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Post Operative Hyperbilirubinemia after Cardiac Surgery: A Cross-Sectional Study in National Institute of Cardiovascular Diseases, Karachi

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ABSTRACT

Background: Postoperative hyperbilirubinemia is a frequent and clinically significant complication following cardiac surgery, with reported incidence ranging from 10% to 40%. It has been associated with increased postoperative morbidity, prolonged ICU stay, low-output syndrome, renal dysfunction, and higher mortality. Despite advances in cardiopulmonary bypass techniques and perioperative care, hyperbilirubinemia remains prevalent and understudied, particularly in local populations. **Objective:** To determine the frequency of postoperative hyperbilirubinemia in patients undergoing adult cardiac surgery. **Methods:** A descriptive cross-sectional study was conducted at the Department of Cardiac Surgery, National Institute of Cardiovascular Diseases (NICVD), Karachi from 17 Feb 2025 to 17 May 2025. A total of 289 adult patients undergoing cardiac surgery were enrolled using non-probability consecutive sampling. Patients with preoperative hyperbilirubinemia, liver disease, or heart failure were excluded. Serum bilirubin levels were monitored during the hospital stay, and hyperbilirubinemia was defined as total bilirubin >2.0 mg/dL. **Results:** Out of 289 patients who underwent cardiac surgery, 76 (26.3%) developed postoperative hyperbilirubinemia. These patients were older (59.2 vs. 55.8 years, p = 0.01), had a higher prevalence of diabetes (58% vs. 36%, p = 0.002), and experienced longer bypass times (98.2 vs. 89.5 minutes, p = 0.015). They also had significantly higher bilirubin levels and liver enzymes (p < 0.001), and more postoperative complications including prolonged ICU stay (59% vs. 30%), mechanical ventilation >24h (41% vs. 13%), and renal support (16% vs. 5%). Logistic regression identified diabetes, prolonged bypass time, low ejection fraction, and inotropic use as significant predictors. **Conclusion:** Postoperative hyperbilirubinemia remains a prevalent complication following cardiac surgery and is significantly associated with adverse clinical parameters. Early identification and risk-based stratification may help mitigate morbidity in affected patients.

INTRODUCTION

Cardiac surgery, particularly procedures involving cardiopulmonary bypass (CPB), carries a significant risk of postoperative complications, among which hyperbilirubinemia is a well-recognized but often underappreciated entity. Postoperative hyperbilirubinemia is typically defined as a serum bilirubin level exceeding 2.0 mg/dL and is reported to occur in 10% to 40% of cases undergoing cardiac surgery [1]. The condition is not merely a biochemical abnormality—it has been associated with increased rates of postoperative morbidity, including renal dysfunction, prolonged mechanical ventilation, sepsis, extended intensive care unit (ICU) stay, and even mortality [2][3]. Previous literature indicates that up to 25% of mortality after open-heart surgery can be attributed to postoperative jaundice, highlighting the clinical relevance of this finding [4]. The pathogenesis of hyperbilirubinemia following cardiac surgery is multifactorial. CPB contributes significantly due to the effects of non-pulsatile perfusion, systemic inflammation, hemolysis, hemodilution, and hepatic hypoperfusion [5]. These physiological insults may impair hepatic function, leading to accumulation of both direct and indirect bilirubin in the serum. The liver, being particularly sensitive to changes in oxygenation and blood flow, is adversely affected by the temporary but significant circulatory alterations during CPB [6].

Patient-specific factors such as older age, pre-existing comorbidities (e.g., diabetes mellitus, hypertension), heart failure, and the need for blood transfusions have been recognized as contributors to postoperative liver dysfunction [7]. Surgical factors including the duration of aortic cross-clamp time, total bypass time, and the complexity of the surgical procedure also play significant roles in predisposing patients to hepatic injury and

subsequent jaundice [8]. Despite advances in CPB circuits, myocardial protection techniques, and intensive care protocols, the frequency of postoperative hyperbilirubinemia has not significantly declined since it was first described over five decades ago [9]. Late-onset hyperbilirubinemia (after 7 days post-surgery) is of particular concern due to its association with a higher risk of mortality and persistent organ dysfunction [10].

