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## Original Article

# Analysis of Prognostic Factors Impacting Pediatric Acute Mastoiditis Outcomes

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**BACKGROUND:** This study aimed to investigate the outcomes of pediatric patients with acute mastoiditis while examining the role of intravenous steroid therapy, patient demographics, and serum inflammatory values as prognostic factors.

**METHODS:** This study is a single-center retrospective observational study including 73 consecutive patients treated for acute mastoiditis in the course of the 10-year study period (January 2010 to December 2019).

**RESULTS:** Data analysis showed that patients requiring surgical treatment (14%) had a 3-fold higher C-reactive protein value at admission compared to those treated conservatively ( $P < .001$ ). Receiver operating characteristic analysis revealed that a C-reactive protein cut-off of  $\geq 98.7$  had a sensitivity and specificity of 100% and 74.6%, respectively, for predicting the need for surgery (area under the curve = 0.927,  $P < .001$ ). The duration of symptoms before hospitalization was nearly 2 days shorter in male patients ( $P = .031$ ), and the use of intravenous steroid therapy significantly shortened the length of hospitalization ( $P = .023$ ), by 1.4 days on average.

**CONCLUSION:** Intravenous steroid therapy may be useful in decreasing the length of hospital stay. Mastoiditis tends to present more severely in male patients, and monitoring C-reactive protein values during treatment correlated well with the need for surgery.

**KEYWORDS:** Acute mastoiditis, acute otitis media, outcomes, steroids, prognosis

## INTRODUCTION

The mastoid is a well-aerated portion of the temporal bone, known to be involved in complications of acute otitis media (AOM).<sup>1</sup> At birth, the mastoid typically has only 1 air cell, termed the *antrum*, and by the age of 2, the extensive mastoid air cell system is well developed.<sup>2</sup> Due to the natural anatomical connections between the tympanic cavity and mastoid air-cell system via the narrow channel named aditus ad antrum, the pneumatic spaces of the mastoid are filled with fluid in virtually all cases of AOM, verified on computerized tomography (CT) imaging of the temporal bone as fluid attenuation.<sup>3</sup> Acute mastoiditis (AC) represents the most common suppurative complication of AOM, and in many cases, it might even be its first presentation.<sup>4,5</sup> Once AC is established, the infection can further progress toward numerous surrounding structures, further causing severe complications and posing a potentially fatal condition.<sup>6</sup> In fact, a recent systematic review of 42 studies including >2000 children with AC reported that intracranial complications occurred in 17% of patients.<sup>7</sup>

While surgical treatment in terms of simple mastoidectomy with ventilation tube insertion may be the most definitive treatment in AC cases, conservative treatment has shown to be efficacious and appropriate as first-line management.<sup>8</sup> Even though antibiotics represent a mainstay of AC treatment, when unaided by adjunct treatment options, complication rates of up to 8.5% are still recorded.<sup>9</sup> Systemic corticosteroids are widely used in the pediatric population for a variety of pathologies, namely rheumatologic,

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ophthalmic, gastrointestinal, respiratory, hematological, endocrinological, neurological, nephrological, and dermatological, and have proven to be safe for short-term treatments.<sup>10,11</sup>

Intravenous (IV) steroids in AC cases have been reported as a helpful adjunct to antibiotic treatment; however, the managing protocol currently varies from center to center and has yet to be widely established.<sup>4,9</sup>

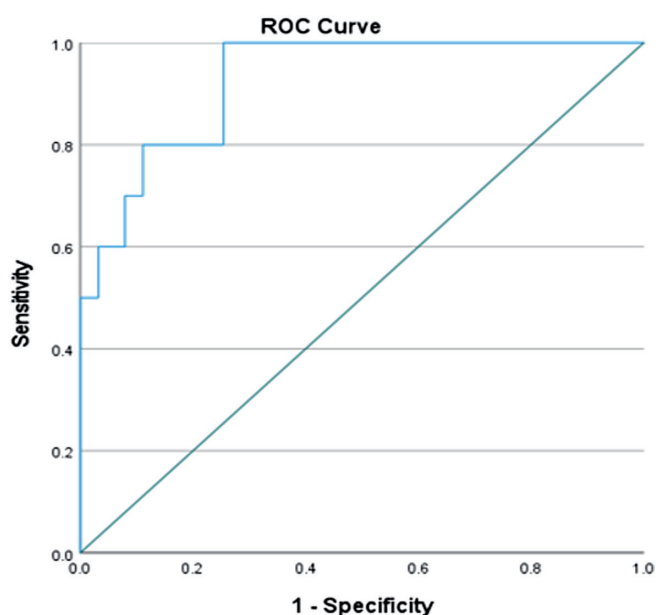
The aim of the present study was to examine the outcomes of pediatric AC and to identify variables associated with prognostic value concerning treatment, patient demographic, and routine laboratory values.

