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Diagnostic and Prognostic Accuracy of Interleukin-6 for Postoperative Infection in Abdominal Surgery in A Tertiary Care Center

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Abstract

Introduction: Sepsis is a significant postoperative risk in abdominal surgery, with traditional markers like WBC and CRP lacking specificity. Interleukin-6 (IL-6) is a promising biomarker, rapidly peaking after infection or injury and correlating with surgical stress and complications like sepsis and SIRS. Studies show IL-6 outperforms CRP and procalcitonin in early detection, particularly in open surgeries. Its diagnostic accuracy supports timely intervention, though further research is needed to optimize its clinical use.

Methods: This single-center cohort study assessed postoperative complications after major abdominal surgery, excluding patients on preoperative antibiotics. Blood samples were collected at baseline and on postoperative days 1, 3, and 7. SIRS was diagnosed based on abnormal temperature, heart rate, respiratory rate, or leukocyte count. Outcomes included 30-day mortality, infections, sepsis, reoperations, and hospital stay duration. IL-6 levels were measured using ELISA, and clinical data on preoperative history, surgery details, and postoperative parameters were analyzed.

Results: This study analyzed IL-6 as a biomarker for predicting complications in 75 patients after major abdominal surgery. IL-6 levels between 300-500 pg/mL were significantly associated with complications, with an optimal cut-off of 432 pg/mL. Fever (21.33%) and pneumonia (20%) were the most common complications, followed by SIRS, surgical site infections, anastomotic leaks, and mortality.

- High IL-6 levels on day 1 were strongly associated with fever (p=0.0101), SIRS (p=0.0012), surgical site

infections (p=0.0077), pneumonia (p=0.0189), and anastomotic leaks (p=0.0305).

- Mortality and congestive heart failure showed no significant correlation with IL-6.
- Day 1 IL-6 levels were more predictive of complications (p=0.0066) than day 3 levels (p=0.04566).

Conclusion: Elevated IL-6 on day 1 is strongly associated with postoperative complications and provides better predictive accuracy than on day 3, making it a valuable marker for early clinical decisions.

Keywords: Sepsis, Interleukin, SIRS

Introduction

Postoperative infections, especially sepsis, are major challenges in abdominal surgery, often leading to longer hospital stays, increased healthcare costs, and higher patient morbidity and mortality. These infections can double the duration of postoperative recovery and pose significant clinical and economic burdens[1-2]. Timely detection and treatment of such infections are essential to improving patient outcomes[3-5]. However, traditional clinical markers like white blood cell count (WBC) and C-reactive protein (CRP) are not always reliable in the postoperative period, as they respond to both infectious and non-infectious inflammation.

Advancements in understanding the immune response have led to growing interest in biomarkers as early indicators of infection. Among these, interleukin-6 (IL-6) is gaining attention due to its rapid release during inflammatory events, including surgical trauma. IL-6 is a pro-inflammatory cytokine central to the immune response, and its levels have been associated with the severity of inflammation. Studies suggest that laparoscopic surgery induces a lower IL-6 response compared to open surgery, indicating reduced surgical stress and potentially quicker recovery[6-9].

This review focuses on the potential of IL-6 as a diagnostic and prognostic biomarker for postoperative infections in abdominal surgery. By examining its accuracy and comparing it with other markers, this analysis seeks to clarify its clinical utility. Additionally, it explores differences in biomarker responses between laparoscopic and open surgical methods, aiming to contribute to improved strategies for early infection detection and better postoperative care.

Aims and objectives of the study

- To assess the diagnostic and prognostic accuracy of interleukin-6 (IL-6) as diagnostic biomarkers for postoperative infection/sepsis/fever following abdominal surgery.
- To assess the diagnostic and prognostic accuracy of IL 6 with respect to surgical site infection. (Superficial, deep, organ space), and anastomosis leak.
- To assess the diagnostic accuracy of IL 6 in reference of SIRS. (Systemic inflammatory response syndrome).
- To assess IL 6 levels as diagnostic and prognostic biomarkers in reference of congestive heart failure, post operative pneumonitis.

