

Original Article

## A Comparison of Adult and Pediatric Measles Patients Admitted to Emergency Departments during the 2008–2011 Outbreak in the Midi-Pyrénées Region of France

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**SUMMARY:** The present French and European measles outbreaks show a bimodal distribution: the two most affected populations are infants aged less than 1 year and adults older than 20 years. The purpose of this study was to determine whether there were differences in the clinical presentation and evolution of measles between adult and pediatric patients. We performed a retrospective study of adult and pediatric measles patients admitted to three tertiary-level university hospitals between January 2008 and May 2011. Data were extracted from medical charts and positive laboratory results. Collected data were age, sex, geographical origin, vaccination status, source of exposure, overseas travel before symptom onset, clinical symptoms, risk factors for complications, severity criteria on admission, type of diagnosis, biological abnormalities, complications, and treatments. A total of 305 patients (171 children and 134 adults) were included in the study. The mean age was  $4.6 \pm 4.4$  years in children and  $26.7 \pm 8.1$  years in adults. Children were less often hospitalized than adults (29% vs. 66%). A comparison between hospitalized pediatric ( $n = 49$ ) and adult ( $n = 89$ ) patients revealed that the former had a higher incidence of complications ( $P < 0.0001$ ), more otorhinolaryngological complications (24% vs. 1%;  $P < 0.0001$ ), and a higher incidence of severe criteria on admission ( $P = 0.02$ ). Hospitalized pediatric patients differed from adults in terms of disease severity and complications.

### INTRODUCTION

The measles virus has reemerged as seasonal outbreaks in France and other European countries (1–11). In the Midi-Pyrénées region of France, the measles vaccination rate after one MMR (measles, mumps, and rubella) dose by the age of 24 months (80%) is one of the lowest in the country (5). The distribution of patient age has changed over the last few years; the two most affected populations are infants aged less than 1 year and adults older than 20 years. Among the cases reported to the French Institute for Public Health Surveillance (InVS), the proportion of clinical or laboratory confirmed cases increased from 4% in 2008 to 9% in 2010 (incidence, 98/100,000 inhabitants) in infants aged less than 1 year and from 17% to 38% in adults aged 20 years or older (incidence, 25/100,000 inhabitants) (1,4,12–14).

The aim of this study was to identify differences in the clinical presentation and evolution of measles (hospitalization rate, complications, assisted ventilation, and mortality) between adult and pediatric patients (age, > 15 and 0–15 years, respectively) during the 2008–2011 measles outbreak in the Midi-Pyrénées

region of France.

### MATERIALS AND METHODS

We performed a retrospective and descriptive study of adult and pediatric measles patients admitted to the three different emergency units of our university hospitals in Toulouse, France (Rangueil, Purpan, and Children's Hospitals) between January 2008 and May 2011. Pediatric patients included children aged 0–15 years, and infant patients corresponded to children younger than 1 year. Data were extracted from two sources: medical charts, where the diagnosis was coded B05.8 or B05.9 in the international classification of diseases (ICD-10), and positive blood results confirmed by the virology department of our university hospital. Criteria for inclusion were a clinical diagnosis of measles as defined by the InVS (Table 1), biological confirmation of measles by positive specific IgM antibody detection from serum samples, positive PCR detection of the measles virus in saliva samples, and epidemiological cases. Collected data included patient age; sex; geographical origin; vaccination status; mode of admission (referred by a family physician or pediatrician); source of exposure; clustered cases; overseas travel 7–18 days before symptom onset; clinical symptoms; existence of known risk factors for complications (pregnancy, malnutrition, and preexisting conditions, such as respiratory, cardiac, or neurological diseases, and immunosuppressive disease or treatment);

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severity criteria on admission (cardiocirculatory, respiratory, and neurological criteria; Table 2); date and mode of diagnosis (clinical, biological, or epidemiological) at the hospital level; radiological or biological abnormalities; patient outcomes; rate, length and location of hospitalization; and therapeutic management (pre-hospital or secondary antibiotic therapy, intravenous hydration, oxygen delivery, assisted ventilation, anticonvulsive medication, and intravenous polyvalent immunoglobulin).