Various international studies have documented the prevalence of this complication. For instance, an Indian study involving 476 patients undergoing cardiac surgery reported a postoperative hyperbilirubinemia rate of 25% [11]. Another large-scale study of 6,100 patients found a frequency of approximately 23% [12]. However, regional data from Pakistan and other South Asian populations remain sparse, making it difficult to evaluate how local demographics, healthcare systems, and surgical practices influence the incidence and outcomes of this condition [13]. Given the high burden of cardiovascular diseases in Pakistan and the increasing volume of cardiac surgical procedures performed at tertiary centers like the National Institute of Cardiovascular Diseases (NICVD) in Karachi, it is imperative to evaluate this complication in our population. Identifying its frequency and associated clinical outcomes can help clinicians implement preventive strategies and modify intraoperative practices to mitigate risk. Thus, this study was conducted to determine the frequency of postoperative hyperbilirubinemia in patients undergoing cardiac surgery at NICVD, and to assess its association with clinical parameters and hospital outcomes.

Objective

To determine the frequency of postoperative hyperbilirubinemia in patients undergoing adult cardiac surgery.

METHODOLOGY

This was a descriptive cross-sectional study conducted at the Department of Cardiac Surgery, NICVD Karachi from 17 Feb 2025 to 2 June 2025, with a sample size of 289 patients selected using non-probability consecutive sampling.

Inclusion Criteria

- Patients aged 20–80 years.
- Male and female patients undergoing adult cardiac surgery.
- Patients providing informed consent.

Exclusion Criteria

- Patients with known preoperative hyperbilirubinemia.
- Patients with congestive heart failure.
- Patients diagnosed with chronic liver disease.

Data Collection Procedure

After obtaining approval from the institutional ethical review board, patients meeting the inclusion criteria were enrolled from the cardiac surgery ward of NICVD, Karachi. Written informed consent was obtained from all participants. Baseline demographic data such as age, sex, body mass index (BMI), and residence were documented. Clinical history regarding hypertension, diabetes mellitus, and medication use was recorded. Surgical variables including type of surgery, duration of aortic cross-clamping, total bypass time, and preoperative ejection fraction were noted. All surgeries were performed by experienced cardiothoracic surgeons using standardized CPB protocols. Patients were monitored postoperatively for serum bilirubin levels. Hyperbilirubinemia was defined as total bilirubin >2.0 mg/dL at any time post-surgery. The presence or absence of hyperbilirubinemia, as well as clinical outcomes such as length of hospital stay, were recorded until discharge.

Statistical Analysis

Data were entered and analyzed using SPSS version 26. Continuous variables such as age, BMI, duration of surgery, cross-clamp time, and hospital stay were presented as mean ± standard deviation (SD). Categorical variables like gender, presence of hypertension, diabetes, and hyperbilirubinemia were reported as frequencies and percentages. To evaluate associations, stratification was done for key effect modifiers. Chi-square test or Fisher's exact test was applied for categorical variables, and independent t-test for continuous variables. A p-value of <0.05 was considered statistically significant.

RESULTS

The average age of patients who developed postoperative hyperbilirubinemia was higher (59.2 years) compared to those who did not (55.8 years), and this difference was statistically significant ($p = 0.01$). The hyperbilirubinemia group also had a slightly higher average BMI (27.9 kg/m^2 vs. 26.8 kg/m^2; $p = 0.04$). Diabetes and hypertension were more common in the hyperbilirubinemia group (58% and 70%, respectively) compared to those without hyperbilirubinemia (36% and 54%), showing significant associations ($p = 0.002$ and $p = 0.03$). Gender and residence were not significantly different between groups.

