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ASSOCIATION BETWEEN DEPRESSION AND DELAYED WOUND HEALING AFTER MAJOR SURGERY.

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Abstract

Background: Depression is a common yet under-recognised psychological condition that significantly influences postoperative outcomes. It disrupts neuroendocrine and immune pathways, impairing the regulation of inflammation, angiogenesis, and collagen synthesis. These biochemical alterations may delay wound healing after major surgery, thereby increasing morbidity.

Objectives: To determine the association between preoperative depression and delayed wound healing after major surgery and to assess its relationship with demographic and clinical factors among adult surgical patients.

Methodology: This prospective study was conducted at the Department of Surgery, Islamic International Medical College, Rawalpindi, from Jan 2024 to June 2024 on 100 adult patients undergoing major elective surgery. Depression was assessed preoperatively using the Hospital Anxiety and Depression Scale (HADS). Demographic and clinical data were documented. Delayed healing was defined as persistent inflammation, dehiscence, or inadequate epithelialization by day 14.

Results: The 100 patients (mean age 48.6 ± 13.2 years), preoperative depression was present in 38%. Delayed wound healing occurred in 32% of the cohort. Depressed patients had a significantly higher rate of delayed healing (52.6%) compared to non-depressed patients (19.4%), with **p = 0.003.** Depression remained the strongest factor associated with impaired healing, accompanied by increased inflammation, prolonged angiogenesis, and slower epithelialization, independent of age,

Conclusion: Depression is a significant predictor of delayed postoperative wound healing. Early detection and integrated psychological support may improve surgical outcomes and reduce postoperative morbidity.

Keywords: Depression, Wound Healing, Surgery Outcomes

Introduction

Wound healing is a complex physiological process involving a series of coordinated events, including hemostasis, inflammation, proliferation, and remodeling. Optimal healing requires intact immune function, adequate tissue perfusion, balanced cytokine activity, and appropriate neuroendocrine regulation [1]. Psychological factors, particularly depression, have increasingly been recognized as influential determinants of surgical outcomes. Depression affects nearly 300 million people worldwide and remains significantly underdiagnosed in surgical populations, especially in low- and middle-income countries where preoperative psychological assessment is often limited [2]. Emerging evidence suggests that depression can impair wound healing by disrupting neuroimmune communication, altering hormonal responses, and promoting a pro-inflammatory state [3]. Mechanistically, depression is associated with deregulation of the hypothalamic–pituitary–aenal (HPA) axis, resulting in elevated cortisol levels that suppress immune cell activity, delay macrophage function, and impair collagen synthesis. Depressed individuals may also exhibit reduced levels of growth factors, such as VEGF, and fibroblast-derived mediators, which are essential for angiogenesis and tissue regeneration. Additionally, altered cytokine profiles with elevated IL-6, TNF-α, and IL-1β promote chronic inflammation, inhibit re-epithelialization, and increase susceptibility to infection. These pathophysiological changes collectively place depressed patients at higher risk for poor postoperative wound outcomes [4,5]. Behavioral factors may further contribute to impaired healing. Patients with depression often demonstrate lower adherence to postoperative care instructions, inadequate nutritional intake, reduced mobility, and impaired self-care habits. Substance use, sleep disturbances, and reduced pain tolerance further exacerbate vulnerability to wound complications. Socioeconomic factors, including limited access to timely follow-up care, may amplify these risks in resource-limited surgical settings [6]. Surgical wounds represent a critical component of postoperative recovery. Delayed wound healing increases the likelihood of infection, dehiscence, prolonged hospitalization, repeated procedures, and overall healthcare burden [7]. Identifying modifiable risk factors such as psychological distress may provide an opportunity to improve patient outcomes using cost-effective interventions. Screening for depression using a validated instrument like the Hospital Anxiety and Depression Scale (HADS) offers a practical method for risk assessment in busy surgical clinics [8,9]. Although previous studies have explored individual predictors of delayed wound healing, limited data are available from developing countries, where the prevalence of untreated psychological disorders may be higher. Furthermore, variations in surgical practices, comorbidities, and perioperative care across regions necessitate local evidence to understand the magnitude of the association between depressions and wound healing [10]. Investigating this link may help integrate mental health assessment into routine surgical preparation and postoperative management.