**Statistical analysis:** Statistical analysis was performed using the StatView 5.1 (SAS Institute Inc., Cary, N.C., USA) and EpiInfo 6.04fr (VF, ENSP-Epiconcept, Paris, France). In descriptive analysis, data are presented as mean  $\pm$  standard deviation, median with extreme values, or odds ratio (OR) with 95% confidence intervals (CIs), where appropriate, unless otherwise indicated. To compare qualitative variables, the Mantel-

Haenszel chi-squared test was used and the 2-tailed Fischer exact test was employed if the expected value was  $< 5.0$ . For quantitative independent variables, the paired Student's *t*-test was applied. A non-parametric Wilcoxon-Mann-Whitney U test was performed in cases of non-normal distribution. A *P* value  $< 0.05$  was considered statistically significant. Factors independently associated with certain risks (severity, complications, and hospitalization) were identified using a logistic regression model. All variables with a *P* value  $< 0.2$  in univariate analysis were entered into the model.

## RESULTS

**Descriptive analysis:** During the study period, 457 medical files were reviewed and 305 patients were included: 171 pediatric (56%) and 134 adult (44%) patients (Fig. 1). The sex and age distributions of the patients are illustrated in Fig. 2. The mean pediatric age was  $4.6 \pm 4.4$  years (interquartile range, 7 weeks-14.8 years; median, 2 years), and the mean adult age was  $26.7 \pm 8.1$  years (interquartile range, 15-57 years; median, 25 years). The male to female ratio was 1.1 (90 males) in the pediatric group and 1.3 in the adult group (75 males). In total, 34% of all patients were referred to our hospital by a family physician or pediatrician. Table 3 summarizes the principle characteristics of patients divided in three groups: adults aged 15 years or older, children aged less than or equal to 1 year and less than 15 years, and infants aged less than 1 year. The source of measles exposure was known in 29% of patients (39% pediatric and 16% adult). Thirty-four patients (30 pediatric and 4 adult) belonged to clusters of 2 or more affected patients. Four patients had traveled overseas 7-18 days before the onset of symptoms, of which 2 cases were imported from Thailand. Vaccination status was known in 80% of patients (91% in the 0-15-year-old pediatric cohort). Among patients with a known vaccination status, 62% had not been vaccinated and 14% had received a single dose. Of these 305 patients, 86 (28%) were clinical patients; 216 (71%) were laboratory confirmed, and 3 (1%) were epidemiologically confirmed. A chest x-ray was performed in 194 patients (64%) and abnormalities were observed in 44% of

Table 1. Measles case definition of the French Institute for Public Health Surveillance

Criteria for diagnosis	
Clinical cases	
	They are defined by the association of a fever $\geq 38.5^\circ\text{C}$ , an erythematous maculopapular eruption, and at least one of the following signs: conjunctivitis, coryza, cough, Koplick spots
Biological cases confirmed by	
	-serum or saliva sample positive detection (absence of vaccination within the last 2 months) of measles specific IgM or,
	-serum, urine, pharyngeal or saliva sample positive PCR detection for measles or,
	-a seroconversion or a 4-fold rise of measles IgG titer between acute and convalescent phase or,
	-saliva, pharyngeal, or serum sample positive culture
Measles confirmed cases are classified as:	
	Clinical case: patient with all clinical criteria, no biological confirmation or epidemiological link to another confirmed measles case
	Biological case: patient with clinical signs of measles with one or several positive biological confirmation methods
	Epidemiological case: patient with clinical criteria and known to have been exposed to a confirmed measles case (biological or epidemiological case) between 7 to 18 days before eruption