## METHODS

### Study Participants and Data Collection

To address the research purpose, the investigators designed and implemented a retrospective cohort study including patients admitted under the diagnosis of AC according to the International Diagnostic Code (ICD)-10 and treated at a tertiary referral center in the period from January 2010 to December 2019. A diagnosis of AM by an otologist was made if otalgia, fever, signs of AOM, and retroauricular redness and swelling were noted. Data were retrieved from computer databases and were retrospectively analyzed. The study was approved by the Ethics Committee of Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa (number 0014/21), and written informed consent was obtained from all the participants. The patients' families were subsequently contacted for any missing details. Cases with incomplete records or lost to follow-up for a minimum period of 3 months were excluded. The study design is displayed in Figure 1.

Study variables were grouped into logical sets and included demographics, ethnicity, laterality, and prior treatment and its duration.



**Figure 1.** Receiver operating characteristic (ROC) analysis assessing the sensitivity and specificity of CRP in discriminating between surgery requiring versus conservatively managed cases. CRP, C-reactive protein.

During hospital admission, body temperature measurements and its patterns, upper respiratory tract infection symptoms, general weakness, presence of central nervous system involvement, description of tympanic membrane, and middle ear and mastoid status were observed. Additionally, laboratory parameters including complete blood count and C-reactive protein (CRP) values, blood/middle-ear, or mastoid bacterial cultures along with presence and type of surgical intervention were monitored. The initial survival follow-up point was the patient's hospital admission, and the endpoint was status at discharge from the hospital, with the length of treatment coded as an outcome variable. Surgical outcomes entailed the need for mastoidectomy with paracentesis and insertion of the ventilating tube, extracranial intratemporal and intracranial complications, hospitalization length, and cases of complicated mastoiditis.

### Treatment Protocol

All patients in the cohort received paracentesis, Dex-Otic® eardrops, and an IV ceftriaxone dose (50 mg/kg/day) (Roche Pharmaceutical Ltd., Hod HaSharon, Israel). Intravenous corticosteroids (1 mg/kg prednisolone) were administered to patients with retroauricular fluctuation and/or subperiosteal abscess formation. In each case of auricular bulging with/without fluctuation, mastoid aspiration with pink 18-gauge needle under local anesthesia was performed in patients with adverse clinical parameters undergoing further surgery. Mastoidectomy was performed in cases of sigmoid sinus thrombosis, CT-verified abscess development, or cases that failed to improve within 48 hours from admission.

### Statistical Analysis

Data in Excel sheets were validated, verified, coded, and fed into Statistical Package for Social Sciences version 22 (IBM Corp, Armonk, NY, USA). The initial analysis comprised recoding and scaling for the preparation of statistical analysis. Calculated scales include duration of symptoms, hospitalization lengths before and after operation, and overall length of treatment. Duration of symptoms and hospitalization were analyzed as both continuous scales and ranked ordinal variables. Summary tables were produced for all main variables. The mean duration of symptoms and hospitalization was tested by analysis of variance (ANOVA) on age, sex, and origin. The mean CRP values and length of hospitalization with and without IV steroids were also tested by ANOVA. A chi-square was utilized for the analysis of categorical variables. Receiver operating characteristic (ROC) analysis and a cut-off value were identified using the Youden J index (measuring the sensitivity and specificity of a dichotomous tested variable), and the patients were divided into low-risk (<the cut-off value) and high-risk subgroups (>the cut-off value) regarding surgical treatment. All cross-tabulations are presented in counts and percentages, and all statistical analyses are accompanied by mean values and their standard deviations. A 2-sided *P*-value of  $\leq .05$  was considered statistically significant. Power was calculated as appropriate. Calculations were made on mean hospitalization length. For a 73-patient sample size, an effect size of 0.56 and a 0.05 error probability are assumed for a best-calculated power of 0.75.

