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Association of Serum Prothrombin Index with Early Post-operative Complications Following Liver Resection

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Abstract
Introduction: *The Prothrombin Index (PI) is a critical measure of coagulation status, reflecting the liver's ability to synthesize clotting factors. In the context of liver resection, a procedure associated with a significant risk of bleeding and other complications, the assessment of PI becomes paramount. This study investigates the association between serum Prothrombin Index and early postoperative complications following liver resection.*
Methods: *This Prospective observational study was conducted in Maternity Center, Madhupur, Tangail, Bangladesh during the period from January 2024 to December 2024. All patients admitted to the hepatobiliary unit of the department of surgery, Dhaka Medical College Hospital were considered as the study population. A total of 40 patients were selected as study subjects through a purposive sampling technique. Data were analyzed by Statistical Package for Social Sciences (SPSS) version 20.0.*
Result: *In the early postoperative period, the association between prothrombin index (PI) and various complications was assessed. Regarding bile leak, no statistically significant association was observed, with the probability of bile leak being 0.237 for patients with a PI <50%. In contrast, a significant association was found between PI and postoperative bleeding, where a PI <50% showed a probability of 0.04 for hemorrhage, making this result statistically significant. Lastly, the association between PI and sepsis revealed no significant findings, with a probability of 0.479 for sepsis in patients with a PI <50%. Overall, a lower PI was significantly linked to an increased risk of postoperative bleeding, but not to bile leak or sepsis.*
Conclusion: *The study findings highlight the clinical importance of assessing both the initial and postoperative Prothrombin Index concerning outcomes following liver resection. Consequently, utilizing the initial and early postoperative Prothrombin Index as a clinical parameter can enhance the optimization of postoperative patient care.*
Keywords: *Serum Prothrombin Index, Liver Resection, Morbidity*

I. INTRODUCTION

Liver resection, especially major liver resection and procedures in patients with chronic liver disease, is a highly complex surgical undertaking. Despite its invasiveness, the safety of liver resection has improved significantly in recent years. Enhanced patient selection, advancements in surgical and anesthetic techniques, the adoption of minimally invasive approaches, and improvements in perioperative care have broadened the indications for liver resections. Consequently, the postoperative mortality rates associated with liver resection range from 0% to 22%, with a median of 3.7% [1]. However, postoperative morbidity remains substantial, with rates reported between 12.5% and 66% [2]. These complications can include liver dysfunction, renal dysfunction, and bile leaks [3,4]. Several factors contribute to perioperative complications and mortality, including patient age, gender, the annual volume of liver resections performed by the hospital, the pathologic origin of the liver tumor, preoperative liver and renal dysfunction, and the presence of chronic liver disease [5,6]. Additionally, the peripheral neutrophil-to-lymphocyte ratio (NLR), blood loss during surgery, the need for transfusions, the extent of liver resection, duration of the surgical procedure, simultaneous extrahepatic procedures [7-9], and the use of the Pringle maneuver [10] also influence outcomes. Despite the many factors that affect liver surgery outcomes, no single scoring system has yet been developed to encompass them all. The American Society of Anesthesiologists (ASA) grade and the Portsmouth Physiologic and Operative Severity Score for the Enumeration of Mortality and Morbidity (P-POSSUM) scores are utilized for risk prediction in various surgical contexts [11], including liver surgery [12]. Previous studies have examined various scoring systems, such as the Child-Pugh score (CP score), the Model for End-Stage Liver Disease (MELD) score, and the albumin-bilirubin score (ALBI). They also explored combining the ALBI score with platelet count (as a surrogate marker for portal hypertension) to create the platelet-albumin-bilirubin (PALBI) grade and a new score called the ALBI-APRI score. These studies

