Factors predicting length of stay in patients hospitalized for acute parotitis

Avinoam Markovich,[1] Ohad Ronen [1,2]

[1]Azrieli Faculty of Medicine Bar-Ilan University, Safed, Israel
[2]Otolaryngology - Head and Neck Surgery, Galilee Medical Center, Nahariya, Israel

Correspondence to
Dr Ohad Ronen, Galilee Medical Center, Nahariya 2210001, Israel; ohadr@gmc.gov.il

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ABSTRACT

Acute suppurative parotitis (ASP) is an acute infection of the parotid gland that necessitates hospitalization in some patients. The aim of this study was to evaluate clinical laboratory values including hydration, nutritional status, inflammatory markers and age, and to compare them with duration of hospitalization of patients with ASP. This is a retrospective chart review in a tertiary academic center. We investigated the factors affecting length of hospitalization in patients admitted to Galilee Medical Center with a diagnosis of ASP between 2010 and 2018. Of the 60 patients with ASP included in the study, 24 were male. The average age of patients was 60, ranging from 18 to 99. We found statistically significant correlations between length of hospitalization and patient age (r=0.3), C reactive protein (r=0.3), white cell count (WCC) at presentation (r=0.3), blood urea nitrogen to creatinine ratio (BUN:Cr) (r=0.2), and platelet levels at discharge (r=0.4). Examination of these factors on multivariate analysis found hospitalization duration was exclusively affected by patients' level of dehydration as represented by BUN:Cr. Patient age, WCC levels at presentation, and platelet levels were not found to be statistically significant. Treatment and interventions should be planned accordingly.

Significance of this study

What is already known about this subject?
- Acute suppurative parotitis (ASP) is an acute infection of the parotid gland that necessitates hospitalization in some patients.
- Length of hospitalization is unknown and may be related to nutritional status, inflammatory markers, dehydration status, and age.

What are the new findings?
- We found significant correlation between dehydration status and longer hospitalization, regardless of age and inflammation markers, in patients with ASP.

How might these results change the focus of research or clinical practice?
- Dehydration status plays the most significant and crucial role in length of hospitalization of patients with ASP.
- Treatment and interventions should be planned accordingly.

INTRODUCTION

Acute suppurative parotitis (ASP) is defined as an inflammatory process of one or both parotid glands. The first clinical description of ASP is attributed to French anatomist Cruveilhier in 1836. Parotitis most commonly occurs in elderly men with poor oral hygiene and poor oral intake, resulting in decreased saliva production.[1] Other known factors that contribute to risk of ASP include dehydration,[2] starvation and malnutrition,[3 4] debilitation, advanced age, immunosuppression, oral neoplasm, and known ductal obstruction.[5] Before the modern antibiotic era, ASP carried a mortality rate of 50%, making it a serious postoperative complication.[5 6]

ASP diagnosis is based on presentation and clinical examination and by isolating causative organisms from the gland.[7] Laboratory tests are non-specific and include elevated white cell count with predominance of neutrophils.[8] Serum amylase levels are usually normal, but may be elevated. Erythrocyte sedimentation rate is usually increased. Treatment of ASP is based on treating the underlying medical condition, hydration, and antibiotic therapy based on culture and sensitivity, and surgical drainage if conservative medical therapy fails.

Aim of the study

Our aim was to examine clinical laboratory values representing patient hydration, nutritional status, inflammatory markers and age in order to find a correlation with duration of hospitalization in patients diagnosed with ASP.

Written informed consent to participate was waived.

MATERIALS AND METHODS

Study design, site and subjects

This was an analytic retrospective study. Data were extracted retrospectively from clinical charts of patients over the age of 18 diagnosed with parotitis at Galilee Medical Center between the years 2010 and 2018. Exclusion criteria included patients diagnosed with ASP but not hospitalized for a period of more than 24 hours.

Follow-up was limited to patients in their hospitalization period.

Variables

Nutritional and hydration status were determined by several measures at the time of diagnosis. Nutritional status was assessed using body mass index and serum albumin levels. Patient hydration status was assessed using serum sodium levels, blood urea nitrogen to creatinine ratio (BUN:Cr), and serum hematocrit (HCT) levels. Clinical features were determined by several measures that represent immunity response and, as a result, severity of the disease, at the time of diagnosis and again before discharge from the hospital.

