

Biochemical Predictors of Wound Healing in Tracheostomy Patients: A Prospective Clinical Study

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ABSTRACT

Background: Tracheostomy is a common intervention in critically ill patients; however, delayed wound healing remains a significant postoperative concern. Biochemical factors such as nutritional status, systemic inflammation, glycemic control, and micronutrient balance may influence tissue repair, yet limited prospective evidence exists in tracheostomy patients.

Objectives: To evaluate the predictive value of selected biochemical parameters on wound healing outcomes in adults undergoing tracheostomy.

Methods: This prospective clinical study was conducted at Indus Hospital and data was also collected from Department of Surgery, Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan, over one year (June 2024–May 2025) and included 100 adult patients undergoing elective or emergency tracheostomy. Preoperative and early postoperative biochemical assessments included serum albumin, prealbumin, fasting blood glucose, HbA1c, C-reactive protein (CRP), interleukin-6 (IL-6), hemoglobin, serum zinc, and serum iron. Wound healing was monitored clinically, with delayed healing defined as persistent inflammation, discharge, or incomplete epithelialization beyond 14 days. Data were analyzed using SPSS version 25, and multivariate logistic regression identified independent predictors of delayed healing.

Results: Delayed wound healing occurred in 28% of patients. Those with delayed healing demonstrated significantly lower serum albumin, prealbumin, hemoglobin, zinc, and iron levels, along with higher fasting blood glucose, HbA1c, CRP, and IL-6 values ($p < 0.05$). Serum albumin and prealbumin showed strong negative correlations with healing time, whereas CRP and IL-6 correlated positively. Multivariate analysis revealed low serum albumin (OR 3.4), elevated CRP (OR 2.9), uncontrolled HbA1c (OR 2.7), and low serum zinc (OR 2.5) as independent predictors of delayed healing.

Conclusion: Nutritional deficiency, systemic inflammation, poor glycemic control, and micronutrient imbalance significantly influence postoperative wound healing in tracheostomy patients. Routine biochemical evaluation and early metabolic optimization may improve healing outcomes and reduce complications.

Key words: Tracheostomy, Wound Healing, Biomarkers, Albumins, C-Reactive Protein, Glycated Hemoglobin A, Zinc



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INTRODUCTION

Tracheostomy is a surgery that is commonly performed among long-term, critically ill, and mechanically ventilated patients. It is also usually noted in the conditions of prolonged mechanical ventilation, airway obstruction to a higher degree, extreme neurological impairment, and

airway damage under traumatic conditions [1]. In modern intensive care, tracheostomy is the main subject in enhancing airway clearance, alleviating patient distress, eliminating secretions, and avoiding complications related to prolonged endotracheal intubation [2]. Although the procedure has clinical advantages, it is not free of

complications. Among them, delayed wound healing is one of the major postoperative issues that may influence morbidity, hospital stay, and the overall recovery [3].

The biological process of wound healing after tracheostomy is a complicated and tightly controlled process of interactions between inflammatory mediators, immune cells, growth factors, components of the extracellular matrix, and systemic metabolic pathways [4]. The inflammation, proliferation, and remodeling are three intersecting phases of the process, each of which depends on a specific cellular and biochemical signaling [5]. Alteration of any stage with infection, malnutritional condition, systemic disease, or metabolic imbalances may slow healing or result in complications, including wound dehiscence, excessive granulation tissue, or continued tracheocutaneous fistula.

The biochemical factors play a major role in regulating wound repair. Nutritional stores are indicated by the serum proteins, including albumin and prealbumin, which shape fibroblast action, collagen synthesis, angiogenesis, and immune efficiency [6]. Glycemic parameters (fasting blood glucose and HbA1c) influence the functionality of leukocytes, microvascular perfusion, and collagen cross-linkage, and therefore, patients with inadequate glycemic control are prone to delayed healing. C-reactive protein (CRP), interleukin-6 (IL-6), and procalcitonin are inflammatory biomarkers to give an indication of the systemic inflammatory load, which can inhibit tissue regeneration and extend the healing period [7]. Also, there are micronutrients like zinc, vitamin C, and iron that are critical cofactor enzymatic processes that lead to stabilization of collagen, epithelialization, and immunity.

Compromised wound healing is likely to occur among tracheostomy patients who are highly likely to have several risk factors. Delayed tissue repair is highly susceptible to critical illness, prolonged ICU stay, malnutrition, sepsis, mechanical ventilation, and comorbidities, including diabetes mellitus and chronic kidney disease. Repeated infection of the stoma site by airway secretions also complicates the treatment of wounds and exposes them to additional risks of infection. Due to such complicated relationships, the discovery of credible biochemical biomarkers related to compromised healing would be beneficial to predict risks at an early stage, optimize perioperative processes, and reduce the number of postoperative complications [8].

