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Immunization Status and the Management of Febrile Children in the Pediatric Emergency Department
What Are We Doing?

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Objectives: Widespread *Haemophilus influenzae* and *Streptococcus pneumoniae* immunization has decreased occult bacteremia and bacterial meningitis rates. Practice has evolved in pediatric emergency departments (PEDs) to favor fewer diagnostic tests for and empiric treatment of invasive bacterial infection. We lack evidence-based guidance on evaluation and treatment of unimmunized (UnI) or underimmunized (UnderI) febrile children. This study aims to determine how parental report of immunization status in febrile PED patients impacts rates of diagnostic testing, interventions, and hospital admissions.

Methods: This is a retrospective cohort study with chart review of encounters of children aged 3 to 36 months presenting to an academic, tertiary care PED in 2019 using International Classification of Diseases-10 code for fever (R50.9). Inclusion criteria were documented fever of 38°C and higher and well appearance. Encounters were excluded if there was a history of chronic illness or documentation of ill appearance or hemodynamic instability. Encounters were grouped by provider-documented immunization status. Fischer exact test and logistic regression compared rates of diagnostic testing (serum, urine or cerebrospinal fluid laboratory studies, and chest radiographs), interventions (intravenous fluid bolus, intravenous antibiotic or steroid administration, respiratory support, or breathing treatment), and hospital admissions between UnderI, UnI, and fully immunized (FI) groups.

Results: Of the 1813 encounters reviewed, 1093 (60%) included provider-documented immunization status and 788 (43%) met final inclusion criteria: 23 (2.1%) UnI, 44 (5.8%) UnderI, and 721 (92.1%) FI. The UnderI and UnI children experienced significantly higher rates of laboratory evaluation including complete blood count and blood culture, medical intervention, and antibiotic prescriptions while in the PED. No significant differences were observed for rates of chest radiographs, hospital admissions, or 72-hour PED return visits.

Conclusions: Higher rates of laboratory testing and interventions were observed in UnderI and UnI versus FI febrile patients at a PED, likely demonstrating increased clinical suspicion for invasive bacterial infection in this group despite lacking national guidelines. Given continued vaccine hesitancy, further studies are needed for guiding management of febrile UnI and UnderI children presenting for emergency care.

Key Words: unimmunized, unvaccinated, febrile, immunization status, management

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The Centers for Disease Control and Prevention recommends children receive a combined 7-vaccine series that includes DTaP (diphtheria, tetanus, pertussis), IPV (poliovirus), MMR (measles, mumps, and rubella), Hib (*Haemophilus influenzae* type B), hepatitis B, varicella, and PCV-13 (13-valent *Streptococcus pneumoniae*) by age 24 months.[1] Nationally, it is estimated that only 70.5% of children complete this series on time, with 1% of children receiving no vaccines.[2] In the state in which this study is based (Indiana), 70% of children are considered fully immunized (FI) with the 7-vaccine series by 24 months, with approximately 1% of children claiming exemption on starting kindergarten, reflecting the national rates of nonimmunization.[3]

Widespread Hib and *S. pneumoniae* immunization has decreased rates of occult bacteremia and bacterial meningitis.[4,5] Hence, pediatric emergency medical (PEM) practice has evolved to favor fewer diagnostic tests for and empiric treatment of invasive bacterial infection (IBI) in children aged 3 to 36 months.[6–8] Until recently, there was a dearth of evidence-based guidance regarding evaluation and management of unimmunized (UnI) febrile young children. A retrospective cohort study by Dunnick et al[9] reported bacteremia from *S. pneumoniae* or Hib were independent of immunization status, and no vaccine-preventable pathogens were isolated in unvaccinated children. However, the county of the institution in which this study took place had an immunization rate of 96.6%. Robust local herd immunity likely contributed to the low number of children with blood cultures positive for vaccine-preventable organisms in their cohort, and their results therefore were not necessarily generalizable. Haut and Wagers[10] proposed considering prevaccination-era rates of IBI when encountering UnI patients in the pediatric emergency department (PED). Likewise, a recent review article by Finkel et al[11] offers an algorithm for managing fever without a source in UnI children that suggests obtaining urinalysis and urine culture, complete blood count (CBC), and a viral detection panel as initial screening tests if unvaccinated 2- to 24-month-old children have a fever of 39°C or higher and are clinically well appearing. Blood culture, chest radiography, and empiric antibiotics are only recommended at or higher than specific thresholds for white blood cell count, absolute neutrophil count, absolute band count, and procalcitonin.[11]

In clinical practice, PEM providers often rely on adult caregivers for confirmation of a patient's immunization status despite

existing literature that suggests this may not be an adequate method.[12,13] For this reason, the Centers for Disease Control and Prevention has supported initiatives to develop state immunization registries to improve population-based health.[14] It has been demonstrated that blood screens for occult bacteremia by emergency medicine physicians were reduced when using an immunization registry for children presenting with fever without a source.[15] However, we are not aware of reported rates of immunization registry use by PEM providers, and it is unknown if PEM providers at our institution are querying the state registry for this information. In addition, immunization registry integration into an electronic health record (EHR) is complex and can be limited by incomplete records (eg, patient recently immigrated to state), poor patient matching, or manual steps required for synchronization. Given the rapid pace required for patient care and inevitable shortcomings of integration of the state registry with the EHR, we believe the immunization status documented by providers is overwhelmingly obtained via caregiver report.