The clinical features represented by an acute inflammatory response were assessed using white cell count (WCC) with differential, and in particular granulocytes percentage, platelet (PLT) count, ferritin levels, fibrinogen levels, and C reactive protein (CRP) levels. Outcomes of the disease were determined by several endpoints[9]: death, number of hospitalization days, and admission to the intensive care unit (ICU). Inflammatory response and clinical outcome were considered as dependent variables. Nutrition and hydration status were considered as independent variables. Additional variables collected were age and gender, as well as comorbidities associated with ASP, such as non-insulin dependant diabetes mellitus (NIDDM), hypertension, and other chronic diseases.

Statistical analysis

Quantitative data were described by mean and SD, median and range. Qualitative data were described by frequencies, percentages, and OR. Correlation between quantity variables (such as hydration status and inflammatory measures) was examined using Pearson's correlation coefficient test or Spearman's correlation coefficient test, linear regression; the choice between these tests was according to sample size, distribution of variables, and the linear regression's preliminary assumptions. Correlation between independent variables (mainly nutrition and hydration status) and qualitative dependent variables (death, ICU hospitalization and so on) was examined with the following tests: quantitative data were compared among subgroups using analysis of variance, independent sample t-test or Wilcoxon rank-sum test. The choice among the tests was according to the number of groups compared, sample size and data distribution in the compared subgroups. Qualitative data were compared using χ^2 test, Fisher's exact test, Cramér's measure, phi measure, and a univariate and multivariate logistic regression model, adjusted to age, gender and comorbidities. A p value less than 5% was considered a significant result.

RESULTS

Overall, 60 patients were included in the study, including 24 men and 36 women. The mean age of male patients was 58.4±20.2 years and of female patients was 60.6±19.3 years (p=0.676). The mean length of hospital stay was 6.2±7.1 days for men and 5.0±4.0 days for women (p=0.707).

Most ASP cases (97%) were a consequence of another associated pathology and not a solitary disease. All patients were treated with systemic antibiotics based on culture and sensitivity tests of pus secreted from the Stensen's duct, as well as salivary secretion agents and hydration.

Table 1 Difference analysis between gender (male and female) with respect to age, length of hospital stay and CRP levels

Measure	Gender	n	Mean	SD	P value
Age	Male	24	58.4	20.2	0.676*
	Female	36	60.6	19.3	
Length of hospital stay	Male	24	6.2	7.1	0.707†
	Female	36	5	7.1	
CRP on admission	Male	17	52.4	52.3	0.420†
	Female	25	71.7	81.1	
CRP at discharge	Male	5	43.6	40.5	0.429†
	Female	6	86.7	66.9	
BUN:Cr on admission	Male	23	17.3	6.2	0.183*
	Female	34	20.7	10.6	

While comparing between men and women with respect to age, length of hospital stay and CRP levels, we did not find any statistically significant difference between men and women in our sample.
*Using t-test.
†Using Mann-Whitney.
BUN:Cr, blood urea nitrogen to creatinine ratio; CRP, C reactive protein.

In all but a few patients, we used CRP levels to assess the inflammatory condition, as opposed to procalcitonin as an inflammatory marker for monitoring ASP. CRP level on admission was 52.4 mg%±54.3 for men and 71.7 mg%±81.1 for women (p=0.420). CRP level at discharge was 43.6 mg%±40.4 for men and 86.7 mg%±66.9 for women (p=0.429). A summary of the results is shown in table 1. We examined whether a correlation existed between length of hospital stay (in days) and various parameters: patient age, WCC levels (WCC1=admission values, WCC2=discharge values), CRP measures (CRP1=on admission, CRP2=at discharge), PLT levels (PLT1=admission values, PLT2=discharge values) and HCT levels (HCT1=admission values, HCT2=discharge values). Hydration status was calculated as the ratio between blood urea nitrogen and creatinine (BUN:Cr). As the length of hospital stay is not normally distributed, these correlations were examined using Spearman's correlation coefficient.

A summary of the results is shown in table 2. We found a statistically significant correlation between length of hospital stay and patient age, CRP, WCC levels, BUN:Cr on admission, and PLT levels at discharge.