Research Objectives:

To determine the association between preoperative depression and delayed wound healing after major surgery and to evaluate its relationship with demographic, clinical, and wound-related factors in adult surgical patients.

Materials and Methods:

Study Design & Setting:

A prospective study was conducted at Department of Surgery, Islamic International Medical College, Rawalpindi, from from January 2024 to June 2024 enrolling patients undergoing major elective surgical procedures over a 6 -month study period.

Participants

One hundred adult patients aged 18–75 years scheduled for major elective surgery were consecutively recruited. Patients with cognitive impairment or those unable to complete the Hospital Anxiety and Depression Scale (HADS) were excluded. All participants underwent preoperative depression screening, routine laboratory testing, and standardised postoperative wound assessments during scheduled follow-up visits.

Sample Size Calculation
The sample size of 100 patients was calculated based on an expected prevalence of depression of 30% among surgical patients, a 95% confidence interval, and an allowable error of 10%. Power analysis ensured adequate ability to detect statistically significant differences in wound healing outcomes between depressed and non-depressed groups.

Inclusion Criteria
Adults aged 18–75 years, undergoing major elective surgery, Able to give informed consent, Preoperative evaluation completed within 24 hours

Exclusion Criteria
Emergency surgeries, Immunosuppressive therapy, or chronic steroid use, Active infection, or chronic non-healing wounds, Cognitive impairment, preventing questionnaire completion

Diagnostic and Management Strategy
Depression was diagnosed using the HADS scale. Wound healing was assessed clinically on postoperative days 3, 7, and 14. Patients received standardised postoperative care, with delayed healing identified based on inflammation, dehiscence, or inadequate epithelialization requiring extended management.

Statistical Analysis
Data were analysed using SPSS version 24. Descriptive statistics included mean, standard deviation, and frequencies. Associations between depression and delayed wound healing were examined using chi-square tests. A p-value < 0.05 was considered statistically significant. Multivariate analysis assessed potential confounders.

Results
A total of 100 patients were included, with a mean age of 48.6 ± 13.2 years. Preoperative depression was identified in 38% of patients. Delayed wound healing occurred in 32% of the cohort. Depressed individuals demonstrated significantly higher rates of delayed healing (52.6%) compared to non-depressed patients (19.4%), yielding a statistically significant association ($p = 0.003$). Depressed patients exhibited prolonged inflammation, increased serous discharge, and slower epithelialization on postoperative assessments. Demographic factors such as age and gender showed no significant association with delayed healing. Clinical comorbidities, including diabetes and hypertension, were evaluated, but depression remained the most prominent independent predictor. No significant differences in surgical procedure type were observed between groups. Overall, the findings highlight a strong correlation between psychological status and postoperative wound outcomes.

Intervention Outcome
Patients with depression required extended wound care, more frequent follow-up visits, and prolonged healing time. Early recognition and psychological support improved compliance with postoperative instructions and enhanced recovery. Integrating mental health screening into surgical pathways may reduce postoperative complications and support better wound-healing outcomes.

Table 1: Demographic Characteristics of Patients (N = 100)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	Mean ± SD	**48.6 ± 13.2**	—
Gender	Male	58	58%
	Female	42	42%
Marital Status	Married	71	71%
	Unmarried	29	29%
Residence	Urban	63	63%

	Rural	37	37%

Table 1 presents demographic details including age, gender distribution, marital status, and residence among the 100 patients undergoing major elective surgery.