concluded that combining blood test scores could enhance the predictive value for post-hepatectomy liver failure (PHLF) [13]. However, these scores may not adequately address the unique challenges posed by liver resection. Post-hepatectomy liver failure (PHLF) is one of the primary causes of mortality following liver resection [14]. The "50-50 criteria," which involve a serum bilirubin level greater than 50 μmol/L and a prothrombin index (calculated as the mean normal prothrombin time divided by the patient's observed prothrombin time) of less than 50% measured on the fifth postoperative day, have been associated with mortality due to PHLF [4]. However, an earlier prediction system might be more beneficial in guiding clinical interventions. Moreover, failure of multiple organ systems can also lead to mortality following liver resection, highlighting the need for a comprehensive perioperative measure to assess the risk of significant postoperative morbidity and mortality. Therefore, the early postoperative Prothrombin Index may serve as a valuable marker for detecting early morbidity after liver resection. This study aims to evaluate the association of serum Prothrombin Index with early post-operative complications following liver resection.

II. METHODS

This Prospective observational study was conducted in Maternity Center, Madhupur, Tangail, Bangladesh during the period from January 2024 to December 2024. All patients admitted to the hepatobiliary unit of the department of surgery, Dhaka Medical College Hospital were considered as the study population. A total of 40 patients were selected as study subjects through a purposive sampling technique. A questionnaire and a consent form were prepared, the sample was selected based on inclusion and exclusion criteria, a questionnaire was filled with informed written consent, and relevant investigations were done. Data were collected by active participation, and interviewing through questionnaires. Univariate and multivariate analysis of the data is carried out using a statistical analysis software program. Descriptive analysis of continuous variables is carried out and presented as the means ± SD. Data were analyzed by Statistical Package for Social Sciences (SPSS) version 20.0. Informed as well as verbal consent of the patient was taken. Ethical clearance was taken from the ethical committee of Dhaka Medical College.

Inclusion criteria:

- The patient underwent liver resection for various indication
- Age between 18 to 70 years

Exclusion criteria:

- Patient with concomitant other malignancy
- Patient with a history of pre-existing chronic liver disease including cirrhosis due to other medical causes like autoimmune hepatitis, hemochromatosis, Wilson's disease
- Patient with concomitant other severe co-morbid illness (severe cardio-respiratory & renal compromise)

III. RESULTS

Table 1: Distribution of patients according to age (N=40)

Age Group (in years)	n	%
18 – 30	4	10.0
31 – 40	4	10.0
41 – 50	16	40.0
51 – 60	10	25.0
61 – 70	6	15.0
Sex		
Male	18	45.0
Female	22	55.0
Age (Mean ± SD): 48.4 ± 10.27		
Male to female ratio = 1 :1.22		

The study shows that the majority (16,40.0%) of the patients were from the 41-50 years age group. Out of forty patients, the mean age was 48.4 years with a standard deviation of 10.27. [Table 1]

Table 2: Post-operative biochemical parameter of patients (POD 3) (N=40)

Prothrombin Index	n	%
>70%	28	70.0
50-70%	8	20.0
<50%	4	10.0

The results indicate that the majority of patients, 28 (70.0%), had a prothrombin index greater than 70%, suggesting adequate coagulation function post-surgery. A smaller group, comprising 8 patients (20.0%), fell within the 50-70% range, indicating moderate coagulation capability. Only 4 patients (10.0%) exhibited a prothrombin index of less than 50%. [Table 2]

Table 3: Post-operative biochemical parameter of patients (POD 5) (N=40)

Prothrombin Index	n	%
>70%	30	75.0
50-70%	6	15.0
<50%	4	10.0

The data shows that a majority of patients, 30 (75.0%), had a prothrombin index greater than 70%, indicating a strong coagulation capacity following surgery. In contrast, 6 patients (15.0%) were within the 50-70% range, suggesting moderate coagulation ability. Additionally, 4 patients (10.0%) demonstrated a prothrombin index of less than 50%. [Table 3]

Table 4: Association of prothrombin index and bile leak in the early postoperative period (N=40)

Prothrombin index	Bile leak		P-value
	Yes	No	
>70%	6 (20%)	12 (80%)	0.330
50-70%	2 (33.33%)	2 (66.66%)	0.919
<50%	2 (50%)	2 (50%)	0.237