Methodology

Source of Data: The study was conducted in the Department of Surgery at Government Medical College and associated hospital, Kota, between November 2022 and February 2024. It included patients undergoing abdominal surgery during this period.

Sample Size: A total of 75 patients were enrolled in the study.

Inclusion Criteria

- Patients of all ages, including adults and children (<18 years), undergoing abdominal surgery.

- Analysis focused on the diagnostic accuracy of IL-6 for detecting infection or sepsis.

Exclusion Criteria

- Neonates.
- Patients on antibiotic treatment before surgery.
- Patients with sepsis from non-abdominal infections.

Data Collection: This prospective observational study measured serum IL-6 levels at four points: pre-surgery and postoperative days 1, 3, and 5. Data from all eligible patients during the study period were analyzed.

This prospective, single-center cohort study assessed postoperative complications after major abdominal surgery. Approved by the Medical Ethics Committee, informed consent was obtained from all patients. Blood samples were collected on the day of surgery (baseline) and on the first, third, and seventh postoperative days. Patients on prior antibiotic therapy were excluded.

SIRS was diagnosed if at least two of the following criteria were met: temperature <36.0°C or >38.0°C, heart rate >90 bpm, respiratory rate >20 breaths/min, or leukocyte count <4,000 or >12,000/μL[10-14].

Primary outcomes included 30-day mortality, pneumonia, sepsis, anastomotic dehiscence, wound infection, respiratory insufficiency, reoperation, and congestive heart failure. Hospital stay duration was also recorded.

IL-6 levels were measured using solid-phase ELISA. Blood samples were stored at –80°C and analyzed in batches. Clinical data, including preoperative history, medications, and surgical details, were obtained from medical records.

Results

The results of our analytical study on the diagnostic and prognostic role of IL-6 in postoperative complications following abdominal surgery, conducted at Government Medical College, Kota, and its associated hospital, are outlined below. A total of 75 patients were included in the study, and the findings are presented as follows:

Table 1:

No of patients and types of complication according to IL6 level (0 to 1000)

S.NO	Level Of Il6 (Pg/Ml)	No Of Patient	No Of Patient With Complication	Types Of Complication
1	0 to 100	24	5	Fever, SSI, CCF
2	101-200	18	5	Fever, CCF, Pneumonitis, Anastomotic Leak
3	201-300	3	1	SSI
4	301-400	7	6	Pneumonitis, SSI, Fever, CCF
5	401-500	2	2	SIRS, Pneumonitis
6	501-600	0	0	
7	601-700	2	2	Fever, Pneumonitis
8	701-800	1	0	
9	801-900	0	0	
10	901-1000	1	1	SSI

Table 2:

No of patients and types of complication according to IL6 level (1001 to 2000)

S.No.	Level Of IL6 (Pg/Ml)	No Of Patient	No Of Patient With Complication	Types Of Complication
1	1001-1100	0	0	
2	1101-1200	0	0	
3	1201-1300	1	1	Anastomotic Leak
4	1301-1400	0	0	

5	1401-1500	0	0	
6	1501-1600	0	0	
7	1601-1700	0	0	
8	1701-1800	0	0	
9	1801-1900	2	2	SSI, Pneumonitis
10	1901-2000	0	0	

Table 3:

No of patients and types of complication according to IL6 level (2001 to 3000)

S.NO.	Level Of IL6 (pg/ml)	No Of Patient	No Of Patient With Complication	Types Of Complication
1	2000-2100	0	0	
2	2101-2200	0	0	
3	2201-2300	0	0	
4	2301-2400	1	1	CCF
5	2401-2500	1	1	SSI
6	2501-2600	1	1	Pneumonitis
7	2601-2700	1	0	
8	2701-2800	0	0	
9	2801-2900	0	0	
10	2901-3000	0	0	

Table 4:

No of patients and types of complication according to IL6 level (3001to3000 and above)