Table 2. Adult and pediatric measles severity criteria on admission

Severity criteria	
Disability	Glasgow coma scale $< 15$ or impaired consciousness or impaired tonus (hypo or hypertonia), agitation, confusion, hallucinations, status epilepticus
Airways/breathing	-High respiratory rate (RR) over 60/min (neonates), 40/min (28 days $<$ age $\leq$ 1 yr), 30/min ( $>$ 1 yr), 25/min (adults) or, -Low RR $< 30$ /min (neonates), $< 25$ /min (28 days $<$ age $\leq$ 1 yr), $< 20$ /min ( $>$ 1 yr), $< 12$ /min (adults) and/or, -Respiratory failure symptoms: cyanosis, nasal flaring, accessory muscle use, suprasternal and intercostal retractions, paradoxical chest-wall movement and/or, -Pulse oximetry $< 92\%$ and/or -Hypoxemia: $\text{PaO}_2 < 70$ mmHg with $\text{FiO}_2 > 0.5$
Circulation	Low blood pressure: systolic blood pressure $< 50$ mmHg (neonates), $< 70$ mmHg (28 days $<$ age $\leq$ 1 yr), $< 80$ mmHg (1 $<$ age $<$ 8 yr), $< 90$ mmHg (8 yr-adults) and, -Tachycardia: pulse rate (PR) $> 180$ b/min (age $\leq$ 1 yr), $> 160$ b/min ( $>$ 1 yr) or, -Bradycardia: PR $< 80$ b/min (age $\leq$ 1 yr), $< 60$ b/min ( $>$ 1 yr), $< 50$ b/min (adults) or, -Peripheral vasoconstriction (capillary refill test $> 3$ s)

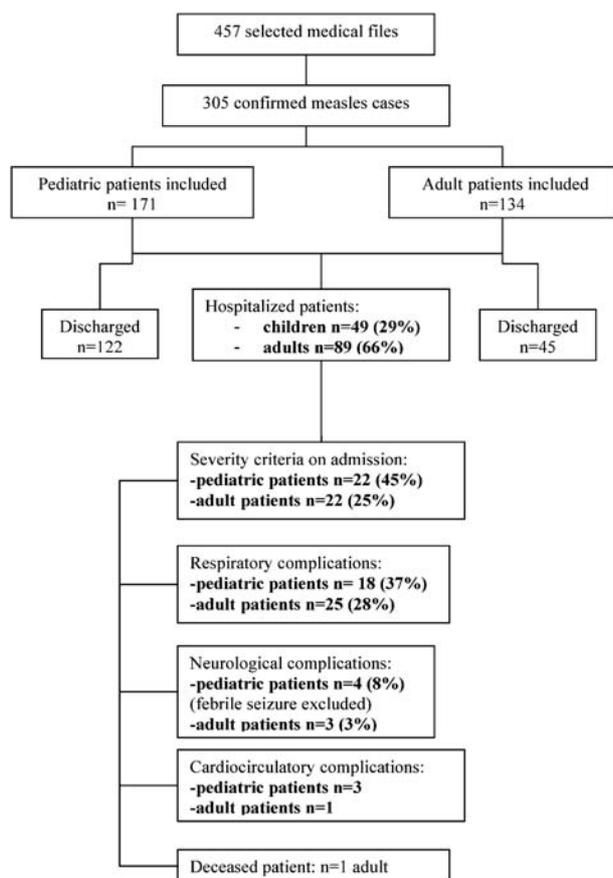


Fig. 1. Study flow chart of pediatric and adult measles patients.

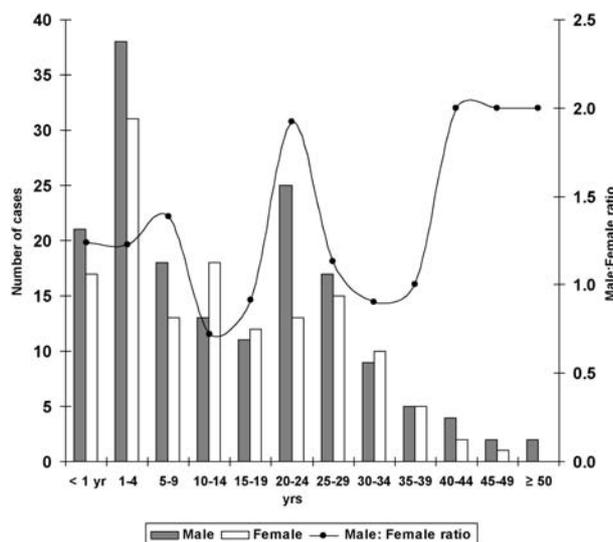


Fig. 2. Measles distribution by age and sex.