## RESULTS

A total of 73 cases of AC were treated between 2010 and 2019. The average follow-up was 6 months (range: 3-12 months). The mean age of the study population was  $2.5 \pm 1.8$  years (median: 1.9, range: 7

**Table 1.** Mean Values and Their SD Presented for Patients Who Underwent Surgery or Treated Conservatively

	Underwent Surgery						F	Sig.
	No			Yes				
	Mean	SD	Total, N	Mean	SD	Total, N		
Hospitalization length	5	2	63	7	2	10	7.717	<b>.007</b>
Prehospital symptom time (days)	4	4	63	3	1	10	0.304	.583
Temperature at admission	38.2	1.1	63	38.7	0.7	10	1.771	.188
Hemoglobin (Hb)	10.9	1.0	63	10.7	1.0	10	0.388	.535
Leukocytes (WBC)	17.67	6.15	63	18.89	8.41	10	0.303	.584
Monocytes (MONO)	1.55	.56	63	1.97	0.81	10	4.238	.043
CRP	74.61	60.28	63	227.62	89.09	10	48.342	<b>.000</b>

SD, standard deviation; Sig., 2-tailed statistical significance.

months-7 years), consisting of male patients in 42 (57.5%) and Jewish ethnicity in 60 (82%) of cases. Auricular bulging was the most common presenting sign, comprising 32 (43.8%) of cases and fluctuating on palpation in 24 (32.8%) of cases. The mean body temperature was 38.3°C (range: 36.1- 40.7) and “picket-fence” pattern was observed in 6 (8.2%) cases. Upper respiratory tract infection was reported in all cases prior to admission. General weakness was most commonly reported in 28 (38.4%) cases. The mean duration of symptoms prior to hospital admission was 3.8 ± 3.8 days (range: 1-21), differing between the genders, with 3 ± 1.6 and 4.9 ± 5.4 in males and females, respectively. The most common complication was subperiosteal abscess formation in 8 (11%) cases, followed by sigmoid sinus thrombosis and epidural abscess in 5 (6.8%) and 4 (5.5%) cases, respectively. In total, 10 (14%) of cases underwent simple mastoidectomy after a mean duration of 72 hours of hospital treatment. Dex-Otic drops were used in all patients, while IV steroid therapy was administered in 14 (19.2%) patients. Duration of pre-admission symptoms, hospitalization, body temperature, laboratory parameters, gender, and ethnicity did not differ significantly between cases with regard to the need for surgery (Table 1). Conversely, CRP values were found to be 3-fold higher in cases requiring surgery compared to conservatively managed cases, with a mean of 227.6 versus 74.6, respectively ( $P < .001$ ). In patients requiring surgery, patients of Arabic ethnicity were more likely to receive surgical treatment since 6 out of 13 (46.2%) underwent surgery in contrast to 4 out of 56 (7.1%) Jewish patients ( $P < .001$ ) (Table 2). Further analysis showed that the mean duration of symptoms prior to admission (3.5 vs. 5.5 days) and mean CRP values (150.5 vs. 81.2) also differed in Arabic versus Jewish children. As shown in Figure 2, the area under the curve, which indicates the predictive ability of CRP with regard to surgical treatment, was 0.927, implying a test with sound discriminating ability between the 2 outcomes (95% CI: 0.856-0.998,  $P < .001$ ). As presented in Figure 2, a CRP cut-off of  $\geq 97.8$  had a sensitivity of 100% and a specificity of 74.6%, for predicting surgery. Data revealed a significantly shorter duration of symptoms before admission in males, ( $P = .031$ ), 2 days on average. Using IV steroids significantly shortened the length of hospitalization ( $P = .023$ ), 1.4 days on average.