S.NO.	Level Of IL6 (pg/ml)	No Of Patient	No Of Patient With Complication	Types Of Complication
1	3001-3100	1	1	Death
2	3101-3200	1	1	Anastomotic Leak
3	3201-3300	0	0	
4	3301-3400	0	0	
5	3401-3500	0	0	
6	3501-3600	0	0	
7	3601-3700	2	1	
8	3701-3800	0	0	
9	3801-3900	2	2	SIRS, Pneumonitis
10	3901-4000	1	1	Anastomotic Leak
11	>4001	4	4	SIRS, Death, Pneumonitis,

In this study, 7 of 9 patients with IL-6 levels between 301 and 500 pg/ml experienced complications, while 7 of 45 patients with IL-6 levels between 0 and 300 pg/ml had complications. The optimal IL-6 cut-off for predicting complications on day 1 was found to be 432 pg/ml, suggesting that the predictive range for complications lies between 300 and 500 pg/ml. While the type of complication was not linked to IL-6 levels, the incidence of complications was significantly associated with IL-6 levels.

Age Distribution

In this study, 25.33% of patients were aged 51-60 years, followed by 17.33% aged 61-70 years, with other age groups accounting for less than 10% .

Sex Distribution

In this study, 73.33% of the patients were male, while 26.66% were female.

Co Morbidity

Table 5: Distribution of Co-Morbidity among the study subjects

CO- Morbidity	No. of Patients	%
None	31	41.33333333
Hypertension	27	36
COPD	6	8

CKD	1	1.333333333
Type 2 DM	10	13.33333333
Total	75	100

In this study, approximately 60% of the subjects had co-morbidities. Among 75 patients, 27 had a history of hypertension, and 10 had type 2 diabetes mellitus, as shown in Table 3 and Figure 3.

Duration of Surgery

In this study, 33.33% of patients (25 out of 75) had a surgery duration of 71-90 minutes, while 18 patients underwent surgery lasting 51-70 minutes. For 6 patients, the procedure exceeded 110 minutes.

Post Operative Complication

Table 6: Distribution of post-operative complication among study subjects

Post-Operative Complications	No. of Patients	%
Fever		
Yes	16	21.33
No	59	78.66
Congestive heart failure		
Yes	6	8
No	69	92
SIRS		
Yes	7	9.333333
No	68	90.66667
Surgical site infection		
Yes	5	6.666667
No	70	93.33333
Post operative pneumonia		
Yes	15	20
No	60	80
Anastomosis leak		
Yes	2	2.666667
No	73	97.33333
Death		
Yes	3	4
No	72	96

In this present study fever is most common complication after surgery approx. 21.33% of study population suffers from fever while post-operative pneumonia is second most common complication (approx. 20 % of study population). Followed by SIRS, congestive heart failure, surgical site infection, anastomosis leak and death.

Hospital Stay

In this present study duration of hospital study for most of patient (50 out of 75 study populations) were less than 7 days while only 3 patients stay more than 15 days.

Operative Procedure

Table 7: Distribution of operative procedure

Name of Operative Procedure	No. of Patients	%
Emergency exploratory laparotomy	39	52
CBD exploration	1	1.333333
Open appendicectomy	12	16
Open cholecystectomy	7	9.333333
Hartmann procedure	2	2.666667
Feeding jejunostomy	1	1.333333
Gastrojejunostomy	2	2.666667
Others	11	14.66667
Total	75	100

In this study, 39 of 75 patients underwent emergency exploratory laparotomy, including procedures like ileal/jejunal perforation repair, Graham patch repair, and resection anastomosis. Other surgeries included open

appendectomy, cholecystectomy, gastrojejunostomy, and CBD exploration, as shown in Table 7 and Figure 7.

Clinical Outcome According To Il6 on Day 1

Table 8: Distribution of clinical outcome

Complications	High IL6	Low IL6	P value	Chi Square
Fever	11	5	0.0101	6.626
Congestive heart failure	3	3	0.6019	0.2722
SIRS	7	0	0.0012	10.44
Surgical site infection	5	0	0.0077	7.092
Post operative pneumonia	10	5	0.0189	5.512
Anastomosis leak	5	1	0.0305	4.683
Death	3	0	0.061	3.51

Association of Fever

Table 9: (Association of fever with IL6 on day -1)

Fever	Present	Absent	Total
High IL6	11	12	23
Low IL6	5	47	52
Total	16	59	75

In this study, 11 out of 23 patients with high IL-6 levels on day 1 had postoperative fever, compared to 5 out of 52 with low IL-6 levels. The chi-square statistic (6.626) and p-value (0.0101) indicate a significant association ($p < 0.05$).