Table 2: Clinical and Surgical Characteristics of Patients

Variable	Category	Frequency (n)	Percentage (%)
Diabetes Mellitus	Yes	22	22%
	No	78	78%
Hypertension	Yes	27	27%
	No	73	73%
Type of Surgery	Gastrointestinal	44	44%
	Hepatobiliary	21	21%
	Urologic	14	14%
	Others	21	21%

Table 2 describes clinical comorbidities and surgical categories, highlighting the distribution of diabetes, hypertension, and major surgical types in the study population.

Table 3: Prevalence of Depression and Wound Healing Outcomes

Variable	Category	Frequency (n)	Percentage (%)
Preoperative Depression (HADS)	Present	**38**	**38%**
	Absent	62	62%
Delayed Wound Healing	Present	**32**	**32%**
	Absent	68	68%

Table 3 shows the prevalence of preoperative depression assessed by HADS and postoperative delayed wound healing among the study participants.

Table 4: Association Between Depression and Delayed Wound Healing

Depression Status	Delayed Healing Present n (%)	Delayed Healing Absent n (%)	p-value
Depressed (n = 38)	**20 (52.6%)**	18 (47.4%)	**0.003**
Non-Depressed (n = 62)	**12 (19.4%)**	50 (80.6%)	—

Table 4 demonstrates a significant association between preoperative depression and delayed wound healing. Depressed patients had more than double the rate of delayed healing compared with non-depressed patients.

Discussion

The present study demonstrates a significant association between preoperative depression and delayed wound healing following major surgery. Patients who exhibited depressive symptoms based on HADS scores had more than twice the rate of delayed healing compared with non-depressed individuals [11]. These findings reinforce the growing body of evidence linking psychological distress with impaired tissue repair and underscore the importance of incorporating mental health assessment into perioperative care [12]. Our results align with recent studies indicating that depression adversely affects postoperative outcomes through neuroendocrine and immunological mechanisms [13]. A 2020 prospective study reported that depressed patients undergoing abdominal surgery experienced a 2.4-fold increase in delayed healing due to elevated inflammatory cytokines and suppressed immune cell activity [14]. Similarly, a 2021 meta-analysis found that psychological distress, particularly depression, was significantly associated with impaired fibroblast proliferation and reduced collagen deposition, ultimately delaying the proliferative phase of wound healing [15]. These findings support the biological plausibility observed in our cohort, where depressed individuals exhibited prolonged inflammation and slower epithelialization. The present study's findings also resonate with a 2022

observational study involving orthopedic surgical patients, which demonstrated that depression independently predicted wound complications even after controlling for comorbidities such as diabetes and obesity [16]. Another 2023 study focusing on gastrointestinal surgery reported significantly higher rates of postoperative surgical site infections among depressed patients, attributed to dysregulated cortisol levels and impaired leukocyte function [17]. Our study similarly found depression to be the strongest predictor of delayed healing despite the presence of other potential confounders. Recent literature further highlights behavioral and lifestyle factors that contribute to delayed wound outcomes in patients with depression. A 2019 study noted that depressive symptoms were linked with poor postoperative compliance, inadequate nutrition, and reduced physical mobility, all of which negatively influence wound recovery [18]. Although behavioral factors were not directly measured in our study, the clinical presentation such as increased discharge and slower healing—may reflect these behavioral influences.

Limitations

This study is limited by its single-center design, relatively small sample size, and reliance on clinical wound assessment rather than biochemical or imaging-based evaluation. Depression was measured only preoperatively, without follow-up scoring. Potential behavioral factors influencing healing were not assessed, which may have contributed to unmeasured confounding.

Conclusion

Depression significantly delays postoperative wound healing and increases the risk of wound complications after major surgery. Early identification and psychological support may improve healing outcomes. Integrating mental health screening into routine surgical care can enhance recovery, reduce morbidity, and promote a more comprehensive, patient-centered perioperative management approach.

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Authors Contributions

Concept & Design of Study: **M Nadeem Umar[1], Mohsin Aliemuddin[2]**
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Final Approval of version: **All Mentioned Authors Approved the Final Version.**

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