Based on a sample of 60 patients, a statistically significant and positive correlation of medium power (r=0.3) exists between length of hospital stay and patient age (figure 1A). Older patients tend to have longer hospital stay.

In addition, based on a sample of 42 patients, a statistically significant and positive correlation of medium power (r=0.3) exists between length of hospital stay and patients' CRP level on admission (figure 1B). Patients with a higher value of CRP tend to have longer hospital stay.

Based on a sample of 60 patients, a statistically significant and positive correlation of medium power (r=0.3) exists between length of hospital stay and patients' WCC levels on admission (figure 1C). Patients with higher value of WCC tend to have longer hospital stay.

Moreover, based on a sample of 57 patients, a statistically significant and positive correlation of medium to strong power (r=0.211) exists between length of hospital stay and patients' dehydration status represented as BUN:Cr on

Table 2 Correlation analysis between length of hospital stay (in days) and various measures

Measure	n	Correlation coefficient (effect size)	P value
Age	60	r=0.307	0.017
PLT on admission	60	r=0.205	0.116
PLT at discharge	28	r=0.411	0.030
CRP on admission	42	r=0.315	0.042
CRP at discharge	11	r=0.188	0.581
WCC on admission	60	r=0.265	0.040
WCC at discharge	28	r=0.241	0.217
HCT on admission	60	r=−0.126	0.336
HCT at discharge	28	r=−0.164	0.404
BUN:Cr on admission	57	r=0.211	0.007

A significant difference was found between length of hospital stay and patient age, PLT levels at discharge, CRP and WCC levels on admission, and BUN:Cr on admission. No statistical correlation was found for the other parameters examined in the sample. Analysis was done using Spearman's correlation coefficient.
BUN:Cr, blood urea nitrogen to creatinine ratio; CRP, C reactive protein; HCT, hematocrit; PLT, platelet; WCC, white cell count.

admission (figure 1D). Patients with more severe dehydration tend to have longer hospital stay.

Finally, based on a sample of 28 patients, a statistically significant and positive correlation of medium to strong power (r=0.4) exists between length of hospital stay and patients' PLT level at discharge. Patients with a higher value of PLT at discharge tend to have longer hospital stay.

Table 3 Multivariable analysis of CRP levels, BUN:Cr ratio and patient age with respect to length of hospital stay

Variable	Coefficient	SE	Test statistics	P value
Age	−0.054	0.055	−0.981	0.333
BUN:Cr	0.301	0.117	2.568	0.014
CRP1	0.022	0.012	1.841	0.073

On multivariate analysis, both age and CRP level on admission were deemed non-significant when BUN:Cr is taken into consideration. This implies that the main contribution to length of hospital stay comes from the severity of the patient's dehydration.
BUN:Cr, blood urea nitrogen to creatinine ratio; CRP, C reactive protein.

We conducted a multivariable analysis, including all features that had statistically significant correlation with length of hospital stay, in order to examine a potential confounder between these independent variables and length of hospital stay. As most of these features were correlated with each other, we could not examine all of them simultaneously. Hence, it was decided to include patient age, CRP1 level and BUN:Cr ratio. The results of both models are summarized in table 3. As can be seen, BUN:Cr is the only measure that seems to affect the length of hospital stay. Patients' dehydration status, CRP1 level, and age did not have any significant influence on length of hospital stay.

From the multivariate analysis, we can see that even when corrected for patient age and CRP measure, the BUN:Cr ratio retained a statistically significant effect on length of hospitalization. For each unit of BUN:Cr, the length of admission increased on average by 0.301 days, with all

