Invasive Bacterial Infections in Afebrile Infants Diagnosed With Acute Otitis Media

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abstract

OBJECTIVES: To determine the prevalence of invasive bacterial infections (IBIs) and adverse events in afebrile infants with acute otitis media (AOM).

METHODS: We conducted a 33-site cross-sectional study of afebrile infants ≤90 days of age with AOM seen in emergency departments from 2007 to 2017. Eligible infants were identified using emergency department diagnosis codes and confirmed by chart review. IBIs (bacteremia and meningitis) were determined by the growth of pathogenic bacteria in blood or cerebrospinal fluid (CSF) culture. Adverse events were defined as substantial complications resulting from or potentially associated with AOM. We used generalized linear mixed-effects models to identify factors associated with IBI diagnostic testing, controlling for site-level clustering effect.

RESULTS: Of 5270 infants screened, 1637 met study criteria. None of the 278 (0%; 95% confidence interval [CI]: 0%–1.4%) infants with blood cultures had bacteremia; 0 of 102 (0%; 95% CI: 0%–3.6%) with CSF cultures had bacterial meningitis; 2 of 645 (0.3%; 95% CI: 0.1%–1.1%) infants with 30-day follow-up had adverse events, including lymphadenitis (1) and culture-negative sepsis (1). Diagnostic testing for IBI varied across sites and by age; overall, 278 (17.0%) had blood cultures, and 102 (6.2%) had CSF cultures obtained. Compared with infants 0 to 28 days old, older infants were less likely to have blood cultures ($P < .001$) or CSF cultures ($P < .001$) obtained.

CONCLUSION: Afebrile infants with clinician-diagnosed AOM have a low prevalence of IBIs and adverse events; therefore, outpatient management without diagnostic testing may be reasonable.

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WHAT'S KNOWN ON THIS SUBJECT: Guidelines do not provide recommendations about whether to evaluate for potential systemic illnesses in afebrile infants with acute otitis media. The prevalence of invasive bacterial infection in these infants is unclear and likely contributes to variation in care.

WHAT THIS STUDY ADDS: Among afebrile infants aged 90 days and younger with clinician-diagnosed acute otitis media, invasive bacterial infections and adverse events were rare. These data suggest that clinicians could minimize diagnostic testing and hospitalizations for these infants.

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Acute otitis media (AOM) is a common childhood infection, affecting >80% of children before 3 years of age.[1] Although AOM is relatively uncommon in infants younger than 3 months of age, once the diagnosis has been made, there is a dearth of evidence to guide further clinical care. National recommendations for young infants with AOM do not exist because the current American Academy of Pediatrics (AAP) guideline on the diagnosis and management of AOM excludes infants younger than 6 months of age.[2]

One important clinical concern in infants younger than 3 months with AOM is whether they have concomitant invasive bacterial infections (IBIs). In previous studies, researchers have suggested a low prevalence of bacteremia among infants with AOM, but these studies were limited by small sample sizes and included mixed populations of infants with and without fever.[3–8] The clinical conundrum of AOM in infants younger than 3 months may be most relevant to those without fever, for whom the appropriate diagnostic evaluation for IBI, if any, is unclear.

The relative lack of data on afebrile infants with AOM has likely resulted in variability among clinicians in their diagnostic approach. If IBIs and adverse events are shown to be rare in a large sample of afebrile infants, clinicians may be more apt to obtain fewer diagnostic tests. Our primary aim was to determine the prevalence of IBIs and AOM-associated adverse events in afebrile infants 90 days and younger with clinically diagnosed AOM. Our secondary aim was to describe patterns of diagnostic testing and factors associated with testing in these afebrile infants.

METHODS

Study Design and Population

We conducted a cross-sectional study at 33 pediatric emergency departments (EDs) associated with the Pediatric Emergency Medicine Collaborative Research Committee of the AAP. The participating sites included 29 EDs in the United States, 2 EDs in Canada, and 2 EDs in Spain. All were university-affiliated teaching hospitals, and 25 (76%) were freestanding children's hospitals. The study was approved by the Pediatric Emergency Medicine Collaborative Research Committee Steering Committee and the research ethics boards of all participating sites.