Table 1

Demographic and Clinical Characteristics of Patients

Characteristic	Total (n=289)	Hyperbilirubinemia (n=76)	No Hyperbilirubinemia (n=213)
Age (years)	56.7 ± 10.4	59.2 ± 9.7	55.8 ± 10.6
BMI (kg/m^2)	27.1 ± 3.8	27.9 ± 3.4	26.8 ± 3.9
Gender (Male/Female)	198 / 91	54 / 22	144 / 69
Diabetes Mellitus	42% (121/289)	58% (44/76)	36% (77/213)
Hypertension	58% (168/289)	70% (53/76)	54% (115/213)
Urban Residence	65% (188/289)	68% (52/76)	64% (136/213)

Patients who developed hyperbilirubinemia had longer aortic cross-clamp times (75.1 minutes vs. 67.6 minutes; $p = 0.008$) and cardiopulmonary bypass durations (98.2 minutes vs. 89.5 minutes; $p = 0.015$). Their mean ejection fraction was also lower (44.1% vs. 48.5%; $p = 0.003$), indicating reduced cardiac performance. Type of surgery distribution did not significantly differ, but prolonged

surgical duration was clearly associated with higher bilirubin levels.

Table 2
Surgical Details and CPB Parameters

Variable	Total (n=289)	Hyperbilirubinemia (n=76)	No Hyperbilirubinemia (n=213)
Type of Surgery (CABG/Valve/Mixed)	181 / 84 / 24	46 / 20 / 10	135 / 64 / 14
Cross Clamp Time (min)	69.5 ± 18.3	75.1 ± 17.4	67.6 ± 18.3
Bypass Time (min)	91.7 ± 22.1	98.2 ± 20.6	89.5 ± 22.2
Ejection Fraction (%)	47.3 ± 9.5	44.1 ± 8.8	48.5 ± 9.6

Mean total bilirubin levels in the hyperbilirubinemia group were elevated at 3.6 mg/dL, compared to 1.6 mg/dL in the non-hyperbilirubinemia group ($p < 0.001$). Similarly, direct bilirubin was significantly higher (2.2 mg/dL vs. 0.9 mg/dL; $p < 0.001$). Liver enzymes such as AST, ALT, and ALP were also significantly raised in patients with hyperbilirubinemia, reflecting hepatic dysfunction likely induced by CPB-related stress.

Table 3
Postoperative Liver Function Test Results

Parameter	Total (n=289)	Hyperbilirubinemia (n=76)	No Hyperbilirubinemia (n=213)
Total Bilirubin (mg/dL)	2.1 ± 1.5	3.6 ± 1.2	1.6 ± 0.5
Direct Bilirubin (mg/dL)	1.2 ± 0.9	2.2 ± 0.7	0.9 ± 0.3
AST (U/L)	58.4 ± 21.6	78.5 ± 22.3	51.3 ± 19.1
ALT (U/L)	51.8 ± 19.4	65.9 ± 18.5	47.4 ± 17.5
ALP (U/L)	146.3 ± 48.5	165.1 ± 42.7	139.4 ± 46.2

Hyperbilirubinemia was associated with prolonged hospital stay (9.4 vs. 7.3 days; $p < 0.001$), higher ICU stay beyond 48 hours (59% vs. 30%; $p < 0.001$), and greater need for extended mechanical ventilation (41% vs. 13%; $p < 0.001$). The need for inotropic support and renal replacement therapy was also markedly higher in these patients, further confirming the link between hyperbilirubinemia and worsened postoperative outcomes.

Table 4
Postoperative Outcomes and Morbidity

Outcome	Total (n=289)	Hyperbilirubinemia (n=76)	No Hyperbilirubinemia (n=213)
Length of Hospital Stay (days)	7.8 ± 2.1	9.4 ± 2.3	7.3 ± 1.7
ICU Stay >48h	38% (110/289)	59% (45/76)	30% (65/213)
Ventilation >24h	21% (60/289)	41% (31/76)	13% (29/213)
Inotropic Support	25% (73/289)	47% (36/76)	17% (37/213)
Renal Replacement Therapy	8% (23/289)	16% (12/76)	5% (11/213)

Among patients with diabetes, 36% developed hyperbilirubinemia versus only 19% among non-diabetics ($p = 0.002$). Similarly, 31% of hypertensive patients experienced hyperbilirubinemia compared to 19% of those without hypertension ($p = 0.03$). These findings highlight the role of metabolic comorbidities as significant risk factors for hepatic dysfunction after cardiac surgery.

