Pk Heart J 2025:58 (01)
ISSN:0048-2706 E-ISSN:2227-9199

Relationship Between Nadir Hematocrit and Postoperative Hyperglycemia in Non- diabetic Patients During Cardiopulmonary Bypass

R. Sunitha
Assistant Professor, Division of Perfusion Technology, Faculty of Allied Health Sciences, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai-600116, Tamil Nadu, India

Dr. Ashwanth P
Associate Professor, Cardio Thoracic and Vascular Surgery. Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai - 600116, Tamil Nadu, India

Jenifer Shekinah. J
M.Sc. Perfusion Technology 1st Year Student, Division of Perfusion Technology, Faculty of Allied Health sciences, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai-600116, Tamil Nadu, India

Dr. J. Ramkumar
Professor, Cardio Thoracic and Vascular Surgery, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai-600116, Tamil Nadu, India

Dr. T. Periyasamys
Professor, Cardio Thoracic and Vascular Surgery, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai-600116, Tamil Nadu, India

ABSTRACT

Background: Cardiopulmonary bypass (CPB) is a crucial part of modern cardiac surgery, providing vital support for complex procedures. However, it also presents physiological challenges such as hemodilution, systemic inflammatory response, and metabolic derangements, which can affect CPB outcomes. Hyperglycemia, a common post-operative metabolic complication, is often overlooked, especially in non-diabetic patients. The surgical stress response during and after CPB increases blood glucose concentration, leading to increased morbidity and mortality. Nadir hematocrit, the lowest level of hematocrit achieved during CPB, is a growing concern, as it can interfere with tissue oxygenation and lead to increased morbidity.

Aim: Investigating the relationship between nadir hematocrit levels and postoperative hyperglycemia could lead to specific intraoperative goals aimed at preserving hemodilution, oxygen delivery, and glucose control, potentially reducing complications and improving patient recovery periods.

Materials and Method: The study was a retrospective single-center study conducted at Sri Ramachandra Institute of Higher Education and Research (SRIHER), involving 30 patients who underwent cardiac valvular and coronary artery bypass grafting with valvular surgeries using CPB from 2022 - 2023.Group A: Consist of 15 patients, with hematocrit maintained at < 25% during CPB , in which 13 patients had blood transfusion during CPB. Group B: Consist of 15 patients, with hematocrit maintained at > 25% during CPB, in which only 6 patients had blood transfusion during CPB. Data measurements included hemoglobin, hematocrit, glucose and lactate. Statistical analysis was performed using a t-test along with chi-square test, with a probability value (PV) of $P < 0.005$ considered significant.

Results: The study compared pre-operative hemoglobin indices between Groups A and B, finding no significant difference. Group B had higher mean hemoglobin, leading to hypoxia, insulin resistance, reduced glucose uptake, and hyperglycemia. Postoperatively, glycemia and insulin consumption increased in both diabetic and nondiabetic patients. Excessive hemodilution during CPB may impair tissue oxygen delivery. Group A's HCT decreased during hypothermia, affecting glucose regulation. Postoperatively, Group A's HCT increased to 34%. The study highlights the complex relationship between nadir hematocrit and metabolism.

Conclusion: Nadir haematocrit < 25 % during CPB causes postoperative hyperglycemia inside nondiabetic patient

Keywords: Cardiac Surgery, Cardiopulmonary bypass, Nadir hematocrit, Non – diabetic and Hyperglycemia

INTRODUCTION

Cardiopulmonary bypass (CPB) is still an indispensable part of modern cardiac surgery for providing crucial circulatory as well as respiratory support in undertaking the more complicated parts of the surgery (1).CPB does offer certain benefits; however, it is also associated with numerous physiological challenges, like hemodilution, systemic inflammatory response, and metabolic derangements, which may affect CPB outcomes. The Post-operative metabolic complication that is very common but is often ignored is hyperglycemia, particularly for people with no previous diagnosis of diabetes mellitus (2). Following heart surgery, hyperglycemia has been linked to greater rates of morbidity and mortality, including higher probability of infection, poor wound healing, extended duration of mechanical ventilation, and adverse neurologic outcomes (3).

