

Association of Serum Albumin Level with Wound Healing after Caesarean Section

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Abstract

Background: Hypoalbuminemia, indicative of malnutrition and illness, is associated with a heightened risk of poor post-operative outcomes, particularly impaired wound healing. Pregnancy, characterized by elevated estrogen levels, may further complicate wound healing processes. **Objective:** To evaluate the association of serum albumin level with wound healing after a caesarean section. **Methods:** A cohort of 100 pregnant patients undergoing caesarean section at Dhaka Medical College Hospital was included between January and December 2020. Preoperative serum albumin levels were measured, with hypoalbuminemia defined as < 3.5 g/dl. Patients were categorized into groups of hypoalbuminemic (Group I) and normal albuminemic (Group II). Postoperatively, patients were monitored for 60 days to identify surgical site infections and signs of delayed wound healing. **Results:** The mean preoperative serum albumin level was 2.57 ± 0.35 gm/dl in group I and 4.2 ± 0.4 gm/dl in group II. The difference was statistically significant ($p < 0.05$) between two groups. Out of 19 patients, 9 (47.4%) developed post caesarean wound infection and delayed wound healing in group I. Out of 81 patients, 7 (8.6%) developed post caesarean wound infection and delayed wound healing in group II. The difference was statistically significant ($p < 0.05$) with OR=9.51 having 95% CI (2.52-37.32). The number of post-operative days in hospital was 13.11 ± 6.14 in group I and 3.22 ± 1.41 in group II. The difference was statistically significant ($p < 0.05$) between two groups. A subject with serum albumin (< 3.5 gm/dl) had 7.626 (95.0% CI 2.324 to 25.02) times increased risk to develop wound infection and delayed wound healing after surgery. Other variables were not significantly associated with delayed wound healing. **Conclusion:** Hypoalbuminemia is an independent risk factor for the delay in wound healing. Low serum albumin level correlates well with the development of surgical site infection and delayed wound healing contributed to prolonged hospital stay.

Keywords: Hypoalbuminemia, malnutrition, post-operative outcomes, wound healing, serum albumin.

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INTRODUCTION

Nutritional status is a critical determinant of surgical outcomes, significantly influencing wound healing and recovery trajectories [1]. Malnutrition, characterized by deficiencies in essential nutrients, poses substantial challenges in patient care, particularly in the context of surgical interventions. The impact of malnutrition on wound healing is profound, with impaired wound closure, increased susceptibility to

infections, and higher rates of post-operative complications documented in malnourished individuals [2]. This underscores the importance of preoperative nutritional assessment and optimization strategies to mitigate the risks associated with surgical procedures. In patients with gastrointestinal diseases, malnutrition is a prevalent concern, further complicating surgical outcomes. It also highlights the detrimental effects of malnutrition on surgical recovery, emphasizing the need

for comprehensive nutritional evaluation in the patients [3]. Various tools exist for assessing nutritional status, with serum albumin emerging as a reliable indicator of nutritional adequacy and surgical risk. Low serum albumin levels have been associated with increased post-operative morbidity and mortality, making it a valuable marker in preoperative risk assessment [4].

Abdominal surgery, including procedures such as caesarean section, ranks among the most frequently performed elective surgeries globally [5]. Despite advancements in surgical techniques and perioperative care, post-operative morbidity remains a significant concern, imposing substantial burdens on patients and healthcare systems alike. The lack of consensus on defining and grading post-operative complications further complicates the assessment of surgical outcomes [6]. Therefore, identifying reliable predictors of post-operative complications, such as hypoalbuminemia, is crucial for optimizing patient care and resource allocation. Serum albumin, owing to its role as a major plasma protein and its sensitivity to nutritional status, serves as a superior prognostic indicator compared to anthropometric measures [7]. Protein-energy malnutrition, characterized by increased protein or energy requirements coupled with inadequate dietary intake, depletes visceral protein stores, including albumin. This cascade of events leads to impaired organ function, compromised immune response, and delayed wound healing. In the context of pregnancy, wound healing presents unique challenges due to hormonal fluctuations and physiological adaptations. Pregnancy is associated with elevated estrogen levels, which can negatively impact wound-healing processes. Estrogen receptors α and β , found in various tissues, mediate estrogen's effects on wound healing, influencing stages such as hemostasis, inflammation, proliferation, and remodeling [8]. These hormonal changes and the complex interplay of genetic, nutritional, and lifestyle factors contribute to variations in wound healing outcomes among pregnant women.