patients (pneumonia, 23%). Blood laboratory tests (cell blood count [CBC], platelet count, serum electrolytes, liver enzymes, and C-reactive protein [CRP]) were obtained for 69% of patients (80 children and 130 adults). CBC was abnormal in 93% of patients (lymphopenia, 85%; leukopenia, 31%; neutropenia, 31%; thrombocytopenia, 29%). CRP value was abnormal (>8 mg/L) in 67% of all patients. Preadmission anti-biotherapy was prescribed to 132 patients (87 children

and 55 adults) and was continued or initiated in 27% of patients after evaluation in emergency units. In total, 29% of the pediatric patients were hospitalized (adults, 66%): 10 patients (4 children) in a resuscitation or intensive care unit (assisted ventilation, 56%). Fifty percent of hospitalized patients ( $n = 138$ ) presented with one or more complications (respiratory, neurological, cardiac, or dehydration) and 28% presented with primarily respiratory complications (Table 4). Risk factors for complications were identified in 43 patients (24 pediatric). Twenty-six hospitalized patients (19%) required intravenous hydration. Seven patients (5 children) received intravenous infusion of polyvalent immunoglobulin: a 2-month-old child with a pneumonia; a 10-month-old child with acute pulmonary distress syndrome (ARDS); a 14-year-old girl under immunosuppressive treatment (Cellcept®) for a nephrotic syndrome; 2 boys, aged 7 and 10 years, misdiagnosed with Kawasaki disease; a 16-year-old woman with severe encephalitis; and an immunocompromised 45-year-old woman with leukemia remission, renal failure, and ARDS. The immunocompromised patient died from respiratory and renal failure after 4 weeks of hospitalization. Three patients presented with severe neurological sequelae (quadriplegia and coma, epilepsy and academic delays, and severe ataxia, respectively).

**Univariate analysis: (i) Comparison of clinical presentation and post-emergency orientation between pediatric and adult patients:** A diagnosis was more often based on clinical symptoms in children ( $P < 0.001$ ), and before hospital admission, the mean duration of symptoms was shorter in the pediatric population than in the adult population ( $4 \pm 2$  vs.  $6 \pm 2$  days;  $P < 0.001$ ). Fever and typical eruption were more often present in adults (99 adult [74%] vs. 103 pediatric [60%] patients;  $P = 0.02$  vs. 0.08). Pediatric patients were less often referred than adult patients (26% vs. 44%;  $P = 0.001$ ). Referred pediatric patients were less frequently hospitalized ( $P < 0.0001$ ) than referred adult patients. The distribution of risk factors was similar between adult and pediatric patients (14% vs. 14%;  $P = 0.97$ ) but slightly varied between infants and children (8% vs. 16%;  $P = 0.22$ ). The mean delay before hospital admission was longer in patients with risk factors ( $5.8 \pm 1.8$  days and  $4.9 \pm 1.8$  days;  $P = 0.006$ ). In patients with a known risk factor, there was a higher proportion of hospitalization in the adult group than in the pediatric group (89% vs. 54%;  $P = 0.02$ ).

**(ii) Comparison of severity and complications among hospitalized patients by age and sex:** In the presence of a risk factor, the complication rate was not influenced by age (adult, 80%; pediatric, 83%;  $P = 0.77$ ). The existence of a cardiac or respiratory risk factor was associated with a higher risk of respiratory complications in pediatric hospitalized patients ( $P = 0.007$ ). Pregnant women ( $n = 4$ ) developed no complications. Immunocompromised patients did not develop more respiratory complications (40% vs. 24%;  $P = 0.40$ ), but one immunocompromised woman died. Among hospitalized children, the incidence of complications was higher (94% vs. 58%;  $P < 0.0001$ ). Pediatric hospitalized patients had more otorhinolaryngological complications (24% vs. 1%;  $P < 0.0001$ ); were less dehydrated (6% vs. 26%;  $P = 0.005$ ), had a higher