It remains unclear what impact provider-documented vaccination status has on the evaluation and management of young febrile children seeking emergency care. Mintegi et al[16] reported that children who were incompletely immunized or UnI specifically against PCV-7 were significantly more likely to have CBC and blood culture obtained and ceftriaxone administered when compared with completely immunized counterparts. However, there has yet to be a study that has investigated the impact of immunization status as reported by a parent or caregiver on the emergency management of febrile children. This study aims to determine if febrile children who are perceived as underimmunized (UnderI) or UnI experience higher rates of diagnostic testing, interventions, and hospital admissions compared with FI children.

METHODS

This institutional review board-approved retrospective cohort study consisted of a chart review of encounters of febrile children aged 3 to 36 months presenting to a large PED during a 12-month period (January 1–December 31, 2019). The PED is part of a free-standing, urban, academic, tertiary care children's hospital with an annual emergency department (ED) volume of approximately 50,000 visits per year. The chart review time frame was chosen in an effort to control for seasonality. We screened for eligible encounters in an analytics database using the diagnosis International Classification of Disease (ICD)-10 code for fever (R50.9). During initial chart extraction, if the diagnosis did not match the clinical documentation (eg, the patient presented for a clinically distinct and different reason and the patient never had a fever or reported a fever), the encounter was deemed miscoded, and no information was extracted from the chart. The clinical inclusion criteria were temperature of 38°C and higher (as documented per parental report or as measured during the ED encounter) and well appearance. Fever was defined as 38°C and higher, which is consistent with the American College of Emergency Physicians' pediatric fever policy.[7] Charts were excluded if there was history of complex chronic illness noted in any section of the EHR (defined as sickle cell disease, congenital heart disease, immunodeficiency, immunosuppressed status from chemotherapy or other immunosuppressive therapy, or tracheostomy ventilation-dependent) or the provider indicated ill appearance or hemodynamic instability during that encounter.

Study-related patient information was accessed in the electronic medical record by manual chart review. REDCap (Vanderbilt University, Nashville, TN),[17] a data collection tool, was used in the chart review process to characterize each encounter in regard to patient demographics, vaccination status, ED course, and ED disposition. Vaccination status was recorded from the natural language of provider documentation (eg, "imm utd", indicating immunizations were up to date or "vaxed only to 2 months", indicating the child has had some but not all immunizations). From this, each patient encounter was categorized by vaccination status into 1 of 3 groups: FI, UnderI, or UnI. The ED course information was collected as it related to the evaluation and management of the
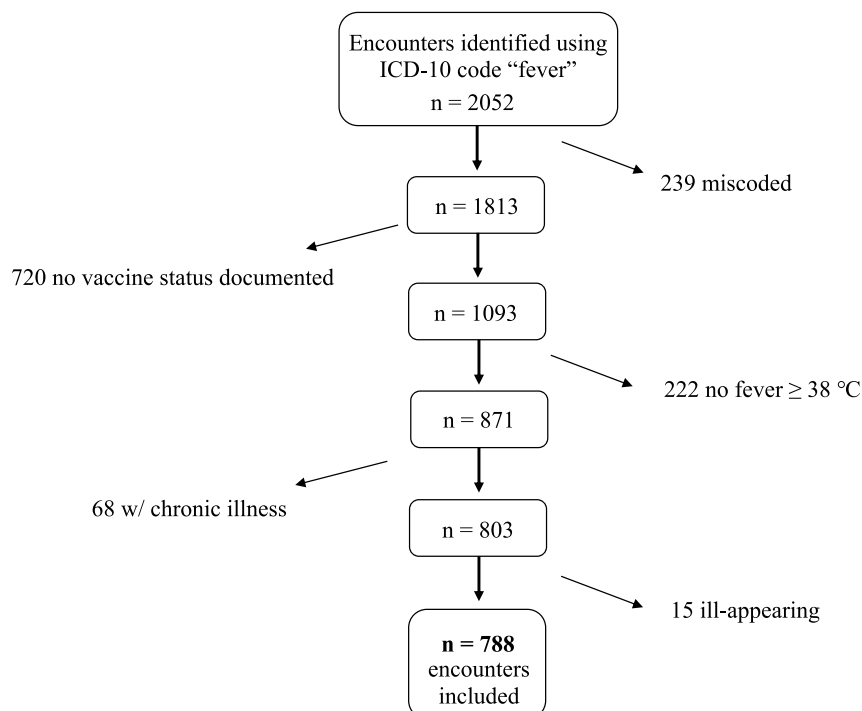

FIGURE 1. Flow diagram of encounters included in chart review.