The normal wound healing process involves three overlapping stages: hemostasis/inflammation, proliferation, and remodeling [9]. During the inflammatory phase, local activation of the coagulation and inflammatory systems initiates the cascade of events leading to wound closure. Estrogen signaling plays a significant role in modulating coagulation factors, thereby influencing hemostasis and inflammation. In the proliferation phase, fibroblasts, keratinocytes, and endothelial cells contribute to tissue repair through the formation of granulation tissue and synthesis of extracellular matrix components [10]. Estrogen's effects on cellular proliferation and extracellular matrix synthesis have implications for wound healing outcomes during pregnancy. The remodeling phase marks the maturation of the wound, characterized by the conversion of immature collagen into mature collagen fibers and the gradual resolution of inflammation.

Estrogen's influence on collagen metabolism and tissue remodeling processes has been elucidated in various studies, highlighting its role in scar formation and tissue integrity [11]. Understanding the molecular mechanisms underlying estrogen's effects on wound healing is essential for developing targeted interventions to improve outcomes in pregnant individuals undergoing surgical procedures.

Given the multifaceted nature of wound healing and the complex interplay of factors influencing surgical outcomes, a comprehensive approach to preoperative assessment is warranted. By evaluating serum albumin levels as a predictor of wound healing outcomes in caesarean section, this study aims to contribute to optimizing preoperative risk stratification strategies and enhancing post-operative care protocols. Through an understanding of the intricate mechanisms underlying wound healing in the context of pregnancy and malnutrition, this research seeks to improve patient outcomes and reduce the burden of post-operative complications.

OBJECTIVES

General objective

- To evaluate the association of serum albumin level with wound healing after caesarean section.

Specific objectives

- To determine preoperative serum albumin level in patients planned for caesarean section.
- To observe the proportion of wound infection and delayed wound healing after caesarean section.
- To compare proportion of wound infection and delayed wound healing after caesarean section between women who had hypoalbuminemia and who had normal albumin level before the operation.

MATERIAL AND METHODS

Study Design

This study utilized a prospective cohort design to investigate the relationship between serum albumin levels and wound healing outcomes following caesarean section. The study of 100 pregnant women was conducted at the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka, over one year from January 2020 to December 2020.

Inclusion Criteria

Patients planned for caesarean section in the department of Obstetrics and Gynaecology, Dhaka Medical College hospital, Dhaka.

Exclusion Criteria

Patients who had jaundice, severe anaemia (Hb <7 g/dl), chronic renal disease, diabetes mellitus,

hypertensive disorders in pregnancy (HDP), thyroid disorders, premature rupture of membrane and patients on steroids or chemotherapy.

Data Collection

Data collection involved several steps. First, pregnant women scheduled for caesarean section were identified as potential participants. After proper history taking a thorough general, systemic and obstetric examination was done. Serum albumin level of each subject was estimated on the day of admission before operation and on 3rd post-operative days, in the Department of Laboratory Medicine, Dhaka Medical College Hospital. The patients were classified into two groups in relation to level of preoperative serum albumin. Group-I (hypoalbuminemic) had preoperative serum albumin level < 3.5 g/dl & group-II (normal albuminemic) had preoperative serum albumin level 3.5 g/dl or more. Nineteen patients were in group-I and 81 in group-II. Each patient was followed-up up to 60 days after operation specially on 3rd, 7th, 15th, 30th POD and 2 months after surgery for identification of any surgical site infection and sign of delayed wound healing. There was no drop out case. All the data was recorded in a pre-designed and pre-tested data collection sheet properly. Additionally, demographic information, medical history, and relevant clinical variables were collected prospectively from patient records and through direct participant interviews. Surgical outcomes, including post-operative wound infection and other complications, were carefully monitored and documented during the follow-up period. The data collected were then subjected to statistical analyses, including chi-square tests, t-tests, and multivariate logistic regression, to examine the

association between serum albumin levels and wound healing outcomes after caesarean section. Ethical considerations were strictly adhered to throughout the study, and informed consent was obtained from all participants before enrollment.