The surgical stress response primarily drives the release of catecholamines, cortisol, and pro-inflammatory cytokines during and after CPB. This, at the same time, triggers the pain response and evokes the release of various hormones. This whole process increases gluconeogenesis, glycogenolysis, and insulin resistance which further increases blood glucose concentration (4). This response, although well known in eclipsed individuals, is newer research that suggests even non-diabetic individuals becoming equally prone to hyperglycemia brought about stress during surgery, especially with CPB. Unlike their diabetic counterparts, non-diabetic patients usually get inadequate glucose management and constant monitoring can leave them vulnerable to hyperglycemia and other complications which stem from it (5)

One of the emerging areas of concern is nadir hematocrit—the lowest level of hematocrit achieved during CPB, which is usually due to hemodilution from the priming solution of the CPB circuit. Hemodilution decreases the oxygen-carrying capacity of the blood, which may interfere with the adequacy of tissue oxygenation and result in compensatory adjustments at the level of physiology. Nadir hematocrit levels are known to be associated with increased morbidity such as acute kidney injury, neurological dysfunction, and heightened transfusion needs. As hypothesized, nadir hematocrit levels and postoperative hyperglycemia are known to have an association, but it has not been well investigated, especially in non-diabetic patients. Exploring the contribution of nadir hematocrit to postoperative hyperglycemia could lead to specific intraoperative goals oriented at the preservation of the patient’s hemodilution, oxygen delivery, and glucose control (6). This may lead to fewer complications following surgery and enhanced patient recovery periods. Even with this potential clinical importance, not much is known about this relationship in non-diabetic populations that undergo CPB. This paper aims to investigate the association across nadir hematocrit levels throughout CPB and the development of postoperative hyperglycemia in non-diabetic patients.

MATERIALS AND METHOD

The present study was a retrospective single-center study done in the Department of Cardio Thoracic and Vascular Surgery at SRIHER. Thirty patients underwent cardiac valvular and coronary artery bypass grafting with valvular surgeries using CPB for the period of 6 months.

Inclusion criteria: Patients of either sex, Patients aged 20 to 50 years, Patients undergoing elective cardiac surgery with CPB, Nondiabetic patient and Patients with low Hb & HCT

Exclusion criteria: Diabetic patients, Obesity, Elevated HbA1C, Chronic kidney disease and Emergency surgeries.

Based on the inclusion criteria, the present study patients are classified into two groups:

1. Group A: Consist of 15 patients, with hematocrit maintained at < 25% during CPB, in which 13 patients had blood transfusion during CPB.
2. Group B: Consist of 15 patients, with hematocrit maintained at > 25% during CPB, in which only 6 patients had blood transfusion during CPB.

Data Measurements

Hemoglobin, hematocrit, blood glucose and serum lactate were monitored, and arterial blood gas samples were taken preoperatively during induction. Peri Operatively (At 28^0C and 32^0C) and postoperatively (6^{th} & 10^{th} hours following patient transfer to the ICU).

Operative Technique

1. CPB requires considerable preoperative planning. The coordination of cannulation, cooling, and cardioprotective techniques must include the surgeon, and anesthesiologist, and perfusionist, along with nursing personnel.
2. A CPB circuit must be primed with fluid and all air expunged from the arterial line before connection to the patient. Prior to cannulation heparin 400 IU/kg were administered until the activated clotting time was above 480 seconds using non- pulsatile flow rate of 2.2 – 2.4l/m2/min.
3. Ascending aorta, superior vena cava and inferior vena cava or right atrium were canulated. Hemofilter were used during CPB to remove excss plasma water. It’s done parallel to CPB, while rewarming.
4. Moderate hemodilution with crystalloid prime and moderate systemic hypothermia (at lowest temperature of 28^0 C) were used.
5. After aorta cross clamping myocardial protection was received from antegrade cold cardioplegia and it was administered through the aortic root or coronary ostium in the AVR surgeries till cardiac arrest occurs.
6. Cardioplegia was administered repeatedly every 20 to 25 mins on the return of conducting of the heart, mean arterial pressure (MAP) of 40-60 mmHg were maintained throughout CPB.
7. Hematocrit was maintained between 20% to 25%, on the addition of blood if necessary, patient was rewarmed at 37C.
8. Once the patient is ready to come off pump, after the cross-clamp removed; patient is weaned from CPB and decannulated. Protamine sulfate (1-1.3mg for 100 IU) was administered after the termination of bypass.
9. The patient’s hemostasis was checked, and the chest was closed and then patients were shifted to ICU and monitored.