Table 5
Stratification by Diabetes and Hypertension

Stratum	Hyperbilirubinemia (%)	p-value
Diabetes Present	36% (44/121)	0.002
Diabetes Absent	19% (32/168)	
Hypertension Present	31% (53/168)	0.03
Hypertension Absent	19% (23/121)	

DISCUSSION

This study demonstrated that postoperative hyperbilirubinemia occurred frequently in patients undergoing cardiac surgery, with notable associations to adverse clinical parameters. A range of perioperative and patient-related factors were significantly linked to the development of hyperbilirubinemia, which in turn correlated with worsened postoperative outcomes such as longer hospital stay, increased ICU time, greater need for mechanical ventilation, inotropes, and renal replacement therapy. Patients who developed hyperbilirubinemia were older (mean 59.2 years), had higher BMI (27.9 kg/m^2), and showed greater prevalence of diabetes (58%) and hypertension (70%) compared to their counterparts (p-values < 0.05). These findings are consistent with previous research, which has identified older age and metabolic comorbidities as key risk factors for liver dysfunction following cardiac surgery [14][15]. Comorbid diabetes mellitus likely impairs hepatic microcirculation and worsens inflammatory responses during cardiopulmonary bypass (CPB), increasing susceptibility to bilirubin elevation [16]. Surgical factors also played a vital role. Patients with longer cross-clamp and bypass times—75.1 and 98.2 minutes respectively—had significantly higher odds of developing hyperbilirubinemia ($p < 0.05$). This finding aligns with previous studies demonstrating that prolonged CPB contributes to hepatic hypoperfusion and hemolysis, both of which elevate bilirubin levels postoperatively [17].

Biochemically, hyperbilirubinemic patients had markedly elevated total and direct bilirubin levels (3.6 mg/dL and 2.2 mg/dL, respectively), along with elevated AST, ALT, and ALP (all $p < 0.001$). These enzyme elevations reflect both hepatocellular and cholestatic injury patterns. Similar biochemical profiles have been reported in earlier studies that highlighted transient hepatic dysfunction as a hallmark of post-CPB inflammation and oxygen debt [18].

In terms of clinical outcomes, patients with hyperbilirubinemia stayed longer in the hospital (mean 9.4 vs. 7.3 days), had more ICU days >48 hours (59% vs. 30%), required prolonged ventilation (41% vs. 13%), and were more likely to need renal support (16% vs. 5%)—all statistically significant. These findings are aligned with previous literature, which confirms that hyperbilirubinemia is not a benign laboratory finding but a predictor of worse morbidity and delayed recovery [19]. Multivariate analysis in this study identified five strong predictors of postoperative hyperbilirubinemia: age >60 years, diabetes, prolonged bypass time >90 minutes, ejection fraction <45%, and requirement of inotropes. The odds ratios ranged from 1.8 to 2.9, with inotropic support showing the strongest association. These predictors have been repeatedly validated in earlier studies as components of hepatic vulnerability in cardiac surgical patients [20]. Importantly, while various international studies report the frequency of postoperative hyperbilirubinemia to range from 21% to 29% [21], local data from Pakistan remains scarce. This study fills a critical gap by highlighting how comorbid burden and surgical stressors contribute to hyperbilirubinemia in our regional context.

CONCLUSION

It is concluded that postoperative hyperbilirubinemia is a frequent and clinically significant complication in patients undergoing cardiac surgery. It is closely associated with advanced age, diabetes, hypertension, prolonged bypass and cross-clamp times, and low ejection fraction. Patients who developed hyperbilirubinemia experienced worse outcomes, including longer hospital stays, increased ICU and ventilator dependency, and higher need for inotropic and renal support. These findings underscore the importance of early identification, monitoring, and intervention in at-risk patients to reduce morbidity and improve postoperative recovery.

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