Table 3. Main characteristics of pediatric and adult measles cases

	Infant ( $< 1$ yr) ( $n = 38$ )	Child (1–15 yr) ( $n = 133$ )	Adult ( $\geq 15$ yr) ( $n = 134$ )	$P^1)$	$P^2)$
Male:female ratio	1.2	1.1	1.3	0.71	0.56
Mean age (yr) (SD)	0.7 (0.2)	5.7 (4.4)	26.8 (8.1)		
Median age (yr)	0.7	4.0	25.0		
Range	7 wk to 11 mo	1 to 14.8 yr	15 to 57 yr		
Geographical origin <sup>3)</sup> , no. (%)	19 (50)	56 (42)	72 (54)	0.39	0.09
Referred by a physician, no. (%)	6 (16)	39 (29)	59 (44)	0.09	0.001
Known source of exposure, no. (%)	16 (42)	51 (38)	21 (16)		
Family, no.	14	36	17	0.17	0.37
Community, no.	2	11	3		
Post-vaccine, no.	0	4	0		
Known vaccine status, no. (%)	37 (97)	118 (89)	90 (67)		
Unvaccinated, no.	34	85 (72)	71 (79)	0.008	0.89
1 dose, %	3	27	12		
2 doses, %	0	6	7		
Confirmed case type					
Clinical case, no. (%)	15 (39)	48 (36)	23 (17)	0.70	0.0001
Koplick spots, no.	6	21	8	0.80	0.6
Biological detection, no. (%)	23 (61)	82 (62)	111 (83)	0.90	$< 0.0001$
Epidemiological link, no. (%)	0 (0)	3 (2)	0 (0)		
Criteria for severity	5 (13)	17 (13)	22 (16)	0.95	0.38
Risk factors <sup>4)</sup>	3 (8)	21 (16)	19 (14)	0.22	0.97
Respiratory factors, no.	3	16	12	0.47	0.54
Asthma	3	13	9	1.00	0.40
Tracheomalacia	0	3	0		
Chronic respiratory insufficiency	0	0	3		
Neurological (encephalopathy)	0	1	0		
Malnutrition	0	2	1		
Cardiac factors, no.	0	1	1		
Congenital cardiac disease	0	1	0		
Dilated cardiomyopathy	0	0	1		
Pregnancy, no.	0	0	4		
Immunocompromised conditions, no.	0	0	3		
Chest x-ray, no. (%)	20 (53)	57 (43)	117 (87)	0.29	$< 0.0001$
Abnormal, no.	75	56	34	0.14	0.0001
Laboratory tests, no. (%)	19 (50)	61 (46)	130 (97)	0.65	$< 0.0001$
Lymphopenia <sup>5)</sup>	9 (47)	46 (75)	123 (95)	0.02	$< 0.0001$
Elevated liver enzymes <sup>5)</sup>	0 (0)	7 (11)	63 (48)		$< 0.001$
Thrombocytopenia <sup>5)</sup>	0 (0)	12 (20)	49 (38)	0.04	0.004
Preadmission antibiotherapy, no. (%)	10 (26)	67 (50)	55 (41)	0.009	0.49
Hospitalization, no. (%)	14 (37)	35 (27)	89 (66)	0.24	$< 0.0001$

<sup>1)</sup>: Compare infants and children.

<sup>2)</sup>: Compare pediatric and adult patients.

<sup>3)</sup>: Toulouse city vs. others (Toulouse is the capital of Midi-Pyrénées region).

<sup>4)</sup>: Known risk factors for complications: malnutrition, pre-existent conditions: respiratory, cardiac or neurological diseases, immunosuppressive disease or treatment, pregnancy.

<sup>5)</sup>: Percentages calculated among sampled patients.

proportion of neurological complications (20% vs. 3%;  $P = 0.001$ ), and presented with severe criteria more often (Tables 4 and 5). When febrile seizures were excluded from the pediatric neurological complications, no difference was observed between the pediatric group and adult group ( $P = 0.25$ ). Compared with female children, male children had more respiratory complications and more severe respiratory compromise criteria on admission (Table 5). Compared with men, hospitalized boys had a higher proportion of severity criteria and respiratory complications ( $P = 0.0001$  and  $P = 0.003$ , respectively). Among adults, there was no differ-

ence in complications between males and females.