Statistical Analysis

We statistically described the data in terms of mean, standard deviation, median, and range, or in terms of frequencies (number of cases) and percentages when appropriate. We used a t-test to determine the significant difference between the paired groups (PREOP, POST-OP, and PERI-OP). We used a chi-square test to determine the significance of the data. In all the above statistical tools, the probability value $P < 0.005$ is considered the significant level. All statistical calculations were done using the computer program SPSS for Microsoft Windows.

RESULTS AND DISCUSSION

Hematologic Parameter

The comparison of pre-operative hemoglobin indices between Groups A & B revealed a non-significant difference, as Group B had a mean hemoglobin (12.8 g/dL) that was greater than Group A (12.3 g/dL) (Table 1, Fig.1).

Decrease in haemoglobin level causes hypoxia, which leads to an increase in insulin resistance, which in turn leads to reduced glucose uptake causing hyperglycemia. Inflammatory response induced by surgical stress also causes hyperglycemia. The initiation of CPB significantly elevates postoperative glycemia along with insulin requirements in both diabetic and nondiabetic individuals. Excessive hemodilution along with the consequent anemia during cardiopulmonary bypass may hinder tissue oxygen supply (6) (7).

Table 1. Levels of hemoglobin

HEMOGLOBIN	GROUP A	GROUP B
Pre-operative	12.3	12.8

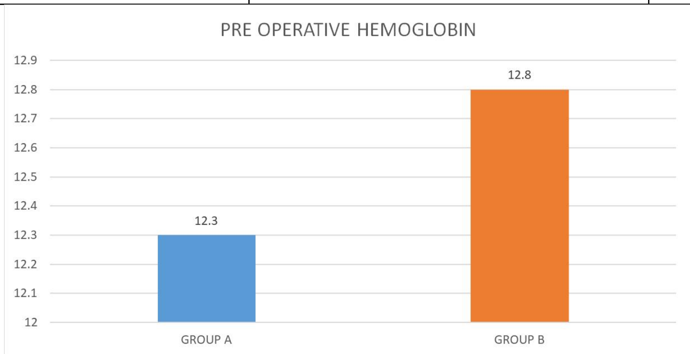

Figure 1. Comparison of hemoglobin between the group

Hematocrit

In the preoperative phase, there were no noteworthy differences in HCT values between both groups, with Group A being 37.04% and Group B being 38.62%. During the perioperative period, especially with hypothermia, the HCT for Group A decreased tremendously to 19.8% while Group B showed a less severe decrease to 27.3%. The difference in nadir hematocrit values of approximately 7% in HCT between the two groups during hypothermia likely have a significant influence on glucose regulation following surgical intervention as Group A is likely to experience a greater amount of stress on glucose metabolism. During rewarming, Group A's HCT was yet again lower than Group B at 21.6% versus 29.2% After CPB circulatory support is removed, and with rewarming, the previously mentioned differences in HCT may affect glucose metabolism. Lower oxygen carrying capacity in Group A could subsequently increase stress induced hyperglycemia due to tissue hypoxia, increased catecholamines, and stress hormones. Subsequent contribution to elevated blood glucose levels may be present in the immediate postoperative period. Postoperatively, after 6 hours Group A's HCT increased to 31.4%, and Group B's increased to 34%, indicating some recovery but still lower than baseline levels. Postoperative HCT's at 12 hours indicated Group A with diminished recovery to 21% and Group B at 28.7% (Table 2, Fig.2).

The main objective of blood transfusion is to enhance the oxygen-carrying capacity of the blood and augment tissue oxygenation. The administration of packed red cell transfusion resulted in a significant elevation in blood glucose levels. The reliability of HbA1c has been challenged owing to noteworthy changes in the hemoglobin composition of patients' erythrocytes resulting from regular and frequent transfusions. The findings may be inaccurately elevated or diminished based on the timing of transfusion and the reduced lifespan of erythrocytes (8).