We included infants aged 90 days and younger who presented to a participating ED between January 2007 and December 2017 and were clinically diagnosed with AOM. Study period varied by site depending on available data. We excluded infants with documented temperatures of ≥38.0°C or <36.0°C in the ED or within 48 hours before ED arrival, antibiotic use other than topical antibiotics within 48 hours of ED presentation, concurrent diagnosis of mastoiditis, evidence of focal bacterial infection on ED examination, or who were transferred to the ED with diagnostic testing completed and/or antibiotic administration initiated at an outside hospital. We chose to exclude febrile infants from our study because the presence of fever in young infants, and not necessarily the diagnosis of AOM, is a primary driver for more expanded testing and/or empirical treatment of IBI.

Eligible infants were identified using two methods. The primary method was using an inclusive list of *International Classification of Diseases* (*ICD*) *9th* or *10th Revision* diagnosis codes for AOM (Supplemental Table 6). To assess for infants with IBI who also had AOM but for whom ICD codes for AOM were not documented, we also retrieved and reviewed the records of all infants evaluated in the ED for whom review of microbiology databases noted bacteria in the blood or cerebrospinal fluid (CSF). All diagnoses of AOM were verified through the review of clinician assessment in the medical records. Because the AAP diagnostic criteria for AOM are for children 6 months and older and may be too stringent to apply directly to this younger age group, we chose for our primary analysis to include all infants with documentation of ≥1 middle ear examination abnormality supportive of AOM diagnosis.[2] However, we performed a subanalysis of infants meeting simplified AAP diagnostic criteria, defined as the presence of tympanic membrane erythema, bulging tympanic membrane, or otorrhea not due to acute otitis externa.

Study Protocol

All study variables were defined a priori and described in the manual of operations. Investigators and research coordinators received standardized data abstraction training and entered their data electronically into REDCap, a secure, web-based electronic database. Collected data included demographic characteristics, medical history, presenting symptoms, ED physical examination, laboratory data, findings on assessment by otolaryngologist consultants when available, and inpatient management for hospitalized infants.

To minimize bias associated with abstracting potentially more-subjective descriptions from the medical records, we provided restrictive key words to guide the determination of ill appearance, respiratory distress, and clinical dehydration. These findings were categorized as present, not present, or unclear. To assess interrater reliability, a second abstractor at each site reviewed the medical records and performed an independent assessment of clinical appearance, respiratory status, and hydration status for a random sample of 10% of

all infants, as well as for all infants with IBI or adverse outcomes.

Outcome Measures

The primary outcomes were IBIs and AOM-associated adverse events. IBIs included bacteremia and bacterial meningitis, which were defined as the growth of a pathogen in the blood culture or CSF culture, respectively (Supplemental Table 7).[9] Any bacteria not predefined as a contaminant or pathogen, or whose categorization of pathogenicity by the treating clinician was unclear or different from the prespecified list, were reviewed by a pediatric infectious disease coinvestigator (A.C.) to determine pathogenicity. For those infants who did not have CSF obtained for culture, the presence or absence of bacterial meningitis was determined through the review of the medical records. If the infant had a follow-up visit to the index hospital within 30 days of the ED visit that did not identify bacterial meningitis, we considered this outcome as negative.

AOM-associated adverse events were defined as any substantial complications resulting from or potentially associated with AOM, including, but not limited to, the development of mastoiditis, sepsis, or death. Urinary tract infection (UTI) was not considered an AOM-associated adverse event because the causal mechanism linking AOM and UTI is unclear. However, we collected information about urine testing because it is a part of the serious bacterial infection evaluation in infants. For infants discharged from the ED, we reviewed the medical records to identify ED return visits within 72 hours. Additionally, we reviewed the medical records for any outpatient clinician encounter or hospitalization within 30 days of ED discharge. For any visit identified, we evaluated the records for evidence of IBIs or adverse events.

Our secondary outcomes were (1) ED completion of blood culture (binary), (2) ED completion of CSF culture (binary), and (3) hospitalization (binary) from the index ED visit. Each of these outcomes was stratified by age and by site to assess for variation in care.

Sample Size

Because we expected IBI to be a rare event in this sample, we determined our sample size on the basis of the prevalence of blood culture testing, a secondary outcome. Targeting evaluation of up to 20 independent variables associated with this outcome, we aimed to study at least 200 infants for whom blood cultures were obtained. Pilot testing at the lead site showed that 30% of eligible infants had blood cultures obtained; therefore, we aimed to enroll a minimum of 667 infants.