Data Analysis

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 26.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean \pm standard deviation and categorical variables as frequencies and percentages n (%). Chi-square test was used to analyze the categorical variables and shown in the cross tabulation. The mean difference between groups was analyzed using the t-test for continuous variables. P values < 0.05 were considered as statistically significant. To recognize independent predictors of post-operative wound infection, variables known by univariate analysis was analyzed further by multivariate logistic regression analysis.

Ethical Considerations

Ethical approval was prioritized throughout the study. Approval was obtained from the Research Review Committee and the Ethical Committee of Dhaka Medical College, Dhaka, before commencement. Informed consent was obtained from all enrolled patients after explaining the study's nature, potential risks, and benefits. Additionally, permissions were obtained from the department and relevant institutions to ensure compliance with ethical standards and guidelines throughout the study period.

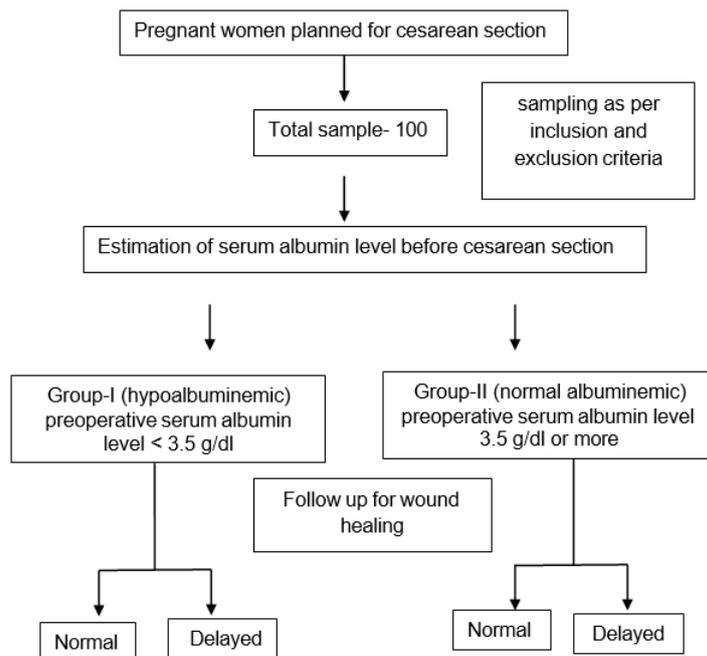


Figure 1: Workflow chart

RESULTS

Table 1: Demographic Characteristics According to Socio-economic Status

Variable	Group I (n=19)	Group II (n=81)
Age (Years)		
≤20	3 (15.8%)	13 (16.0%)
21-30	13 (68.4%)	60 (74.1%)
31-40	3 (15.8%)	8 (9.9%)
Lived in		
Rural	1 (5.3%)	5 (6.2%)
Urban	18 (94.7%)	76 (93.8%)
Education		
Illiterate	9 (47.4%)	23 (28.4%)
Primary	7 (36.8%)	31 (38.3%)
Secondary	3 (15.8%)	10 (12.3%)
Higher Secondary	0 (0.0%)	8 (9.9%)
Graduate	0 (0.0%)	9 (11.1%)
Occupation		
Housewife	19 (100.0%)	70 (86.4%)
Service	0 (0.0%)	6 (7.4%)
Student	0 (0.0%)	5 (6.2%)

The table compares demographic and socio-economic variables between Group-I (n=19) and Group-II (n=81) participants. Group I predominantly comprises individuals aged 21-30 (68.4%), residing in urban areas (94.7%), with primary education (36.8%), and occupied as housewives (100%). Group-II similarly features a

majority aged 21-30 (74.1%), urban residents (93.8%), with primary education (38.3%), and mostly housewives (86.4%). Variations between groups suggest potential influences on study outcomes warranting consideration during analysis.

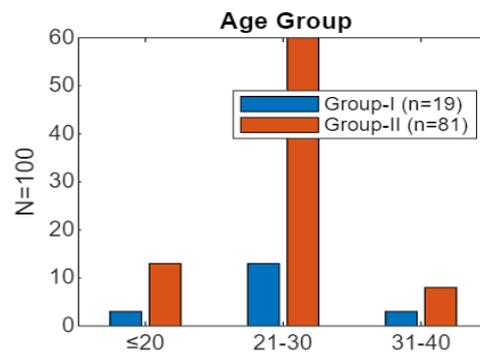


Figure 2: Distribution of the study patients by age (N=100)

The distribution of the study patients by age. It was observed that most of the patients in both groups (I and II) belonged to age (21-30) years.