Table 2. Hematocrit Levels

HEMATOCRIT	GROUP A	GROUP B
Pre-Operative	37.04	38.62
Peri Operative (During Hypothermia)	19.8	27.3

Peri Operative (During Rewarming)	21.6	29.2
Post Operative After 6 Hours	31.4	34
Post Operative After 12 Hours	21	28.7

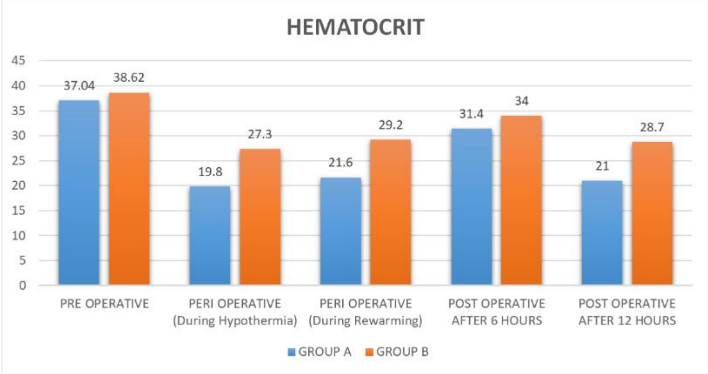

Figure 2. Comparison of Hematocrit levels between groups

Lactate

The lactate progression in Group A and Group B highlights some intriguing differences that may reflect potential mechanisms behind the relationship between nadir hematocrit levels and postoperative hyperglycemia during CPB. Throughout the perioperative phase, the hypothermia phase stood out, with Group A having significantly higher lactate values (3.35 mmol/L) versus Group B (1.63 mmol/L). This pattern continued into the rewarming phase with Group A's lactate (3.44 mmol/L) being markedly greater than Group B (1.75 mmol/L) (Table 3, Fig.3).

These differences may indicate that Group A had a higher degree of metabolic turmoil or resulted in tissue hypoxia secondary to lower nadir hematocrit levels that led to some metabolic stress culminating in hyperglycemia. Six hours after the operation, Group A's lactate trend continued to be greater than Group B at 4 mmol/L versus 2.4 mmol/L, further suggesting Group A had a continued metabolic disturbance. By the 12-hour mark after surgery, the trend had reversed with Group A's lactate falling to 1.4 mmol/L and Group B's lactate increasing to 2.07 mmol/L; indicating that Group A possibly had a more rapid resolution of the metabolic insult than Group B due to adaptive mechanisms or enhanced lactate clearance secondary to removal of the hypoxic stress. Our findings provide evidence that indicates insights into the complexity of the relationship between nadir hematocrit and metabolism.

Another method may include desaturation and arterial hypoxemia due to excessive hemodilution, leading to an augmented sympathetic autonomic response, which subsequently elevates the release of cortisol, and catecholamines, along with glucagon, while inhibiting insulin production. The stimulation of hepatic glycogenolysis and the inhibition of glucose clearance, caused by high circulating catecholamine levels and reduced insulin levels, lead to hyperglycemia as well as increase in lactate level postoperatively (9).

Table 3. Levels of Lactate

LACTATE	GROUP A	GROUP B
Peri Operative (During Hypothermia)	3.35	1.63
Peri Operative (During Rewarming)	3.44	1.75
Post Operative After 6 Hours	4	2.4
Post Operative After 12 Hours	1.4	2.07