Despite the large amount of literature assessing clinical and biochemical predictors of wound healing in general surgical populations, few prospective data exist in tracheostomy patients in particular [9]. By setting biochemical markers with delayed healing, clinical monitoring protocols can be improved, better decision-making can be made, and nutritional, metabolic, and inflammatory management approaches can be directed towards high-risk patients [10].

The current prospective clinical study aims to explore the relationship between the chosen biochemical parameters, such as nutritional parameters, inflammatory parameters, glycemic parameters, and levels of micronutrients, and wound healing outcome in adult tracheostomy patients. This study also seeks to improve the clinical outcome and postoperative care measures by identifying the biochemical predictors most important to help increase better clinical outcomes in the vulnerable subset of patients.

MATERIALS AND METHODS

The Current study was one-year prospective clinical study performed at Indus Hospital, Chowk Qureshi, Multan, Pakistan and data was also collected from Department of Surgery, Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan. n=142 patients who were undergoing an elective or emergency tracheostomy were enrolled sequentially, with their informed consent accorded by the patients or legal guardians. Adult patients aged 18 and above who needed tracheostomy due to long-term mechanical ventilation, airway obstruction because of upper airway obstruction, neurological deficit, trauma, and emergency signs were included. The exclusion criteria were: the existence of chronic non-healing neck wounds, local malignancy at the tracheostomy site, known immunodeficiency disorders, ongoing chemotherapy or long-term corticosteroid use, and death within 72 hours of surgery due to confounding factors affecting wound healing.

At enrolment, baseline demographic and clinical data, including age and gender, body mass index, tracheostomy indication, pre-operative mechanical ventilation, smoking status, and comorbid data (diabetes mellitus, hypertension, and chronic kidney disease) were collected.

All the procedures were carried out by trained surgical teams under aseptic conditions using a standardized technique to perform tracheostomy. Follow-up involved wound evaluation on a daily basis in the first week, followed by twice per week after that until full healing or discharge. The response in terms of healing was measured by the decreased erythema and edema, the development of healthy granulation tissue, the lack of purulent discharge, and the continuation of the epithelialization. Delayed wound healing was determined as the constant inflammation, discharge, wound gaping, or inability to attain complete epithelialization in 14 days. Cases of wound infection, dehiscence, excessive granulation tissue, and tracheocutaneous fistula were observed.

Measurement of serum albumin, prealbumin, fasting blood glucose, HbA1c, C-reactive protein, interleukin-6, hemoglobin, and total leukocyte count in the venous blood samples was also measured 24 hours before the operation and every three days after the operation. All

the biochemical tests were made in the central diagnostic laboratory through automated standardized tests with definite quality control measures.

This was done by grouping the patients into two categories: normal wound healing and delayed wound healing. SPSS version 25 was used to analyze the statistical data. Continuous variables were displayed using mean and standard deviation, whereas the categorical variables were displayed using frequencies and percentages. Group comparisons of the variables were done using independent sample t-tests and chi-square tests. Pearson correlation was used to evaluate the relationship between biochemical markers and the length of healing, and multivariate logistic regression was used to determine independent predictors of delayed wound healing. A p-value below 0.05 was considered as being statistically significant. The study was conducted by following the principles of ethics that are encompassed in the Declaration of Helsinki and institutional guidelines on clinical study. All participants were kept secret, and no identifiable information about the patients was given. The study was conducted voluntarily, and the subjects were allowed to pull out of the study at any point without any impact on their normal medical treatment. Ethical approval was received by the Institutional Review Board (IRB) of Indus Hospital, Chowk Qureshi, Multan, Pakistan, under the ethical approval reference: IRB Reference Number: IH-IRB/017.

RESULTS

The study involved 100 patients. The average age of the participants was 54.2 years, 16.8 years. Sixty-two percent of the cohort was made up of males, and the remaining 38 percent was made up of females. Long-term mechanical ventilation (48%), neurological impairment (26%), obstruction of the upper airways (18%), and trauma (8%) were the most common indicators of tracheostomy. Out of the participants, 34 percent were diabetic with diabetes mellitus, 46 percent were hypertensive, and 12 percent were chronic kidney disease patients.

A total of 28 patients (28%) and 72 patients (72%) reported delayed and normal wound healing, respectively. Table 1 provides a comparison of the demographic and clinical status of the normal and delayed

healing. The frequency of diabetes mellitus was much higher in the delayed healing group, and these patients subjected to pre-tracheostomy mechanical ventilation, needed more time ($p < 0.05$).