Statistical Analysis

To enhance clinical interpretability, several continuous variables were categorized. Age was categorized as 0 to 28, 29 to 56, and 57 to 90 days based on cutoffs generally used when risk-stratifying febrile infants for IBI.[10,11] The results of tests generally available during the ED stay were categorized as not performed, performed and within normal limits, and performed and abnormal. For the complete blood count, a white blood cell (WBC) count between 5 and 15 $\times$ 10^3 cells/μL was considered to be normal; values outside of this range were considered abnormal.[12] Urinalysis was considered abnormal if there was any leukocyte esterase, nitrite, or $>$5 WBCs per high-power field, similar to previous studies.[13,14] Given the challenges of interpreting CSF WBC count if the lumbar puncture was traumatic,[15] these results were not categorized.

We described the prevalence of IBI, adverse events, and diagnostic tests obtained with proportions and 95% confidence intervals [CIs]. For all tests of association regarding practice variation (eg, testing, hospitalization), we used generalized linear mixed-effects models to account for site-level clustering effects. For each outcome, we first examined the association between the outcome and a potential explanatory variable, including those from infant characteristics, clinical symptoms, and physical examination findings, using a univariable generalized linear mixed-effects model. For the subsequent multivariable models, we first assessed for potential collinearity between predictor variables using generalized variance inflation factors. Those predictors with univariable P value $<.1$ and no evidence of multicollinearity were included in multivariable models to assess for an association with the following outcomes as fixed effects: (1) obtaining a blood culture, (2) obtaining a CSF culture, and (3) hospitalization. Hospital sites were used as random effects.

Interrater reliability for the assessment of general appearance, respiratory distress, and dehydration was measured by using Cohen unweighted κ, a 0 to 1 scale where 0 indicates poor agreement and 1 indicates perfect agreement.[16] All statistical analyses were conducted using either the Statistical Program for the Social Sciences Version 26 (IBM SPSS Statistics, IBM Corporation, Armonk, NY) or R (R version 3.6.3, 2019).

RESULTS

We screened 5270 infants for eligibility; of these, 1637 (31.1%) met study criteria (Fig 1). Sites contributed 0 (1 site) to 386 cases, with a median of 30 cases across sites, and ranging from 5 to 11 years of review.

Patient Characteristics

The median age of included infants was 68 days (interquartile range [IQR]: 49–80 days) (Table 1). One thousand four hundred fifty-nine (89.1%) infants met the simplified

AAP diagnostic criteria for AOM. The remaining 178 infants had ≥1 of the following examination findings reported as supporting evidence for AOM: opacification of tympanic membrane (n = 113), dull tympanic membrane (n = 57), decreased visualization of middle ear structures (n = 25), middle ear effusion (n = 9), visualized tympanic membrane perforation (n = 8), or decreased tympanic membrane mobility with insufflation (n = 5).

Prevalence of IBI and AOM-Associated Adverse Events

None of the 278 infants with blood cultures had bacteremia (0 of 278; 0%, 95% CI: 0%–1.4%). No infant was diagnosed with bacterial meningitis on the basis of CSF culture results (0 of 102; 0%, 95% CI: 0%–3.6%) or combined with 30-day follow-up (0 of 672; 0%, 95% CI: 0%–0.6%). Two of 645 infants (0.3%; 95% CI: 0.1%–1.1%) with 30-day follow-up or hospitalization history experienced adverse events. One of these infants was treated for culture-negative sepsis, a potentially AOM-related adverse event, although on review of medical records, it was suggested that the primary cause of her illness was likely severe dehydration from underlying milk protein allergy. In Table 2, we describe the 2 infants with adverse events in detail. In Supplemental Table 8, we describe the 2 infants who were subsequently diagnosed with UTIs.

ED Management

Diagnostic testing and hospitalization rates varied by site (Supplemental Fig 2). One-fifth of all infants (355 of 1637, 21.7%) had ≥1 diagnostic test obtained for infectious illness (Table 3). One-third of infants 28 days and younger underwent lumbar puncture (34/100; 34.0%). Of 1179 infants with symptoms of upper respiratory tract infection, 58 (4.9%) underwent lumbar puncture, and 162 (13.7%) had blood cultures obtained.