**DISCUSSION**

Despite a significant decrease in surgical interventions for acute pediatric mastoiditis, there have been reports of the increasing incidence of the number of cases in general.<sup>10</sup> This study aimed to evaluate clinical characteristics and outcomes of pediatric AM

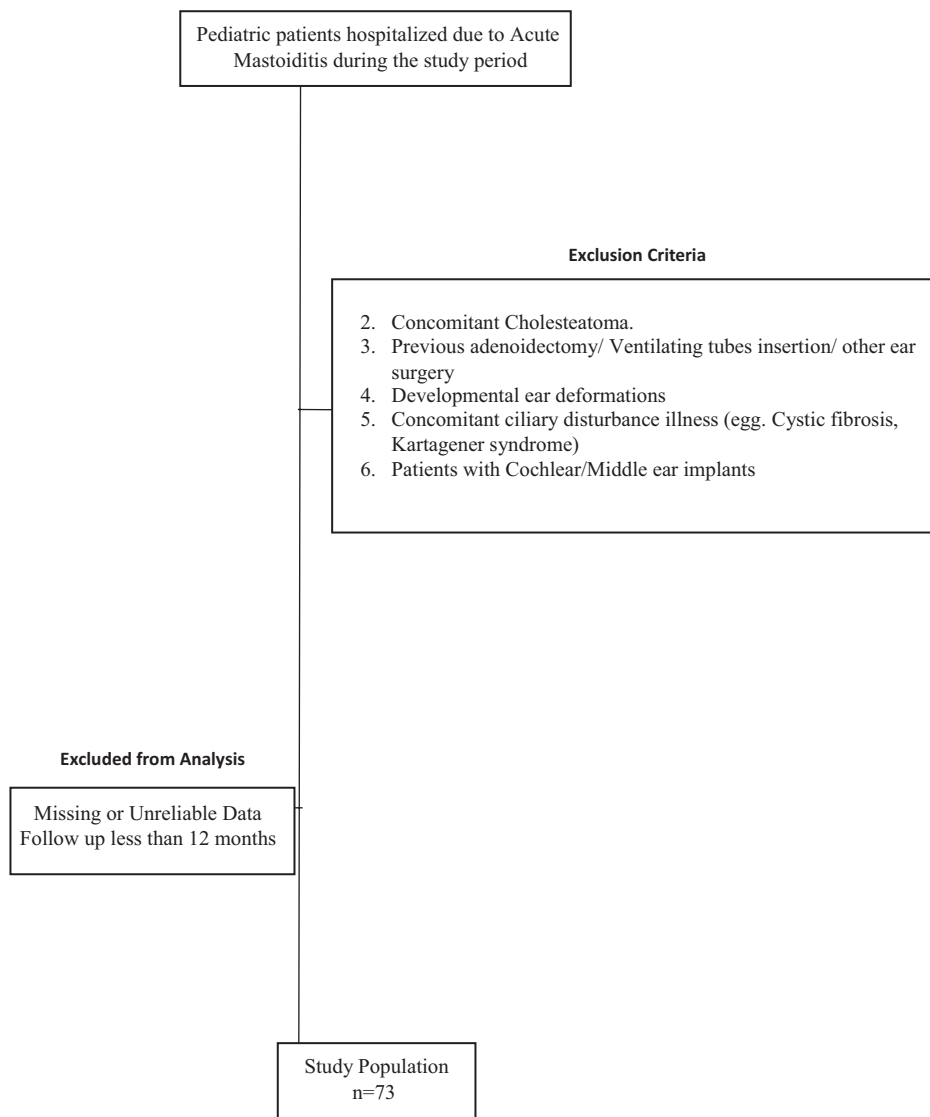
and to identify possible indicators influencing the length of hospitalization and the decision to undergo surgery.

There have only been several previous studies detailing the difference between pediatric patients undergoing surgery and those conservatively managed, and our present study found that CRP was a good predictor of the need for surgical intervention.<sup>10,11</sup> The mean CRP in cases that required mastoidectomy was 227.62, a 3-fold increase compared to those managed conservatively. A CRP cut-off of  $\geq 97.8$  was found to have a sensitivity and specificity of 100% and 74.6%, respectively, for predicting the need for mastoid surgery. Since early diagnosis and intervention in patients presenting with complications of AM is critical, we believe that identifying a cut-off value of a

**Table 2.** Distribution Among Categorical Groups for Patients Who Underwent Surgery or Were Treated Conservatively and Their Correlating Chi-Square Values