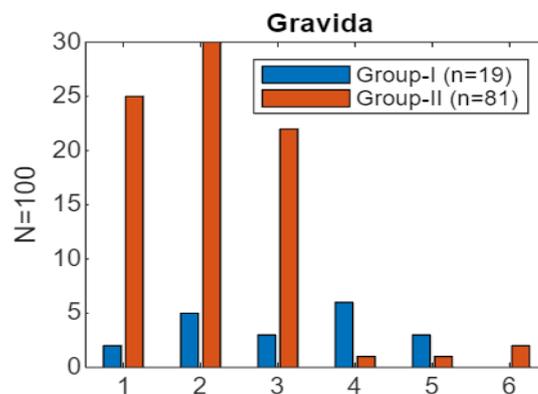


Figure 3: Distribution of the study patients by gravida (N=100)

The distribution of the study patients by gravida. Multiparity (three or four births) was mostly seen in group I, and low parity (one or two births) in group II.

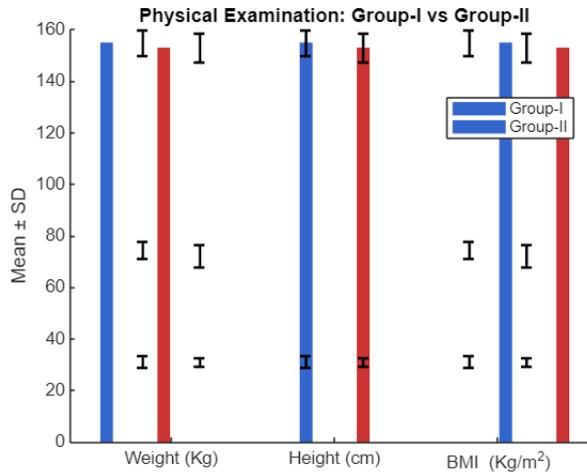


Figure 4: Distribution of the study patients by physical examination (N=100)

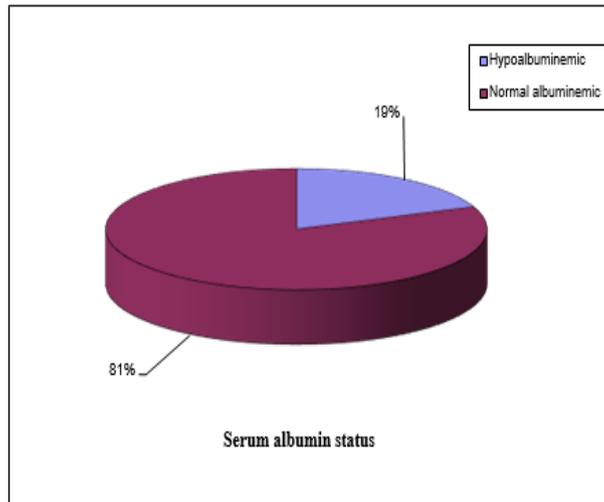


Figure 5: Pie-chart showing the distribution of the study patients by pre-operative serum albumin status

Table 2: Distribution of the study patients by serum albumin (N=100)

Serum Albumin (g/dl)	Group-I (n=19)	Group II (n=81)	p-value
Preoperative	2.57 ± 0.35	4.2 ± 0.4	0.001s
At 3 rd POD	2.4 ± 0.31	4.0 ± 0.4	0.001s

The mean preoperative serum albumin was 2.57±0.35 gm/dl in group I and 4.2±0.4 g/dl in group II. The mean serum albumin on 3rd POD was 2.4±0.31

gm/dl in group I and 4.0±0.4 gm/dl in group II. The difference was statistically significant (p<0.05) between two groups.

Table 3: Distribution of the study patients by wound healing status (N=100)

Wound Healing Status	Group-I (n=19)	Group II (n=81)	OR	95% CI	p-value
Delayed	9 (47.4%)	7 (8.6%)	9.51	2.52 – 37.32	0.001s
Normal	10 (52.6%)	74 (91.4%)			

The study patients were distributed by wound healing status. It was observed that almost half (47.4%) patients had wound infection and delayed wound healing in group I and out of 81, only 7 patients (8.6%) had

wound infection and delayed wound healing in group II. The difference was statistically significant (p<0.05) with OR=9.51 having 95% CI 2.52-37.32%.