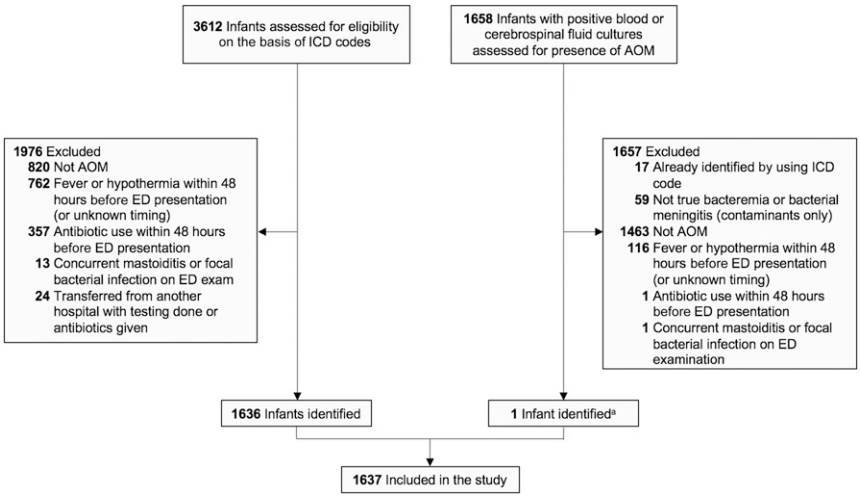

FIGURE 1
Patient screening and identification. [a]One infant had a positive CSF culture result, which was clinically verified by the infectious disease expert after inclusion in the study to be a contaminant (coagulase-negative staphylococci).

TABLE 1 Characteristics of Afebrile Infants With AOM (N = 1637)

Demographic	
Median age, d (IQR)	68 (49–80)
Age, d, n (%)	
0–28	100 (6.1)
29–56	444 (27.1)
57–90	1093 (66.8)
Male, n (%)	957 (58.5)
Ethnicity, n (%)	
Hispanic	595 (36.3)
Not Hispanic	859 (52.5)
Unknown or other	183 (11.2)
Term gestation, n (%)	1217 (74.3)
Chronic illness[a], n (%)	49 (3.0)
History of presenting illness, n (%)	
History of tactile warmth	257 (15.7)
Measured fever >2 d before ED visit	92 (5.6)
Ear discharge	422 (25.8)
Difficulty feeding	429 (26.2)
Vomiting	276 (16.9)
Diarrhea	119 (7.3)
Decreased urine output	96 (5.9)
Symptoms of upper respiratory infection	1179 (72.0)
General examination, n (%); κ[b]	
Ill appearanceκ	30 (1.8); 0.56
Respiratory distressκ	75 (4.6); 0.44
Dehydrationκ	28 (1.7); 0.21
Ear examination ≥1 ear, n (%)	
Tympanic membrane erythema	970 (59.3)
Bulging tympanic membrane	564 (34.5)
Otorrhea	477 (29.1)

All values are frequency (%) except where otherwise indicated.
[a] Includes congenital heart disease (19), major congenital anomaly other than congenital heart disease (10), renal or urologic disorder (6), failure to thrive (4), disease or use of medications that would affect the immune system (3), neurologic disorder (3), chronic lung disease (1), presence of indwelling catheters or shunts (1), and other (7). Does not total 49 because an infant may have >1 chronic illness.
[b] Cohen unweighted κ (interrater reliability) was used to measure interrater reliability of 2 assessors' determination of these findings. Variables with κ of 0.21 to 0.40 were considered to have fair agreement, those with κ of 0.41 to 0.60 were considered to have moderate agreement, and those with κ of 0.61 to 0.80 were considered to have substantial agreement.