Association of Congestive Heart Failure

Table 10: (Association of Congestive heart failure with IL6 on day -1)

Congestive heart failure	Present	Absent	Total
High IL6	3	20	23
Low IL6	3	49	52
Total	6	69	75

In this study, postoperative congestive heart failure occurred in 3 of 23 patients with high IL-6 levels and 3 of 52 with low levels. The chi-square statistic (0.2722) and p-value (0.6019) show no significant association.

Association of Sirs

Table 11: (Association of SIRS with IL6 on day -1)

SIRS	Present	Absent	Total
High IL6	7	16	23
Low IL6	0	52	52
Total	7	68	75

In this study, 7 of 23 patients with high IL-6 levels and 3 of 52 with low IL-6 levels developed SIRS. The chi-square statistic (10.44) and p-value (0.0012) indicate a significant association.

Association of Surgical Site Infection

In this study, 5 of 23 patients with high IL-6 levels developed surgical site infections, compared to none of the 52 patients with low IL-6 levels. The chi-square statistic (7.092) and p-value (0.0077) indicate a significant result.

Association of Post-Op Pneumonia

In this study, 10 of 23 patients with high IL-6 levels on day 1 developed postoperative pneumonia, compared to 5 of 52 with low IL-6 levels. The chi-square value (5.512) and p-value (0.0189) show a significant association.

Association of Anastomosis Leak

In this study, 5 patients out of 23 which had high IL-6 value on day 1 present with post-operative anastomosis leak while 1 patient out of 52 which had low IL-6 value present with post-operative anastomosis leak.

The chi-square value is 4.683. P value is 0.0305. Results are significant.

Association of Death

In this study, 3 of 23 patients with high IL-6 levels had mortality, compared to none of the 52 patients with low IL-6 levels. The chi-square value is 3.51, with a p-value of 0.061, which is not significant.

Table 12: (Comparison of post-operative complication between IL-6 OF day 1 and day 3)

Day -1	Patient with complications	Patient without complications	p value
HighIL6	16	7	0.0066
Low IL6	10	42	0.0895
Total	26	49	

In this study, day 1 IL-6 levels were more strongly associated with postoperative complications than day 3 levels. The p-value for day 1 IL-6 is 0.0066, while for day 3 it is 0.04566.

Discussion

Postoperative infections can significantly increase hospital stays, costs, and risks to patient life. Early detection of these infections is crucial, and traditional markers like WBC, CRP, and PCT are affected by surgery factors[6,7,8]. IL-6, a cytokine, rises quickly and normalizes faster than CRP, making it a more sensitive indicator of early inflammation and infection.

Studies such as Szczepanik et al. (2018) and Mokart et al. (2018) found that elevated IL-6 levels on the first postoperative day correlate with higher risks of complications like sepsis[4,15]. Our study identified 432 pg/mL as the optimal IL-6 cutoff for predicting complications after major abdominal surgery.

IL-6 on day 1 showed similar diagnostic accuracy to CRP, and its predictive value was comparable to imaging methods for complications like anastomotic dehiscence[16]. SIRS symptoms also correlated with higher IL-6 levels but were less reliable for predicting complications.

Our study has limitations, including the use of composite endpoints, variability in sample timing, and a small cohort size. Despite these, IL-6 remains a promising marker for early detection of postoperative complications, warranting further larger studies to refine its clinical application.

Conclusion

Elevated IL-6 levels on the first postoperative day are strongly associated with postoperative complications following abdominal surgery. IL-6 on day 1 provides better predictive accuracy than on day 3, making it a valuable marker for early clinical decision-making.

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