arabi YM, Dabbagh OC, Tamim HM, Al-Shimemeri AA, Memish ZA, Haddad SH, et al. Intensive versus conventional insulin therapy: a randomized controlled trial in medical and surgical critically ill patients. *Critical care medicine*. 2008;36(12):3190-97.
- Oddo M, Schmidt JM, Carrera E, Badjatia N, Connolly ES, Presciutti M, et al. Impact of tight glycemic control on cerebral glucose metabolism after severe brain injury: a microdialysis study. *Critical care medicine*. 2008;36(12):3233-8.
- Vespa PM. Intensive glycemic control in traumatic brain injury: what is the ideal glucose range. *Critical care*. 2008;12(5):175.
- Vespa PM, McArthur D, O'Phelan K, Glenn T, Etchepare M, Kelly D, et al. Persistently low extracellular glucose correlates with poor outcome 6 months after human traumatic brain injury despite a lack of increased lactate: a microdialysis study. *Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism*. 2003;23(7):865-77.
- Finfer S, Liu B, Chittock DR, Norton R, Myburgh JA, McArthur C, et al. Hypoglycemia and risk of death in critically ill patients. *The New England journal of medicine*. 2012;367(12):1108-18.
- Karunakar MA, Staples KS. Does stress-induced hyperglycemia increase the risk of perioperative infectious complications in orthopaedic trauma patients? *Journal of orthopaedic trauma*. 2010;24(12):752-56.

- [23] Richards JE, Kauffmann RM, Zuckerman SL, Obrebsky WT, May AK. Relationship of hyperglycemia and surgical-site infection in orthopaedic surgery. *The Journal of bone and joint surgery American volume*. 2012;94(13):1181-86.
- [24] Richards JE, Kauffmann RM, Obrebsky WT, May AK. Stress-induced hyperglycemia as a risk factor for surgical-site infection in nondiabetic orthopedic trauma patients admitted to the intensive care unit. *Journal of orthopaedic trauma*. 2013;27(1):16-21.
- [25] Olsen MA, Nepple JJ, Riew KD, Lenke LG, Bridwell KH, Mayfield J, et al. Risk factors for surgical site infection following orthopaedic spinal operations. *The Journal of bone and joint surgery American volume*. 2008;90(1):62-69.
- [26] Mraovic B, Suh D, Jacovides C, Parvizi J. Perioperative hyperglycemia and postoperative infection after lower limb arthroplasty. *Journal of diabetes science and technology*. 2011;5(2):412-18.

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