Underwent surgery	No	Yes	$\chi^2$	Sig.
	N	N		
<b>Sex</b>				
Male	35	7	0.737	.391
Female	28	3		
<b>Age groups</b>				
<2 years	31	7	0.221	.221
>2 years	32	3		
<b>Ethnicity</b>				
Arabic	7	6	14.093	<b>.000</b>
Jewish	56	4		
<b>Infection side</b>				
Left	29	4	0.127	.722
Right	34	6		
<b>Steroid IV</b>				
Yes	11	3	0.876	.349
No	52	7		
<b>Dex-Otic drops</b>				
Yes	60	9	0.457	.499
No	3	1		

IV, intravenous; Sig., 2-tailed statistical significance.



**Figure 2.** Study design.

routinely used laboratory inflammatory parameter will be beneficial in reducing morbidity and mortality. Other diagnostic modalities like MRI are expensive and are often complicated to perform on younger children, especially when requiring general anesthesia.<sup>12</sup>

Acute mastoiditis cases in the pediatric population requiring hospitalization are a considerable burden to the healthcare system. According to the Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project, and Kids' Inpatient Database, the annual cost of ENT hospitalizations in the USA is rising continuously.<sup>13</sup> Out of all hospital inpatient stays between 2008 and 2012, the average hospital cost of pediatric stays had the highest growth rate (more than 6% annually).<sup>14</sup> We found that IV steroid treatment shortened the length of hospitalization by 1.4 days on average, providing not only a better patient experience but also a major economic benefit to the healthcare system. Roland et al<sup>15</sup> in their study found that addition of topical steroids to antibiotic drops treatment is superior to the topical antibiotic treatment alone, which we could not corroborate in our study. There are still no clear guidelines on AC management, with trends leaning toward preferential conservative management.

Subperiosteal abscess formation, sigmoid sinus thrombosis, and epidural abscess were found in all 10 cases who underwent mastoidectomy, while no children developed similar complications after 72 hours of conservative treatment. This progression of infection in some patients may be indicative of aggressive disease and when coupled with laboratory findings, maybe a sound basis for early surgical intervention.<sup>16,17</sup>

Gender-related differences are common in many pathologies, and AC is no different. Although data regarding the issue are limited, 1 prior study showed a higher incidence of mastoiditis in male patients, with a 2.31 male to female ratio.<sup>18</sup> Our findings were similar, with a 1.35 male to female ratio. These disparities may be attributed to the anatomical variations between males and females.<sup>19</sup> Additionally, we discovered that females had a longer duration of symptoms, 2 days on average, before being admitted. To our knowledge, the difference in disease progression was not reported before. Ethnicity did not play a significant role in any variable apart from the likelihood of mastoid surgery, where it appeared that Arabic children were more likely to receive surgical treatment, 46.2% versus

7.1% of Jewish children ( $P < .001$ ) (Table 2). This finding could be explained by longer duration of symptoms prior to hospitalization (3.5 vs. 5.5 days) along with higher CRP values (150.5 vs. 81.2) when compared to the non-surgical group.

This study has several limitations. First, we employed retrospective methodology using data from computerized systems, and data were obtained without the ability to assess its reliability. Secondly, results were obtained in individuals who were admitted to the department and may thus not be indicative of all patients with acute mastoiditis. Furthermore, selection bias regarding the timing of surgical treatment may also play a significant role. Group selection and categorization regarding surgical management were not independent variables. Nevertheless, despite this inevitable retrospective bias, our large-scale cohort identified potentially useful clinical characteristics for treatment-based decisions.

## CONCLUSION

The outcomes of pediatric AC may be influenced by IV steroid treatment, showing an impact on shortening the hospitalization length. Male patients had a propensity toward more severe disease onset and clinical course, while serum CRP values seem to be a reliable predictor variable in patients requiring surgery.

**Ethics Committee Approval:** Ethical committee approval was received from the Ethics Committee of Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa (Approval no: 0014/21).

**Informed Consent:** Written informed consent was obtained from all participants and their legal guardians.

**Peer-review:** Externally peer-reviewed.

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**Declaration of Interests:** The authors declare that they have no conflict of interest

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