TABLE 1. Demographic Information

	FI		UnderI		UnI		*P*
Sex							
Male	391	54%	20	46%	15	65%	0.2904
Female	330	46%	24	54%	8	35%	
Age							
3–5 mo	65	9%	1	2%	4	18%	0.3504
6–11 mo	214	30%	16	36%	6	26%	
12–17 mo	152	21%	13	30%	3	13%	
18–23 mo	134	18%	6	14%	3	13%	
24–36 mo	156	22%	8	18%	7	30%	
Race							
White	396	55%	18	41%	7	30%	0.2259
Hispanic	26	4%	3	7%	0	—	
Black	265	37%	20	46%	16	70%	
Asian	17	2%	2	4%	0	—	
Native American	2	0.3%	0	—	0	—	
Pacific Islander	4	1%	0	—	0	—	
Other	11	2%	1	2%	0	—	
Insurance type							
Private	85	12%	4	9%	4	17%	0.0559
Medicaid	616	85%	39	89%	16	70%	
Self-pay	16	2%	1	2%	3	13%	
Military	4	1%	0	—	0	—	

patient during that encounter. Specifically, any laboratory evaluation (urine, serum, or CSF), chest radiography, medical resuscitation (intravenous [IV]/intramuscular antibiotic, steroid or IV fluid administration, supplemental oxygen or breathing treatments), admission, systemic antibiotic prescription on discharge, or 72-hour return visits were identified, and these characteristics were compared between FI, UnderI, and UnI groups.

The χ^2 and Fisher exact tests were used to analyze the differences among immunization status groups. For purposes of logistic regression, UnderI and UnI groups were combined into a non-FI group that was compared against the FI group. The odds ratio (OR)

and 95% confidence intervals (CIs) were calculated, and results were reported in terms of OR, where appropriate. Statistical tests were 2-sided, and $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

During the study time frame, there were 1813 encounters that were appropriately coded by diagnosis with ICD-10 code for fever. Of those, 1093 (60%) included provider-documented immunization status, and 788 (43%) met all inclusion criteria: 23 (3%) UnI, 44 (5.5%) UnderI, and 721 (91.5%) FI. Of the 305 encounters that were excluded, 222 did not have a fever of 38°C and higher documented, 68 had chronic illness, and 15 were ill appearing (Fig. 1). Patient demographics are shown in Table 1; sex, age, race, and insurance type distribution was similar between groups.

Comparisons of testing and management strategies of febrile young children by immunization status are summarized in Table 2. Laboratory testing was obtained in 48% of UnI and 32% of UnderI patients (vs 24% of FI, $P < 0.05$). The odds of obtaining laboratory studies were approximately 0.86 times higher in non-FI than FI patients (OR, 1.86; 95% CI, 1.10–3.14). More specifically, a CBC was obtained in 35% of UnI patients (vs 13% UnderI and 7% FI, $P < 0.01$) and a blood culture was obtained in 30% of UnI patients (vs 7% UnderI and 2% FI, $P < 0.001$). Both CBC and blood culture were obtained more frequently in non-FI patients (OR, 3.18; 95% CI, 1.35–7.48; OR, 7.33; 95% CI, 3.35–17.82). Non-FI patients were also 83% more likely to experience a medical intervention during their PED visit and 99% more likely to receive an antibiotic prescription on discharge from the PED (OR, 1.86; 95% CI, 0.89–3.73; OR, 1.99; 95% CI, 1.13–3.53).

There were no significant differences in rates of chest radiography (16% FI vs 22% UnderI vs 30% UnI, $P = 0.1669$), hospital admissions (3% FI vs 2% UnderI vs 9% UnI, $P = 0.2429$), or 72-hour ED return visits (7% FI vs 2% in UnderI vs 0% UnI, $P = 0.3116$).