**(iii) Comparison of laboratory tests abnormalities by age group:** Laboratory tests were performed less frequently for pediatric patients (Table 3). CBC abnormalities (leukopenia, lymphopenia, thrombocytopenia), elevated serum alanine aminotransferase (ALAT) ( $2 \times N$ ), or abnormal CRP ( $> 8$  mg/L) had a linear age-related augmentation (linear trend  $\chi^2$  test,  $P < 0.001$ ; OR, 1.0 in infants [age,  $< 1$  year], 5.2 in children [age, 1–15 years], and 59.5 in adults [age,  $> 15$  years]). Abnormal CBC or CRP values were not associated with a more severe disease state ( $P = 0.42$  and  $0.45$ , respectively),

## Comparison of Pediatric and Adult Measles

Table 4. Measles complications in pediatric and adult hospitalized patients

Complication, no. (%)	Infant (< 1 yr) (n = 14)	Child (1-15 yr) (n = 35)	Adult (≥ 15 yr) (n = 89)	<i>P</i> <sup>1)</sup>	<i>P</i> <sup>2)</sup>
Intensive care unit	2 (14)	2 (6)	6 (7)	0.56	0.74
Dehydration <sup>3)</sup>	0 (0)	3 (9)	23 (26)	0.55	0.005
Respiratory	6 (50)	10 (29)	23 (28)	0.50	0.40
Pneumonia	3 (21)	6 (17)	21 (24)	0.73	0.48
Bronchiolitis	3 (21)	3 (9)	0 (0)		
Asthma <sup>4)</sup>	0 (0)	0 (0)	1 (1)		
ARDS <sup>5)</sup>	0 (0)	1 (3)	1 (1)		
Neurological	0 (0)	10 (29)	3 (3)	0.02	0.001
Seizures	0 (0)	6 (17)	0 (0)		
Encephalitis	0 (0)	2 (6)	1 (1)		0.29
Meningitis	0 (0)	1 (3)	1 (1)		
Miscellaneous	0 (0)	1 (3)	1 (1)		
Cardiac	0 (0)	3 (9)	1 (1)	0.55	0.12
Myocarditis	0	0	1		
Coronary arteritis	0	2	0		
Pericarditis	0	1	0		
Otorhinolaryngologic					
Acute laryngitis	3 (21)	9 (7)	1 (1)	0.53	<0.0001
Miscellaneous					
Antiphospholipid syndrome	0	0	1 (1)		
Hemophagocytic syndrome	0	2 (6)	0		
Antibiotherapy	8 (57)	22 (63)	24 (27)	0.71	<0.0001
Severe criteria	5 (36)	17 (49)	22 (25)	0.65	0.02
Oxygen delivery	1 (7)	10 (29)	19 (21)	0.10	0.88
Assisted ventilation	1 (7)	2 (6)	2 (2)	0.64	0.24
Death, no.	0	0	1		

<sup>1)</sup>: Compare infants and children.

<sup>2)</sup>: Compare pediatric and adult patients.

<sup>3)</sup>: Necessity of intravenous hydration.

<sup>4)</sup>: Considered as a complication if patients had no previous asthmatic condition.

<sup>5)</sup>: ARDS, acute respiratory distress syndrome.

Table 5. Comparison of measles complications depending on sex between pediatric and adult hospitalized patients

	Adult		Child (0-15 yr)		<i>P</i> <sup>1)</sup>	OR (95% CI)	<i>P</i> <sup>2)</sup>
	Male	Female	Male	Femal			
Hospitalization	52 (69)	37 (63)	27 (30)	22 (27)	0.68	—	0.42
Resuscitation unit	2 (4)	4 (11)	3 (11)	1 (5)	0.38	—	0.19
Severity criteria on admission	9 (17)	13 (35)	16 (59)	6 (27)	0.028	3.88 (1.2-13.0)	0.058
Hemodynamic failure	1	0	5	1	0.20		0.58
Respiratory failure	9	12	13	3	0.01	5.88 (1.2-32.3)	0.09
Neurological failure	0	1	1	1	0.70	—	0.42
Respiratory complication	10 (19)	12 (32)	14 (52)	4 (18)	0.02	4.85 (1.1-22.7)	0.15
Pneumonia	10	11	7	2	0.12	—	0.25
Oxygen delivery	8	11	9	2	0.08	—	0.11
Assisted ventilation	1	1	2	1	0.58	—	0.66

<sup>1)</sup>: Compare male and female among pediatric patients.