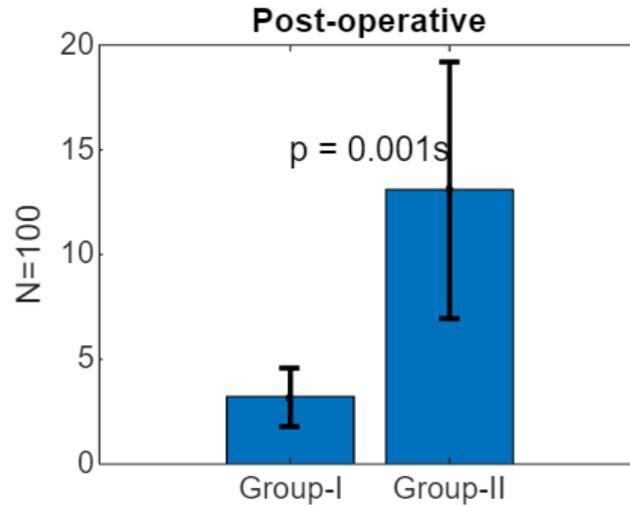


Figure 6: Distribution of the study patients by number of post-operative days in the hospital

Distribution of the study patients by number of post-operative days in hospital. The number of post-operative days in hospital was 13.11 ± 6.14 in group I and

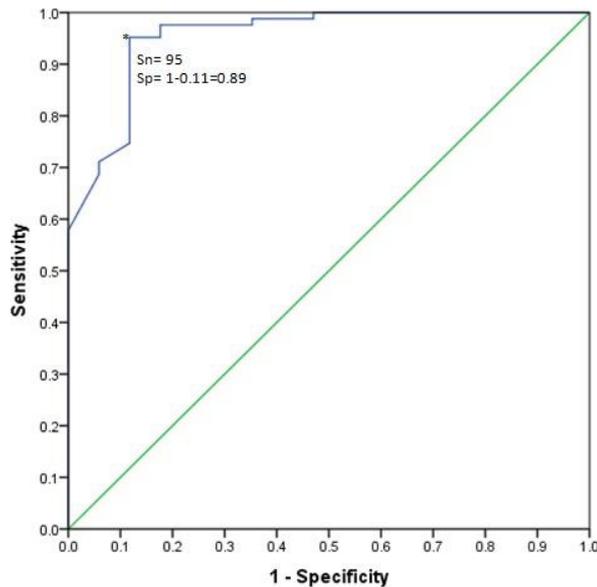
3.22 ± 1.41 in group II. The difference was statistically significant ($p < 0.05$) between two groups.

Table 4: Effect of Independent Variables on Delayed Wound Healing (N=100)

Variable	Regression Coefficient (B)	S.E.)	(df)	p-value	(OR)	95% CI Lower	95% CI Upper
Serum Albumin (g/dl)	2.032	0.606	1	0.001s	7.626	2.324	25.020
Age (Years)	-0.172	0.079	1	0.290ns	0.842	0.722	0.982
Gravida	0.029	0.293	1	0.920ns	1.030	0.580	1.827
BMI (Kg/m ²)	-0.141	0.178	1	0.428ns	0.869	0.613	1.230
Constant	1.883	6.128	1	0.759ns	6.576		

The table shows multivariate logistic regression analysis showing the effect of independent variables on delayed wound healing. A subject with pre-operative serum albumin level (< 3.5 g/dl) had 7.626 (95.0% C.I.

2.324 to 25.02) times increased risk of wound infection and delayed wound healing after surgery. Other variables were not significantly associated with delayed wound healing.



Diagonal segments are produced by ties.

Figure 7: Receiver-operator characteristic (ROC) curve of pre-operative serum albumin for prediction of wound infection and delayed wound healing

The area (0.954) under the receiver-operator characteristic (ROC) curves for the wound infection and delayed wound healing is depicted in the above figure. Based on the receiver-operator characteristic (ROC) curves using pre-operative serum albumin value of the patients underwent caesarean section having delayed wound healing with the best combination of sensitivity and specificity for wound infection and delayed wound healing after surgery, which gave a pre-operative serum albumin cut off value of <3.35 g/dl with 95.0% sensitivity and 89.0% specificity as the value and for prediction of delayed wound healing after surgery.