TABLE 2 Characteristics of Infants With Adverse Events

Patient	Age, d	Ill Appearance	Culture Results	Adverse Event	Clinical Course
1	45	No	Blood: negative, CSF: negative, urine: negative, MEE: not obtained	Lymphadenitis	Initially discharged from the hospital on amoxicillin. Twenty days after index ED visit, returned with cervical lymphadenitis and perforated AOM, confirmed by an otolaryngologist. Hospitalized and treated with IV and otic antibiotics.
2	32	Yes	Blood: negative, CSF: negative, urine: negative, MEE: *Staphylococcus aureus*	Culture-negative sepsis	Presented with severe illness during the index ED visit. AOM confirmed by an otolaryngologist. Source of culture-negative sepsis thought to be severe milk protein allergy. Hospitalized and treated with IV and otic antibiotics.

IV, intravenous; MEE, middle ear effusion or ear discharge.

One hundred seventy-three infants (10.6%) received either an intravenous or intramuscular antibiotic in the ED (Supplemental Table 9). Of the 1450 infants discharged from the ED (88.6% of total), 1311 (90.4%) received a prescription for an oral antibiotic. Amoxicillin was the most-frequently prescribed antibiotic (n = 1228; 93.7%), followed by amoxicillin and clavulanate (n = 56; 4.3%).

The 72-hour return rate was 4.3%. Of the returning 63 infants, 15 (23.8%) were hospitalized for related reasons (median age: 49 days, IQR: 37–66) (Supplemental Table 10). One patient returned 3 weeks after the initial ED visit with lymphadenitis, as described in Table 2.

Factors Associated With Diagnostic Testing and Hospitalization

No potential predictor variables assessed for inclusion in the generalized linear mixed-effects models were collinear (generalized variance inflation factors <3) (Supplemental Table 11). Adjusting for covariates, older infants were less likely to have blood cultures sent (Table 4), undergo lumbar puncture (Supplemental Table 12), or be hospitalized (Table 5) as compared with infants 0 to 28 days old. In all 3 models, history of ear discharge was significantly associated with IBI testing and hospitalization. Decreased urination, respiratory distress, and completion of complete blood count (regardless of whether the results were normal or abnormal) were also independently associated with hospitalization. For the subanalysis of infants meeting the simplified AAP diagnostic criteria, minor differences in the point estimates of the predictor variables were observed for each model (see Tables 4 and 5, Supplemental Table 12).

TABLE 3 Summary of ED Management

	N (%)			
	Overall (*N* = 1637)	0–28 d Old (*n* = 100)	29–56 d Old (*n* = 444)	57–90 d Old (*n* = 1093)
Diagnostic testing				
Any testing for bacterial infection[a]	355 (21.7)	58 (58.0)	177 (39.9)	120 (11.0)
Complete blood count	311 (19.0)	54 (54.0)	164 (36.9)	93 (8.5)
Blood culture	278 (17.0)	53 (53.0)	147 (33.1)	78 (7.1)
Urine culture	207 (12.6)	46 (46.0)	102 (23.0)	59 (5.4)
CSF culture	102 (6.2)	34 (34.0)	58 (13.1)	10 (0.9)
Respiratory pathogen test[b]	161 (9.8)	27 (27.0)	46 (10.4)	88 (8.1)
Consultations				
Otolaryngologist	64 (3.9)	8 (8.0)	40 (9.0)	16 (1.5)
Treatment				
IV or IM antibiotics	175 (10.7)	37 (37.0)	86 (19.4)	52 (4.8)
Prescription for oral antibiotic[c]	1311 (90.4)	37 (71.2)	299 (81.3)	975 (94.7)
Disposition				
Discharged from the ED	1450 (88.5)	52 (52.0)	368 (82.9)	1030 (94.2)
Hospitalized	186 (11.4)	47 (47.0)	76 (17.1)	63 (5.8)
Transferred to another hospital	1 (0.1)	1 (1.0)	0 (0)	0 (0)

IM, intramuscular; IV, intravenous.

[a] Defined as obtaining ≥1 of the following tests: complete blood count, blood culture, CSF culture, or urine culture.

[b] Includes any respiratory testing, including point-of-care respiratory syncytial virus and influenza testing, as well viral pathogen panels.

[c] Percentage reflects total out of infants discharged from the ED (1311 out of 1450 for all ages, 37 out of 52 for 0–28 days, 299 out of 368 for 29–56 days, and 975 out of 1030 for 57–90 days).