<sup>2)</sup>: Compare male and female among adult patients.

more complicated disease ( $P = 0.86$  and  $0.36$ , respectively), or higher hospitalization rate ( $P = 0.21$  and  $0.07$ , respectively).

**Multivariate analysis:** Factors independently associated with severity criteria on admission were the existence of complications (OR, 16.7; 95% CI, 2.1-124.4;  $P$

$= 0.007$ ), abnormal chest x-ray (OR, 4.4; 95% CI, 2.0-9.7;  $P < 0.001$ ), and existence of risk factors (OR, 2.8; 95% CI, 1.2-6.7;  $P = 0.02$ ). Factors independently associated with complications were the existence of risk factors (OR, 3.03; 95% CI, 1.1-8.3;  $P = 0.03$ ) and an abnormal CRP value (OR, 2.9; 95% CI, 1.56-5.3;  $P <$

0.001). Factors independently associated with the risk of hospitalization were the existence of severity criteria on admission (OR, 35.1; 95% CI, 4.5–273.0;  $P = 0.0007$ ), an abnormal CRP value (OR, 3.6; 95% CI, 1.6–7.9;  $P = 0.001$ ), presence of risk factors (OR, 3.2; 95% CI, 1.1–9.8;  $P = 0.04$ ), and being referred by a physician or pediatrician (OR, 2.1; 95% CI, 1.1–4.1;  $P = 0.03$ ).

## DISCUSSION

The present French and European measles outbreaks show a bimodal distribution between children and adults: infants younger than 1 year and adults older than 20 are the two most affected populations. Approximately 95%–99% of maternal specific antibodies disappear from infants by 6 months of age, which explains the susceptibility of this population to develop the disease (15,16). In young healthy adults, the absence of vaccination has been reported to be the leading cause of measles infection, however, in the present study, it was the primary cause in children older than 1 year and adults without any difference. Before hospital admission, a clinical diagnosis was less frequent in adults (17%). Prehospital clinical recognition of measles is easier in children, thereby resulting in a lower proportion of laboratory tests to confirm a diagnosis. During the study period, initial symptoms of a fever or cough in a pediatric patient frequently initiated a parental cause of concern that led to earlier consultations at a pre-eruptive disease stage and a consequent higher chance of detecting Koplick spots. When the clinical presentation is doubtful, the serum detection of specific IgM antibodies is recommended and is 98% sensitive if realized at least 3 days after the rash onset. On the other hand, the RT-PCR technique to detect measles virus nucleic acid in saliva is a more expensive method and should be chosen when direct evidence of the virus is necessary (for example, in immunocompromised patients) (17). The hospitalization rate for measles infections varies by age and underlying conditions with an average rate of 30% in the United States and Europe (5,18). This rate has massively increased since 2009 (when it was less than 40%), reaching 80% in 2010 (12–14). Recent studies have demonstrated that patients aged less than 1 year and patients older than 20 years had the highest hospitalization rates (1,5–11). Because they were much less referred, the pediatric patients included in this study represented the general pediatric population better than the adult patients represented its counterpart. Therefore, we only compared complication types and rates among hospitalized patients. In the general population, children with measles have fewer complications than adults (17–20), with the complication rate varying from 9% to 14% in France (1,5,21) and from 11% to 50% in Europe (6–11). Infants aged less than 1 year included in this study did not present with more severe symptoms or complications than older children but were hospitalized at a higher rate. We believe that infants were more likely to have been hospitalized on the basis of only their age criteria and the lack of knowledge of the disease severity before the publication of recent pediatric outbreaks throughout Europe. Some studies have provided complication rates by sex and showed equal rates for men and women (18). Here, we showed that boys had a