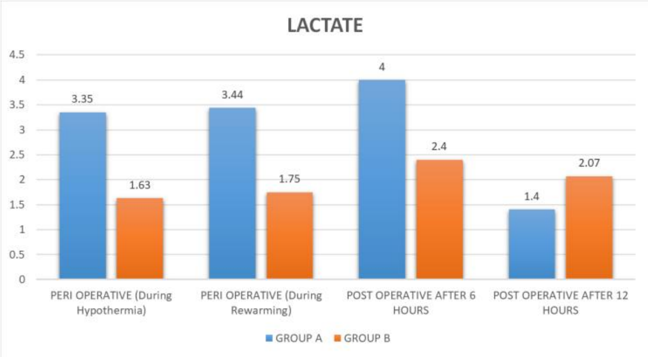

Figure 3. Comparison of Lactate between groups

Glucose

Perioperative glucose fluctuations can significantly impact patient outcomes, with stress-induced hyperglycemia being a well-documented phenomenon in surgical settings. In the current data, both groups show elevated preoperative glucose levels, but Group A demonstrates a more pronounced hyperglycemic response, particularly during the hypothermia phase (188.6 mg/dL vs. 148.9 mg/dL in Group B) and notably at 6 hours postoperatively, where Group A spikes to 319.7 mg/dL compared to 163.2 mg/dL in Group B. This marked increase in Group A may reflect an enhanced stress response, increased insulin resistance, or impaired glucose clearance, factors that have been linked to adverse outcomes such as infections, delayed wound healing, and prolonged hospital stays (10) (11). The data also reveal a transient normalization during the rewarming phase, suggesting that the hypothermic state may exacerbate metabolic derangements. Recent studies have emphasized that maintaining tighter glycemic control in the perioperative period—especially in settings involving temperature modulation—can improve clinical outcomes by mitigating the inflammatory and stress responses (12). These findings underscore the need for vigilant glucose monitoring and tailored glycemic management strategies to optimize recovery in high-risk surgical patients.

Table 4. Levels of Glucose

GLUCOSE	GROUP A	GROUP B
Pre-Operative	124.9	134.37
Peri Operative (During Hypothermia)	188.6	148.9
Peri Operative (During Rewarming)	160.6	166.1
Post Operative After 6 Hours	319.7	163.2
Post Operative After 12 Hours	201.5	181.8

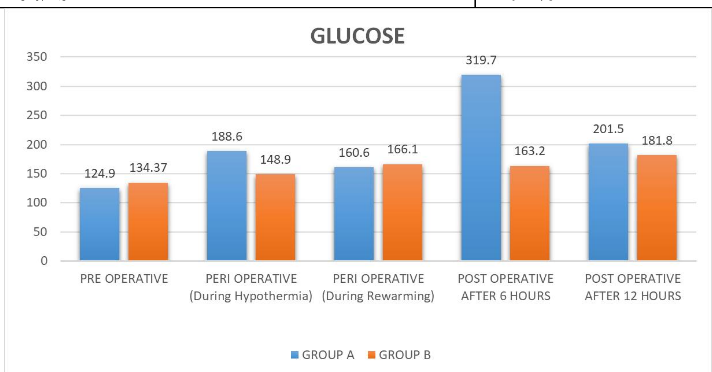

Figure 4. Comparison of Glucose levels between groups

The changes in blood parameters, lactate, and glucose levels throughout the perioperative period highlighted in this study provide important insights into how cardiopulmonary bypass (CPB) affects metabolism. Both groups had similar preoperative hemoglobin and hematocrit levels, suggesting they started off on equal footing. However, Group A saw a more significant drop in hematocrit during the procedure, especially during hypothermia, with their lowest value hitting 19.8%, while Group B's was 27.3%. This substantial hemodilution in Group A likely led to tissue hypoxia, which can trigger stress responses that disrupt glucose metabolism. When hemodilution is excessive, it diminishes the blood's ability to carry oxygen, leading to increased insulin resistance and higher blood sugar levels—a well-known issue in cardiac surgeries involving CPB.

In line with this, lactate levels, which indicate poor blood flow, were notably higher in Group A during both the hypothermic and rewarming stages, reinforcing the idea that metabolic stress was due to insufficient oxygen delivery. The elevated lactate levels peaked at 4 mmol/L after surgery, signaling ongoing anaerobic metabolism, while Group B maintained lower levels, suggesting they had better blood flow and oxygenation. Interestingly, by 12 hours post-surgery, Group A's lactate levels began to drop, hinting at a potential recovery.

Glucose levels followed a similar trend to the hematologic and lactate data. Group A showed significant hyperglycemia, reaching a peak of 319.7 mg/dL six hours after surgery—almost double that of Group B. This spike can be linked to a mix of factors, including hypoxia, increased stress hormones (like catecholamines and cortisol), and inflammatory responses, all worsened by low hematocrit and perfusion issues. Experiencing hyperglycemia during the perioperative phase is associated with negative outcomes, such as a higher risk of infections and slower recovery.

CONCLUSION

In conclusion, these results stress the key interaction between managing blood health, tackling metabolic disturbances, and the outcomes for patients in cardiac surgery. To lessen postoperative complications and boost recovery for those on cardiopulmonary bypass, it's crucial to keep hematocrit levels optimal, minimize hemodilution, and adopt targeted approaches for controlling blood sugar.

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ISSN:0048-2706 E-ISSN:2227-9199

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