DISCUSSION

In this study, 81(81%) patients were normal albuminemic (3.5 g/dl) and 19(19%) patients were hypoalbuminemic (<3.5 g/dl). In a study, Sullivan *et al.* reported that patients with hypoalbuminemia were more likely to have a major wound complication (OR 2.9 95% CI 1.1-7.3, $p=0.02$) [3], even after adjusting for BMI, age, preoperative hematocrit, and diabetes which correlates with our study. They concluded that low preoperative albumin is associated with major post-operative wound complications in women undergoing surgery. Therefore, when obtaining informed consent, patients with low albumin should be counseled regarding higher risks of post-operative wound complications. It also stated that hypoalbuminemia may prolong maternal hospitalization, increase healthcare costs, and lead to other socio-economic implications. Studies have shown that hypoalbuminemia contributes negatively to the process of wound healing and the severity of disease [12]. It is linked to mortality and post-operative complications such as surgical site infections (SSI) and reoperations, together with longer hospital stays.

In this study, regarding the distribution of the study patients by age, it was observed that 68.4% of patients belonged to age 21-30 years in group I and 74.1% in group II. Following our study, we observed that the number of patients in the 21-30 years group was highest among their study subjects [13]. In prospective research, reported that the age variable is a protective factor with OR = 0.62; 95% CI 0.43-0.89. In this study, 94.7% of patients came from urban areas in Group I and 93.8% in Group II. In this context, it is discussed that in humans, genetic expression has been demonstrated to vary significantly across urban, rural, and pastoral social environments, but the extent to which social environment affects gene behavior is largely unknown. The emergence of populational genomics and the opportunity to analyze large amounts of human genomic data provide opportunities to analyze and identify the genetic making of social traits [14].

In this study, more patients are multigravida in group I than in group II. Researchers reported that most of the multiparity categories showed surgical site infection and delay in wound healing [15]. The bivariate analysis results statistically and clinically correlate with

the incidence of post-caesarean section surgical wound infection ($p<0.05$). Patients in the multiparous group were 255 (81.9%), among them surgical wound infection was found in case of 149 patients (47.9%). The results of this analysis show that clinically multiparity is a risk factor for wound complications such as surgical site infections resulting delay of wound healing compared to primiparas. In this study, the mean body weight was 74.53 ± 3.37 kg in group I and 72.21 ± 4.44 kg in group II. The mean height was 154.97 ± 5.0 cm in group I and 152.93 ± 5.6 cm in group II. The mean BMI was 31.1 ± 2.14 kg/m² in group I and 30.91 ± 1.81 kg/m² in group II. The two groups' weight differences were statistically significant ($p<0.05$). In consistent with our study, found that primary emergency caesarean section rates were higher for obese women compared with women with a healthy BMI (27% versus 19%, $P < 0.04$), with the majority of the deliveries occurring during the first stage of labour for failure to progress in labour and fetal distress [16]. Reported that obesity is a major risk factor for pregnancy complications and carries huge social and financial costs.

There is a clear need to establish national and regional prevalence rates of maternal obesity so that maternity services can be appropriately organized to ensure suitable care for 'at-risk' women. The results of our study are similar to those of British hospitals, where out of 4,107 studied patients, there were 394 obese patients with BMI (body mass index) > 35 kg / m², detected SSI of about 9.6%. The results of this study are similar to those of the World Health Organization (WHO) survey, which says that the incidence of SSI is 5% -34% [17]. In this study, the mean preoperative serum albumin was 2.57 ± 0.35 gm/dl in group I and 4.2 ± 0.4 gm/dl in group II. The mean serum albumin on 3rd POD was 2.4 ± 0.31 gm/dl in group I and 4.0 ± 0.4 gm/dl in group II. The difference between the two groups was statistically significant ($p<0.05$).

The majority of patients with hypoalbuminemia suffered wound-related problems as compared to those with normal albumin levels [7,12], which is consistent with our data. Among 43 patients, 38 showed wound complications with serum albumin levels of less than 3.5 g/dl [18]. They emphasized that hypoalbuminemia is a risk factor for mortality and post-operative complications. In this context, reported participants with more than 2 h of operative time had a 73% higher chance of an adverse surgical outcome compared to those with less operative time. (OR: 1.73; 95% CI: 0.35 8.45); however, participants with a higher percentage change in pre-and post-operative albumin level (delta albumin) had a significant chance of developing adverse outcomes compared to those with low delta albumin (OR: 6.68; 95% CI: 1.59, 28.09). They also recommended that early perioperative decreases in serum albumin levels may be a good, simple, and cost-effective tool to predict adverse outcomes in major abdominal surgeries. Stated that a serum albumin decrease ≥ 10 g/L on POD 1 was

independently associated with a threefold increased risk for post-operative complication [19].