DISCUSSION

In this international, multicenter study of afebrile infants aged 90 days and younger with clinically diagnosed AOM, the prevalence of IBI and AOM-associated adverse events was low. Despite the low probability for IBI in this population, more than one-fifth underwent IBI diagnostic testing and were hospitalized. This practice varied by site and was largely driven by age, with younger infants more likely to both undergo invasive testing and be hospitalized. With the data from our study, we suggest that given the low rates of IBI and adverse events, outpatient management without IBI testing is reasonable for most afebrile infants with a clinical diagnosis of AOM.

Our data may be used to help guide clinical management of afebrile infants with clinician-diagnosed AOM, who are not included in the current AAP AOM practice guideline.[2] We expected variation in IBI testing and were not surprised that young age

TABLE 4 Generalized Linear Mixed-Effects Model to Predict Blood Culture Testing

Predictor	Adjusted Odds Ratio (95% CI)	*P*
Demographic		
Age[a]		<.001[b]
29–56 d	0.37 (0.23–0.60)	<.001[b]
57–90 d	0.06 (0.04–0.10)	<.001[b]
Gestational age[c]		.01[b]
<37 weeks' gestation	1.60 (0.94–2.72)	.08
Unknown	0.59 (0.36–0.96)	.03[b]
History of presenting illness		
Ear discharge	2.32 (1.62–3.34)	<.001[b]
Tactile warmth	2.29 (1.53–3.43)	<.001[b]
Upper respiratory infection symptoms[d]	0.88 (0.62–1.26)	.50

[a] Reference group: 0 to 28 d old.

[b] Statistical significance ($P < .05$). In this model, age, gestational age, history of ear discharge, and history of tactile fever were independently associated with obtaining a blood culture. In the subanalysis including only the 1459 infants meeting simplified AAP diagnostic criteria (data available on request), no meaningful changes were noted, except the predictor variable <37 wk gestational age was significant ($P = .04$).

[c] Reference group: ≥37 wk gestation.

[d] Include cough, new nasal congestion or sneezing, rhinorrhea, wheezing, noisy breathing, and difficulty breathing.

appeared to be the major driver leading to evaluation for IBI with either blood or CSF testing. The increased testing in the youngest infants is likely related to the lack of data regarding how AOM modifies the risk of IBI, the concern for IBI in younger infants based on data from the febrile infant population, and the reluctance to initiate antibiotics without any IBI evaluation. However, it is suggested by our data and previous data that the risk of IBI is low in afebrile infants with AOM.[4–6] Additionally, IBI prevalence in afebrile infants with AOM appears lower than the 0.8% to 2.5% prevalence described in the febrile infant AOM population.[4,5]

TABLE 5 Generalized Linear Mixed-Effects Model to Predict Hospitalization

Predictor	Adjusted Odds Ratio (95% CI)	*P*
Demographic		
Age[a]		<.001[b]
29–56 d	0.11 (0.06–0.22)	<.001[b]
57–90 d	0.07 (0.03–0.14)	<.001[b]
Gestational age[c]		.02[b]
<37 weeks' gestation	1.64 (0.80–3.38)	.18
Unknown	0.38 (0.17–0.87)	.02[b]
History of chronic illness	2.27 (0.85–6.07)	.10
History of presenting illness		
Decreased urine output	4.13 (1.88–9.07)	<.001[b]
Ear discharge	1.97 (1.17–3.31)	.01[b]
New difficulty feeding	1.36 (0.81–2.30)	.25
Diarrhea	0.58 (0.21–1.59)	.29
Physical examination		
Respiratory distress	40.54 (19.17–85.70)	<.001[b]
Dehydration	2.89 (0.87–9.61)	.08
Ill appearance	1.64 (0.52–5.18)	.40
Diagnostic test		
Complete blood count[d]		<.001[b]
Completed and within normal limits	10.95 (5.95–20.15)	<.001[b]
Completed and abnormal	9.25 (4.04–21.14)	<.001[b]
Urinalysis[e]		.05
Completed and within normal limits	2.11 (1.15–3.87)	.02
Completed and abnormal	2.14 (0.49–9.26)	.31

[a] Reference group: 0 to 28 d old.

[b] μStatistical significance ($P < .05$). In this model, age, gestational age, history of decreased urine output, history of ear discharge, respiratory distress on examination, and completion of complete blood count were independently associated with hospitalization. In the subanalysis including only the 1459 infants meeting simplified AAP diagnostic criteria (data available on request), the following differences were observed: chronic illness was not included in the model (univariable $P > .1$) and dehydrated appearance was statistically significant in the regression model ($P = .02$).