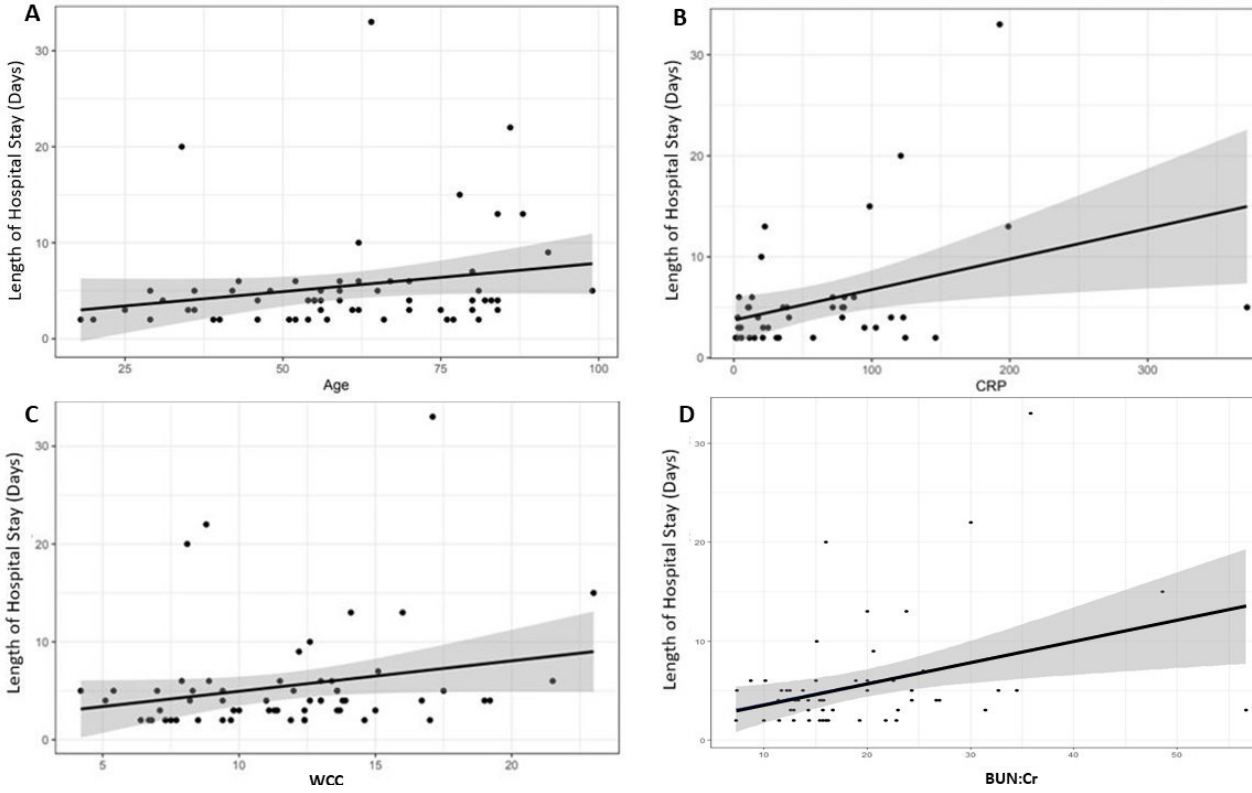

Figure 1 Length of hospital stay (in days) in relation to (A) patient age (in years), (B) C reactive protein (CRP) level (mg%), (C) white blood cell (WBC) level ($\times 10^9$/L), and (D) blood urea nitrogen to creatinine ratio (BUN:Cr).

other variables held constant. Our results imply that the main contribution to length of hospitalization stems from the severity of the patient's dehydration.

Furthermore, we investigated other possible risk factors such as diabetes mellitus, hypertension, and other chronic conditions, as these conditions could worsen the acute inflammation and increase the length of hospital stay. About one-third (31.4% and 37.1%) of the cohort had either NIDDM or hypertension, respectively, and 60.0% had some chronic illness including heart conditions. Surprisingly, when we compared the length of stay based on the presence of each chronic condition, there was no statistical significance.

DISCUSSION

Summary

Our study examined whether baseline hydration, nutritional status, laboratory inflammatory markers, and age correlate with clinical features and outcomes of hospitalized patients diagnosed with ASP. We found statistically significant correlations between length of hospitalization in relation to several parameters: older age, higher value of CRP, higher WCC value, higher BUN:Cr, and higher PLT count, all tend to lead to longer hospital stay.

We did not find any correlation between men and women with respect to age, length of hospital stay and CRP levels. In order to perform such a comparison, several other confounding variables should be examined, such as comorbidities (hypertension, ischemic heart disease, diabetes mellitus and so on) and lifestyle habits including dietary habits, cigarette smoking and alcohol consumption.[10]

Hydration status represented by BUN:Cr was found to be positively correlated with length of stay in our cohort. While this is a known risk factor for developing acute parotitis,[2 4] it has not been described in the literature as correlating with length of stay, and this finding might further emphasize the importance of rehydration in the treatment of such patients.