Out of 19 patients, 9 (47.4%) developed post caesarean wound infection in group I, and out of 81 patients, 7(8.6%) developed post caesarean wound infection in group II. The difference was statistically significant ($p<0.05$), with OR=9.51 having 95% CI (2.52-37.32). Reported that hypoalbuminemia is an independent risk factor for the development of surgical site infection (SSI) [20]. The magnitude of SSI was lower when compared with a study done in Nepal [21] and India [22] where 12.6% and 13% of cesarean deliveries ended up with SSI respectively. These discrepancies might be tailored to differences in sample size and the difference in duration between the studies. In this study, the number of post-operative days in hospital was 13.11 ± 6.14 in group I and 3.22 ± 1.41 in group II. The difference was statistically significant ($p<0.05$) between two groups. Reported that the mean number of days until the wound was dry was 3.79 for the hypertensive group and 2.03 for the normotensive group [23]. Hypertensive patients required more days for their wounds to dry than normotensive patients (odds ratio = 1.65, $p<0.05$).

Post-cesarean wound complications may increase maternal morbidity and mortality. In addition, wound infections, which also contribute to delay healing, can be frustrating for the mother trying to recover from the procedure and at the same time taking care of the newborn. It may prolong maternal hospitalization, increase health care costs, and lead to other socio-economic implications. Hypoalbuminemia is a risk factor for mortality and post-operative complications. Therefore, nutritional control has been an important focus of perioperative management [24]. Reported that among 43 patients, 38 patients showed wound complications that also had serum albumin levels were less than 3.5 g/dl. Bhamidipati *et al*. [25] emphasized that hypoalbuminemia is a risk factor for mortality and postoperative complications.

In this study, subjects with serum albumin (<3.5) had 7.626 (95.0% C.I. 2.324 to 25.02) times increased risk of delayed wound healing and wound infection after surgery. Other variables were not significantly associated with delayed wound healing and post-operative wound infection after surgery. Reported that out of 83 patients with hypoalbuminemia, 33 patients developed wound-related complications, and four patients with normal albumin levels developed wound-related complications [26]. The p-value is 0.0003. The various complications were wound infection in 24 patients (72.7%), wound dehiscence in 9 cases (27.28%), anastomotic leak in 5 cases (15.15%) in hypoalbuminemic group. Whereas 3 patients developed wound infection (75%) and one patient developed anastomotic leak (25%) in the other group. Their study showed similar results ($P < 0.005$), patients with serum albumin less than 3 g/dl had more postoperative

complications [27]. In this present study, it was observed that two third 66.67% of patients developed wound infection on 3rd POD in group I and 57.14% in group II.

In this study, Receiver operator characteristics (ROC) were constructed using the serum albumin value of the patients who underwent surgery having post-operative wound infection with the best combination of sensitivity and specificity for wound infection and delayed wound healing after surgery, which gave serum albumin cut off value of <3.35 with 95.0% sensitivity and 89.0% specificity as the value and for prediction of delayed wound healing and wound infection after surgery.

CONCLUSION

Hypoalbuminemia is an independent risk factor for the delay in wound healing. Low serum albumin level is associated well with the development of post caesarean surgical site infection, and delay in wound healing contributed to prolonged hospital stay. Hypoalbuminemia is a good and simple predictor of wound infection and delay in wound healing after caesarean section.

Recommendations

Further multi-center case-control studies are very much needed. The recommendations provide an up-to-date, evidence-based approach to the full range of issues related to the wound complications after caesarean section. Further studies may be conducted using prospective methods to look at other risk factors related to nursing.

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Abbreviations

POD: Postoperative Day
 ROC: Receiver-Operator Characteristic
 BMI: Body Mass Index
 CI: Confidence Interval
 OR: Odds Ratio
 SSI: Surgical Site Infection
 Hb: Hemoglobin
 HDP: Hypertensive Disorders in Pregnancy
 g/dl: grams per deciliter

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