higher proportion of severe criteria than girls or male adults (Table 5), which could be related to the higher proportion of risk factors (primarily asthma) among boys than among girls (33% vs. 16%) or male and female adults (33% vs. 21% and 18%), although there was no significant difference. Respiratory complications are reported to be more frequent in adults and increase with age (17–19). Despite a more frequent rate of viral or bacterial pneumonia in adults, a higher risk of respiratory failure was not observed, which required assisted ventilation during the study period. The study rate of adult pneumonia (24%) was similar to that published by Filia et al. (10). Because measles has a high tropism for the respiratory tract, pulmonary radiographic changes are common, and no correlation has been found between the severity of disease and chest x-ray abnormalities (17,18,20). In our multivariate analysis, the presence of respiratory risk factors (primarily asthma) was associated with a higher risk of respiratory complications in pediatric patients. Dehydration has multiple causes (fever, profound asthenia and anorexia, and emesis) and often leads to hospitalization (32%) for intravenous correction (17,18). Surprisingly, this complication was more frequent among hospitalized adults (26%), which could be related to delayed consultation after symptom onset. Hepatic involvement is commonly described in adult patients and often limited to an ALAT elevation (17,18). Similar to ALAT elevation, the incidence of lymphopenia and thrombocytopenia had a linear age-related augmentation. In the present study, the incidence of neurological complications was higher in hospitalized pediatric patients. At the national and European levels, the rate of post-measles infectious encephalitis is reportedly 0.1% (5,17,18), and the overall incidence is between 1 and 3 per 1,000 patients. Thus, this complication is not rare but poses a potentially serious risk of motor and cognitive sequelae (15%–40%) (17,18). The small number of encephalitis patients included in this study prevented us from comparing the incidence between pediatric and adult patients. However, the number of cases was similar to others described in reports of measles outbreaks in France or Europe (5,7,10). The increase in measles infections among young infants has been associated with a higher risk of subacute sclerosing panencephalitis within the following 7–10 years (22–24). Other uncommon complications were observed in our study that involved 4 children and 1 adult: a case of coronary arteritis (male, 7 years); coronary arteritis with pericardial effusion (male, 12 years); severe myocarditis complicated by an antiphospholipid syndrome (male, 43 years); and 2 cases of hemophagocytic syndrome (female, 21 months and male, 12 years). The 2 pediatric cases of coronary arteritis initially diagnosed and treated as Kawasaki disease were finally confirmed as measles because both were positive for specific IgM antibodies, had no biological signs of inflammation, did not develop thrombocytosis early or later in the biological evolution of their disease, and did not present any desquamation of the extremities. To our knowledge, this uncommon complication has rarely been reported and has been reported only in adult patients (25). Several risk factors have been recognized and described in association with more severe presentations (immunosuppression, infancy, pregnan-

cy, malnutrition, vitamin A deficiency, and sex) (17,18,26,27). The presence of a risk factor influenced the rate, length, and location of hospitalization. In our pediatric patients, the presence of a risk factor tended to be associated with a higher risk of being transferred to a resuscitation or intensive care unit, particularly among the infant group. If there were no such risk factors, hospitalized children (0–15 years) did not show a higher proportion of complications than hospitalized adults. Antibiotherapies were more often prescribed to pediatric patients before hospital admission, which could be related to early presentation in the pre-eruptive stage, where fever and cough were the primary clinical symptoms. The use of intravenous infusion of polyvalent immunoglobulin has been reported in patients with severe respiratory and neurological complications (28–30). Other than the 2 patients misdiagnosed with Kawasaki disease, 2 other children with risk factors received this treatment (an immunocompromised condition and a 2-month-old infant); however, its use was misemployed, as is indicated for prophylactics. Contrary to the popular belief that measles is a benign illness, this disease can lead to death because the overall mortality rate is 0.03%–0.5% in infected populations and 0.97%–1.1% in hospitalized patients (31–34). Before the age of 5 years and after the age of 20 years, the mortality rate of measles is higher (18) and seems to be currently higher in female patients (31,34).

Disease severity and complications differ among hospitalized pediatric and adults patients. Among hospitalized pediatric patients, there were differences in sex, with a higher proportion of complications and severe criteria in males. However, compared to older children, we did not find a higher proportion of complications among infants aged less than 1 year.

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