In a multivariate analysis, we found that the length of hospital stay was affected only by the dehydration status represented by BUN:Cr and not by inflammation severity or age. Dehydration is the hallmark of acute parotitis infection. It is a major contributing factor to the development of the disease, serving as the main prognostic factor for prolonged hospital stay, as demonstrated in this study. Lastly, rehydration is one of the main treatment goals in these patients.

Comparison with existing literature

The results of our study are similar to those of a survey conducted by the Centers for Disease Control and Prevention (CDC) published in 2007: 'National hospital discharge survey'.[11] According to the CDC survey, older patients (65 years and older) represent almost half of hospitalized adults and tend to be hospitalized more often in relation to the rest of the population. Infections such as ASP are the second leading diagnosis for admission among older patients. With advanced age, patients tend to have more comorbid chronic illnesses and disabilities, making them more vulnerable to adverse events during hospitalization, including nosocomial complications and adverse drug reactions.[12]

CRP is a well-studied, acute-phase protein that is involved in multiple stages of inflammation. CRP has both proinflammatory and anti-inflammatory actions. Elevation of plasma CRP concentration occurs in association with acute and chronic inflammation due to a range of causes, including both infectious diseases and non-infectious inflammatory disorders.[13] In this study we found that patients with higher CRP values at presentation tend to have longer hospital stays. Previous studies support our findings. In one study involving patients with exacerbated interstitial lung disease, high CRP levels (≥ 0.5 mg/dL) and advanced age predicted longer hospital stay.[14] In another study, it was found that in patients with community-acquired pneumonia, consecutive measures of CRP correlated with length of hospital stay, and in particular a greater decrease in CRP level between the first and second day of hospitalization was associated with shorter hospital stay and rapid improvement.[15]

A study involving patients in general wards found a correlation between early-onset leukocytosis and mortality rates among hospitalized patients.[16] That study identified leukocytosis at early stages of admission as an alarming sign of mortality among patients admitted to general hospital wards. Leukocytosis on admission was more frequent among patients who died of their disease compared with survivors.

Patients with higher PLT values at discharge tended to have had longer hospital stay. PLTs have been increasingly recognized as an important component of innate and adaptive immunity. PLT response in antimicrobial host defense is similar, in many ways, to the leukocyte response: both cell types contain antimicrobial peptides that act against a broad range of pathogens.[17] A possible explanation for this finding is that elevated PLT level (but not thrombocytosis; PLT $>450 \times 10^9$/L) may reflect an acute systemic inflammatory response.

In the past, postsurgical ASP was a relatively common complication after major surgeries; however, its incidence is decreasing.[18] Our cohort included patients with dehydration from causes other than surgery, although the pathogenesis is the same. Although other comorbidities might contribute to the development of ASP, we did not have these data in our study.

Strengths and limitations

Because of the retrospective nature of our study, some parameters such as nutritional status and CRP at discharge were not available for many patients in our cohort. Lack of data was initially defined as part of the potential bias for this research. We relied on correct coding of ASP and could not validate the diagnosis. In addition, the attempt to predict disease outcome as expressed by hospitalization days, ICU admissions, and mortality was not accomplished because most patients (58 of 60) were discharged from the hospital after several days. According to our data, only one patient was admitted to the ICU and another one died. In order to measure disease outcomes more accurately, a study with a larger sample should be conducted. For the same reason we were not able to create a survival model, as we had hoped to do.

Implications for research and/or practice

Dehydration on admission rather than older age and inflammation severity serves as a predictor of prolonged hospitalization. Thus, treatment protocols should take this into consideration.

We are of the belief that these parameters might influence the disease course. In order to find such a correlation, a prospective study, where data are collected throughout the hospitalization period, should be conducted in the future.

In conclusion, there is a relationship between dehydration and longer duration of hospitalization, regardless of patient age or inflammation severity. A future prospective study should examine the effect of nutritional status on the disease course. Additional parameters such as comorbidities, lifestyle and dietary habits should be investigated.

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Competing interests None declared.

Patient consent for publication Not required.

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Data availability statement Data are available upon reasonable request from the Department of Otolaryngology-Head and Neck Surgery, Galilee Medical Center, Nahariya.

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ORCID iD

Ohad Ronen http://orcid.org/0000-0001-7084-0695

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