There were also major variations in the biochemical parameters between the two groups. The serum albumin, prealbumin, hemoglobin, zinc, and iron levels among the patients with delayed wound healing were significantly lower than those of the normal healing group. Conversely, inflammatory cytokines like the C-reactive protein (CRP) and interleukin-6 (IL-6) were significantly higher in the delayed healing group. Fasting blood glucose and HbA1c glycemic indicators were also considerably increased in patients with delayed healing. Table 2 summarizes these findings.

The correlation was performed to estimate the strength of the negative relationship between the level of serum albumin and prealbumin and the wound healing duration ($r = -0.61$ and $r = -0.58$, respectively; $p = 0.001$). On the other hand, CRP and IL-6 showed strong positive correlations with the healing period ($r = 0.66$ and $r = 0.63$, respectively; $p < 0.001$).

After controlling for the variable age and diabetes status, multivariate logistic regression (Table 3) selected low serum albumin (OR 3.4), high CRP (OR 2.9), uncontrolled HbA1c (OR 2.7), and low serum zinc (OR 2.5) as independent predictors of delayed wound healing. In general, the results show that nutritional status biomarkers (albumin and prealbumin), inflammatory (CRP and IL-6), glycemic control (HbA1c), and micronutrient (zinc and iron) biomarkers have a crucial role in postoperative wound healing among patients with tracheostomy. Low serum albumin and high CRP were identified as the most potent independent biochemical predictors of slow wound healing in this group of people. In general, the results show that nutritional status biomarkers (albumin and prealbumin), inflammatory (CRP and IL-6), glycemic control (HbA1c), and micronutrient (zinc and iron) biomarkers have a crucial role in postoperative wound healing among patients with tracheostomy. Low serum albumin and high CRP were identified as the most potent independent biochemical predictors of slow wound healing in this group of people.

Table 1: Baseline Clinical Characteristics of Study Participants (n = 100)

Variable	Normal Healing (n=72)	Delayed Healing (n=28)	p-value
Mean Age (years)	52.6 ± 15.9	58.4 ± 17.3	0.08
Male gender, n (%)	44 (61.1%)	18 (64.3%)	0.76
Female gender, n (%)	28 (38.9%)	10 (35.7%)	
Diabetes mellitus, n (%)	18 (25%)	16 (57%)	0.003*
Hypertension, n (%)	30 (41.6%)	16 (57.1%)	0.14

(*Statistically significant)

Table 2: Comparison of Biochemical Parameters Between Groups

Parameter	Normal Healing (n=72)	Delayed Healing (n=28)	p-value
Serum Albumin (g/dL)	3.8 ± 0.4	3.1 ± 0.5	<0.001*
Prealbumin (mg/dL)	24.6 ± 5.3	17.2 ± 4.8	<0.001*
Fasting Blood Glucose (mg/dL)	118 ± 22	162 ± 35	<0.001*
HbA1c (%)	6.4 ± 0.8	8.1 ± 1.2	<0.001*
CRP (mg/L)	8.6 ± 3.2	21.4 ± 6.8	<0.001*
IL-6 (pg/mL)	12.5 ± 4.1	29.3 ± 7.6	<0.001*
Hemoglobin (g/dL)	12.1 ± 1.4	10.4 ± 1.2	<0.001*
Serum Zinc (µg/dL)	88 ± 14	63 ± 11	<0.001*
Serum Iron (µg/dL)	76 ± 18	52 ± 15	<0.001*

(*Statistically significant)

Table 3: Multivariate Logistic Regression Analysis for Predictors of Delayed Wound Healing

Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
Low Serum Albumin	3.4	1.8 – 6.5	0.001*
Elevated CRP	2.9	1.6 – 5.2	0.002*
HbA1c > 7%	2.7	1.4 – 4.9	0.004*
Low Serum Zinc	2.5	1.3 – 4.6	0.006*

(*Statistically significant)

DISCUSSION

This prospective clinical study assessed the correlation of the chosen biochemical parameters and wound healing in patients with tracheostomy. The results indicate that nutritional condition, inflammatory reaction, glycaemic regulation, and micronutrients are powerful factors affecting postoperative wound healing. Poor glycaemic control (high HbA1c), low serum zinc, low serum albumin, and elevated C-reactive protein (CRP) became independent predictors of delayed wound healing [6].