[c] Reference group: ≥37 wk gestation.

[d] Reference group: complete blood count not obtained. Test was considered abnormal if the WBC count was <5 or >15 × 10^3 cells/μL.

[e] Reference group: urinalysis not obtained. Test was considered abnormal if any of the following was present: leukocyte esterase, nitrite, or >5 WBCs per high-power field.

Of note, approximately three-fourths of the infants in our study were reported to have symptoms of upper respiratory infections, which may lead to viral AOM.[17] Inclusion of these infants, who may have a lower likelihood of IBI than those with bacterial AOM, might have led to an underestimation of IBI prevalence. However, existing data do not provide clarity regarding the ability to distinguish viral from bacterial AOM without performing tympanocentesis. Because >85% of older infants and children with clinically diagnosed AOM have identifiable bacterial otopathogens,[18] which could potentially spread to the blood or CSF, it is understandable why clinicians would manage infants with AOM conservatively, regardless of the presence of concurrent viral illnesses.

One major challenge in any study of infants with AOM is ensuring that AOM is indeed present. The diagnosis of AOM is unquestionably difficult. However, in this young age group, clinicians may be less inclined to make this diagnosis without having clear evidence of AOM on examination, because once the diagnosis is made, they must make difficult decisions regarding the need for invasive diagnostic tests, systemic antibiotics, and hospitalization. In previous studies, researchers have used the examination by otolaryngologists, who often use surgical microscopes and/or tympanocentesis results to support the clinical diagnosis of AOM.[3,4,6,7] However, these methods are not

routinely used in current clinical practice.[19] Although examining the ears of young infants is technically challenging, previous researchers have demonstrated successful use of otoscopy to diagnose AOM in infants younger than 8 weeks, with 52% to 85% of middle ear effusion cultures yielding growth of true otopathogens after tympanocentesis.[4,20]

Our study had limitations. First, given its retrospective design, we were unable to ensure completeness and accuracy of clinical data. Interrater agreement for appearance of dehydration was only fair but was higher for general appearance and respiratory distress. Second, not all infants had IBI testing, potentially leading to an underestimation of IBI prevalence. However, we minimized misclassification of infants with meningitis by reviewing any available clinician encounter within 30 days for discharged infants. We recognize that the use of return visits and medical record reviews as a proxy for identifying those with bacterial meningitis may not fully capture any events occurring outside of the index EDs and hospital systems. However, the majority of the participating EDs are referral centers for the sickest children in their respective regions, making presentation to an alternative hospital less likely. Additionally, all except one site had the ability to review some or all of the outpatient records of pediatric offices affiliated with the hospital, augmenting our ability to capture those infants presenting in the outpatient setting. We did not make similar assumptions regarding bacteremia, which may be transient or respond to standard therapy for AOM. Third, we may have missed infants whose discharge codes did not include AOM, but we addressed this concern by screening all infants with positive blood or CSF cultures for missed AOM diagnosis. Fourth, although we identified factors associated with testing and hospitalization, these management decisions may have been driven by factors that are unable to be captured retrospectively and not primarily by the diagnosis of AOM. Our study included only a relatively small number of infants ≤28 days, which may reflect the challenges of diagnosis or lower prevalence of AOM in this age group. Thus, the conclusions of our study should most readily be applied to infants older than 28 days. Finally, our findings are not generalizable to febrile infants.

CONCLUSIONS

In this cohort of afebrile infants with clinician-diagnosed AOM, IBIs and AOM-associated adverse events were uncommon. Diagnostic testing and hospitalization rates varied by site and were substantial in contrast to the low prevalence of IBIs and adverse events. On the basis of these findings, outpatient management without diagnostic testing for IBI may be reasonable for most afebrile infants with AOM.

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ABBREVIATIONS

AAP: American Academy of Pediatrics
AOM: acute otitis media
CI: confidence interval
CSF: cerebrospinal fluid
ED: emergency department
IBI: invasive bacterial infection
ICD: International Classification of Diseases
UTI: urinary tract infection
WBC: white blood cell

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