Table 4 shows the probability of bile leak with the prothrombin index. The probability of bile leak was .237 with PI <50% which is not statistically significant. [Table 4]

Table 5: Association of prothrombin index and postoperative bleeding in the early postoperative period (N=40)

Prothrombin index	Postoperative bleeding		P-value
	Yes	No	
>70%	0 (0%)	15 (100%)	0.01
50-70%	2 (33.33%)	2 (66.66%)	0.564
<50%	2 (100%)	0 (0%)	0.04

Table 5 shows the probability of postoperative bleeding with the Prothrombin Index. The probability of hemorrhage was .04 with PI <50% which is statistically significant. [Table 5]

Table 6: Association of prothrombin index and sepsis in the early postoperative period (N=40)

Prothrombin index	Sepsis		P-value
	Yes	No	
>70%	2 (6.66%)	28 (93.33%)	0.838
50-70%	2 (33.33%)	2 (66.66%)	0.455
<50%	2 (50%)	2 (50%)	0.479

It was observed that, the probability of sepsis with Prothrombin Index. The probability of sepsis was .0479 with PI <50% which is not statistically significant. [Table 6]

IV. DISCUSSION

The predominance of patients in the 41–50 years age group aligns with findings from previous studies, which often report that liver resection is more common among middle-aged individuals. For instance, studies have shown that liver resection is frequently performed in patients aged 40 to 60 years, reflecting the typical age of

onset for liver tumors, particularly hepatocellular carcinoma and metastatic liver disease [7,8]. The observed male-to-female ratio of 1:1.22 indicates a higher proportion of female patients in this cohort, which is somewhat atypical, as many studies have reported a male predominance in liver disease, particularly in hepatocellular carcinoma [13]. This discrepancy may reflect specific demographic or geographical factors affecting patient selection and disease prevalence in the study population. No statistically significant association was found between PI and bile leaks (P = 0.237 for PI <50%). Similar observations were made in studies by Poon et al. [8], which reported that bile leaks are more often associated with intraoperative factors than coagulation metrics alone. A significant relationship was observed between low PI (<50%) and postoperative bleeding (P = 0.04), indicating that impaired coagulation increases bleeding risk. Benzoni et al. [10] similarly reported a strong association between low PI and increased rates of postoperative hemorrhage. While sepsis rates were higher in patients with low PI (<50%), the association was not statistically significant (P = 0.479). This finding is consistent with van den Broek et al. [14], who noted that factors beyond coagulation, such as infection control and immune status, play crucial roles in sepsis risk. It showed that the prothrombin index <50% after liver resection is associated with an increased risk of bile leak, hemorrhage, sepsis, and other complications resulting in a longer hospital stay. Several authors have shown that deranged prothrombin index before and after hepatic resection in the early postoperative phase can be variably associated with renal and hepatic dysfunctions, postoperative peaks in serum bilirubin concentration, length of hospital stay, and mortality [15,16]. Previous studies reported similar findings in a series of patients with a very low postoperative mortality rate. PI < 50% is associated with an adverse outcome. Liver blood supply was occluded earlier during anatomical liver resection for minimal blood loss, but the affected segment remain hypoxic for a long duration. Major liver resection usually takes more time. So, low PI significantly predicts postoperative bleeding but not bile leaks or sepsis, highlighting the need for vigilant coagulation management in liver resection patients.

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

V. CONCLUSION

The study findings highlight the clinical importance of assessing both the initial and postoperative Prothrombin Index concerning outcomes following liver resection. Consequently, utilizing the initial and early postoperative Prothrombin Index as a clinical parameter can enhance the optimization of postoperative patient care.

VI. RECOMMENDATION

Initial Prothrombin Index can be measured after liver resection for early prediction of compromised outcome. Conduction of further research and validation studies is necessary to establish the reliability and generalizability of the initial Prothrombin Index with post-hepatectomy complications. The study should be conducted among larger sample sizes with a long-duration follow-up. The multidisciplinary approach to research work can make a study precise & more authentic in this regard.

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