Wound healing is an extremely ordered biological process that entails inflammation, growth, and remodeling of the tissues. Sufficient protein intake is necessary in the production of collagen, the growth of fibroblasts, angiogenesis, and immunity [7]. Delays in healing were significantly accompanied by low levels of serum albumin and prealbumin in patients who had delayed healing, as opposed to the normal recovery in patients. The deposition of collagen and tissue regeneration may be impaired by hypoalbuminemia, indicative of poor nutritional stores and catabolic stress on the body. These results are in line with the past surgical studies that have reported low preoperative albumin to be linked with delayed healing and increased postoperative complications. The negative relationship between albumin and healing time is also high, which further supports its prognostic nature in patients who undergo tracheostomy [8].

The delayed healing group showed a significant increase in the inflammatory markers, especially CRP and IL-6. Whereas controlled inflammation is essential in the early stages of healing, long-term and excessive inflammation suppresses tissue repair and increases healing. High CRP can be a result of systemic inflammation, unexplained infection, and extreme physiological stress, which are detrimental to the wound biology. Its positive relation with extended healing underscores the role of inflammatory burden on tracheostomy site healing [9]. Local inflammatory

responses may be exacerbated by the frequent exposure of the area of the neck to respiratory secretions.

Wound outcomes also had a significant relationship with glycaemic status. Patients who had high levels of fasting glucose and HbA1c had a higher chance of delayed healing [10]. Hyperglycemia inhibits the neutrophil functions, decreases phagocytosis, angiogenesis, and collagen cross-linking. In addition, the presence of high glucose levels contributes to the growth of bacteria, making the wound vulnerable to infection. The incidence of diabetes mellitus was found to be much higher in the delayed healing group, and this indicates the need to carefully control the level of glycaemic control before and after tracheostomy [11].

Micronutrient status, particularly serum zinc and iron, also showed significant relations with healing outcome. Zinc is very necessary in the production of DNA, foreign body growth, immune response, and collagen. The reduced level of zinc in delayed healers was probably the cause of the inadequate epithelialization and extended inflammation [12]. Similarly, iron deficiency and anemia affect the oxygen supply to tissues, which is essential to provide fibroblast activity and collagen synthesis. The fact that hemoglobin levels are considerably lower in patients with delayed healing indicates the need to pay sufficient attention to tissue oxygenation [13].

The results of multivariate regression validated the low serum albumin and high CRP as the most important independent variables of delayed wound healing [14]. These results reveal that malnutrition and systemic inflammation can be used as primary factors to define poor postoperative outcomes in patients with tracheostomy. Significantly, the biochemical markers are relatively cheap, readily accessible, and clinically feasible, thus useful in the early risk stratification [15].

The study has a number of clinical implications. The preoperative screening of serum albumin, glycaemic, and inflammatory levels could be performed on a regular basis to detect individuals at risk. Prenatal nutritional

supplementation, micronutrient replacement, greater glycemic control, and successful control of systemic inflammation could improve the wound healing outcome [16]. Biochemical screening as part of the perioperative care practice could help to minimize complications like wound infection, dehiscence, and persistence of tracheocutaneous fistula, especially in intensive care units where tracheostomy is widely used.

The study, however, has its limitations. It might not be generalizable because it is a single-center study [17]. Even though the study sample of 100 patients was sufficient to give the necessary statistical power, multicenter studies that included more patients would enhance the external validity. Also, local wound-care cultures, patterns of microbial colonization, and length of tracheostomy tube were not directly tested and could have an effect on the outcome of healing [18-20].

CONCLUSION

This clinical trial shows that the use of biochemical parameters is a decisive factor in the wound healing of tracheostomy individuals postoperatively. The nutritional status, systemic inflammation, and poor glycemic control, coupled with the lack of micronutrients, were also significant risk factors contributing to delayed healing. Low serum albumin and high CRP became the most significant independent predictors, and this reflects the combined effect of malnutrition and the load of inflammatory processes on the body in restoring tissues. The results underline that metabolic and biochemical factors play a crucial role, as tracheostomy patients do not heal their wounds based only on the surgical factors. Regular monitoring of essential biochemical indicators, as well as early optimization of nutrition, glycemic regulation, and micronutrient balance, could positively affect recovery, minimize complications, and increase the overall clinical results.

Conflict of Interest: The authors declare no conflicts of interest.

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Authors' Contributions:

M.E.A.K. designed the study, supervised patient recruitment, and contributed to manuscript drafting.

M.G.A. assisted in clinical evaluation, data collection, and preliminary data analysis. M.S.A. performed statistical analysis, data interpretation, and manuscript writing.

S.R. critically reviewed the manuscript and approved the final version. All authors read and approved the final manuscript.

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Data Availability: The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request.

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