DISCUSSION

Our study showed that young children documented by providers as non-FI (UnderI or UnI) underwent higher rates of laboratory

TABLE 2. Differences in Management

	FI (n = 721)	UnderI (n = 44)	UnI (n = 23)	*P*	OR (95% CI)*
Serum, urine, or CSF laboratory test[†]	175 (24%)	14 (32%)	11 (48%)	0.0229	1.86 (1.10–3.14)
CBC	50 (7%)	6 (13%)	8 (35%)	0.0006	3.18 (1.35–7.48)
Blood culture	16 (2%)	3 (7%)	7 (30%)	<0.0001	7.73 (3.35–17.82)
Any urine study	108 (15%)	13 (30%)	4 (17%)	0.0392	
Any CSF study	1 (0.1%)	1 (2%)	0 (0.0)	0.1629	
Chest radiograph	112 (15%)	11 (25%)	5 (22%)	0.1669	1.71 (0.94–3.10)
ED Intervention[‡]	63 (9%)	4 (9%)	6 (26%)	0.0272	1.83 (0.89–3.76)
Hospital admission	22 (3%)	1 (2%)	2 (9%)	0.2429	
Antibiotic prescription at ED discharge[§]	122/698 (18%)	13/43 (30%)	6/21 (29%)	0.0532	1.99 (1.13–3.53)
Return to ED w/in 72 h	50 (7%)	1 (2%)	0 (0.0)	0.3116	

*Odds ratio comparing differences in management between UnderI and UnI as a group versus FI.

†Basic metabolic panel, liver function test, CBC, urinalysis, urine culture, urine dip, C-reactive protein, erythrocyte sedimentation rate, procalcitonin, CSF studies (culture, Gram stain, protein, glucose, viral studies), blood culture, or other. Subgroups listed only represent specific laboratory testing analyzed and will not add up to the group totals shown; overlap also exists such that patients could have had only 1 or multiple tests obtained during the same encounter.

‡Intravenous fluid bolus, IV antibiotics, respiratory support, steroids, breathing treatment, or other.

§Twenty-five patients admitted to hospital and 1 incomplete record not included.

testing and interventions when presenting for fever in the PED. Non-FI children were almost 3 times more likely to have a CBC obtained, almost 8 times more likely to have had a blood culture drawn, and received both ED interventions and antibiotic prescriptions on discharge at almost twice the rate as FI children. This suggests providers' clinical decision making may be influenced by the immunization status of their patients and could reflect a higher index of suspicion for IBI, as was seen in the prevaccine era. Because urinary tract infections are not vaccine-preventable, we completed a sensitivity analysis in which patients who only underwent urine testing were removed. A significant pattern across groups remained (11% FI vs 17% UnderI vs 43% UnI, P = 0.0004). In fact, an even stronger association was found for laboratory testing between the non-FI and FI children (OR, 2.9; 95% CI, 1.5–5.4).

For purposes of logistic regression, UnderI and UnI groups were collapsed for comparison against FI. This was done to reflect our belief that providers' threshold at which they consider a child low risk for IBI is when they are reported as being FI. Therefore, we feel providers likely view UnderI and UnI children at a similarly increased risk of IBI when making clinical decisions about their evaluation and management. Our results support the idea of a substantial difference in provider behavior in diagnostic specimen testing between FI and non-FI groups.

Of equal interest, we did not find higher rates of chest radiography for non-FI patients, which could indicate that providers did not have increased concern for bacterial pneumonia or that they are more comfortable using clinical evidence alone in diagnosing this condition. It is also possible that providers are using laboratory values to guide their decision to obtain chest radiography, as suggested by Finkel et al.[11] Likewise, similar rates of hospital admissions between groups suggest a lack of elevated concern for clinical decompensation in an otherwise healthy child, despite being unvaccinated.

A large portion of parents who choose not to vaccinate their children perceive that this choice reduces risk of medical intervention.[18] Our study suggests otherwise in that UnderI or UnI status increases a child's odds for experiencing invasive testing and management strategies if they were to present to a PED with fever. Taken with the findings of Dunnick et al,[9] that blood culture isolates of unvaccinated children had higher rates of contaminants than true pathogens, it is important for parents to be made aware of this increased risk of medical intervention as they make vaccination decisions for their children. This is especially salient in the current context of the COVID-19 pandemic that has resulted in a dramatic decline in routine childhood immunization rates globally.[19,20]

There were limitations to our study. This is a single-center study involving a single PED, which may limit the generalizability of our results. In addition, given the retrospective study design, our data were limited to extractable information from charts, including whether a provider documented immunization status. It is also possible that there were encounters of febrile children that were missed because they were given an ICD-10 code other than fever. Although immunization status was extracted and coded from the natural language of provider documentation in an effort to capture the motivation behind clinical decisions, it is possible that the clinician's management was not related to the immunization status documented. We opted to rely on provider documentation of immunization instead of an immunization registry to capture the provider's perception of immunization status, which is more likely to influence their decision making than documentation elsewhere that they may not have reviewed.

Our observational study provides insight into the clinical decisions providers are making while taking care of febrile UnderI and UnI children in the PED while lacking an evidence-based guideline. Analyzing the outcomes of the identified non-FI

patients was not within the scope of this study. Further studies are needed to determine if there are truly higher rates of IBI in non-FI children and whether this necessitates additional testing and treatment in this population.

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