USJ 1875
Université Saint-Joseph de Beyrouth
Vice-rectorat à la recherche

Les **journées** de la **recherche**

Pollution
Environnement
Santé

Jeudi 9 et vendredi 10 mai 2019

Recherche à l'USJ

Campus des sciences médicales

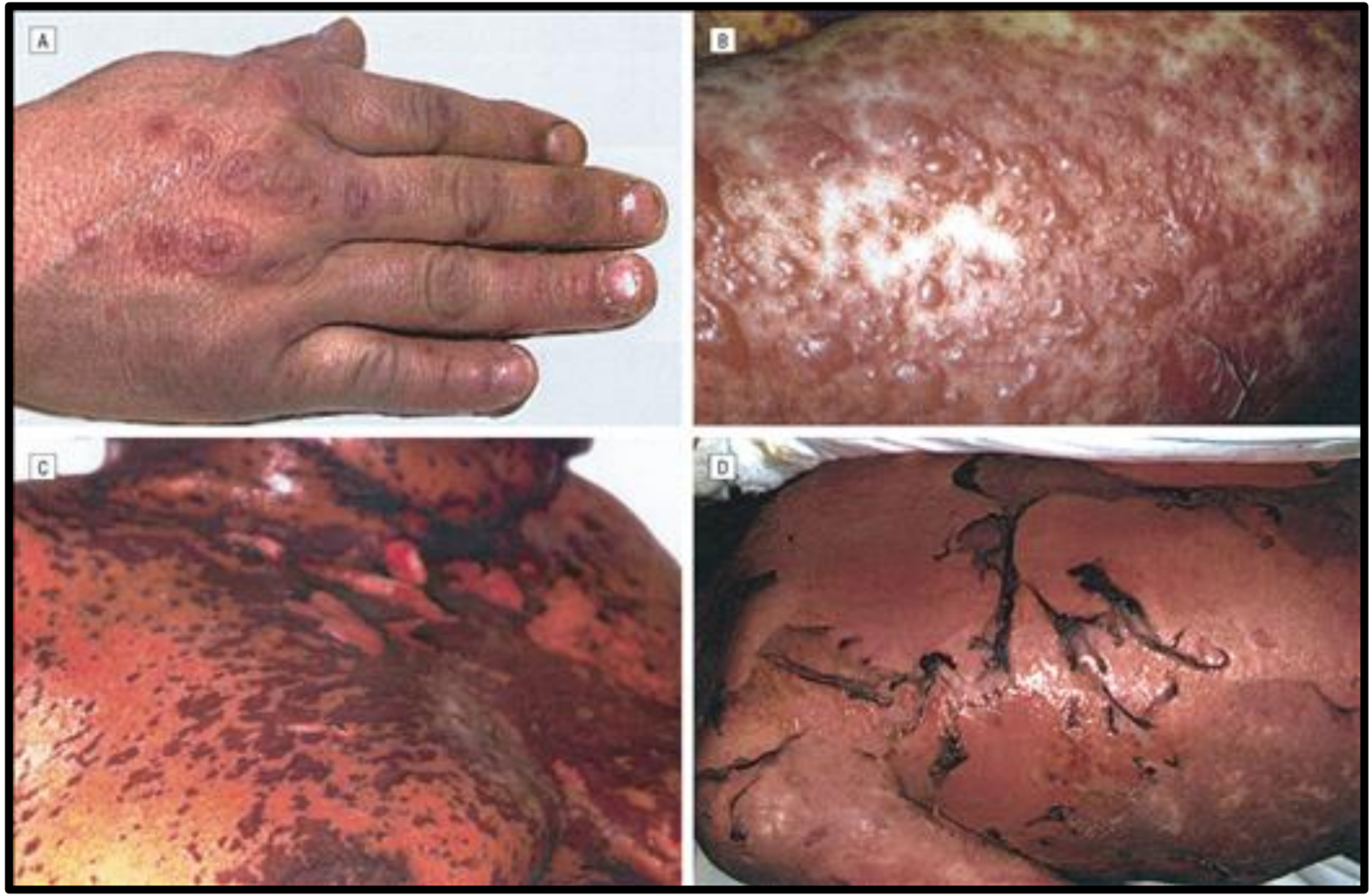
L’érythème polymorphe, au delà des cocardes

Elio Kechichian, MD

Chargé d'enseignement à la Faculté de Médecine de l’USJ

Dermatologue- Hôtel Dieu de France

Beyrouth, Liban


A
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C
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BJD British Journal of Dermatology

Research Letter

A large epidemiological study of erythema multiforme in France, with emphasis on treatment choices

E. Kechichian, S. Ingen-Housz-Oro ✉, E. Sbidian, F. Hemery, C. Bernier, C. Fite, J. Delaunay, D. Staumont-Sallé, F. Toukal, N. Dupin, C. Abasq, M. Samimi, C. Picard, V. Hebert, C. Prost, J.-B. Monfort, B. Milpied, P. Wolkenstein, O. Chosidow

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E.K. and S.I.H.O. contributed equally to this study.

Funding sources: none.

Conflicts of interest: none to declare.

REVIEW

Triggers, clinical manifestations, and management of pediatric erythema multiforme: A systematic review

Samer Zoghaib, MD, Elio Kechichian, MD, Karim Souaid, MD, Boutros Soutou, MD, Josiane Helou, MD, and Roland Tomb, MD, PhD

Beirut, Lebanon

Background: Erythema multiforme (EM) is an acute inflammatory mucocutaneous condition. EM is rarely described in children and infants.

Objective: To investigate the triggers, clinical manifestations, and treatment of pediatric EM.

Methods: Systematic literature review of pediatric EM.

Results: After full-text article review, we included 113 articles, representing 580 patients. The mean age was 5.6 years, ranging 0.1-17 years. Infectious agents were the main triggers: herpes simplex virus (HSV) in 104 patients (17.9%) and *Mycoplasma pneumoniae* in 91 patients (15.7%). In total, 140 cases (24.1%) were drug-related and 89 cases (15.3%) had other triggers, such as vaccines (19 patients, 3.2%). In total, 229 patients had EM major (39.5%). Treatment was supportive care only (180 patients, 31.1%), systemic corticosteroids (115 patients, 19.8%), antivirals (85 patients, 14.6%), and antibiotics (66 patients, 11.3%), mostly macrolides (45 patients, 7.7%). Long-term sequelae were rare (1.3%). Pediatric EM was reported in 19 infants (3.2%). The main trigger was vaccination (9 patients). Infantile EM was EM major in 2 cases and EM minor in 17. Infants were less prone to develop EM major than older children ($P < .01$). Pediatric EM was recurrent in 83 cases (14.3%), which was triggered by HSV in 36 patients (61%). Recurrence affected older children.

Limitations: Potential confusion between Steven Johnson syndrome and EM major in addition to publication bias.

Conclusion: Pediatric EM is a rare disease, mainly triggered by infections. This condition can affect all mucosal surfaces, most commonly the oral mucosae. The diagnosis is clinical, and management relies on supportive care. Vaccines are a particular trigger in infants. Recurrent cases are most commonly linked to HSV. Dermatologists and pediatricians should be aware of this potentially recurrent and severe condition. (J Am Acad Dermatol https://doi.org/10.1016/j.jaad.2019.02.057.)

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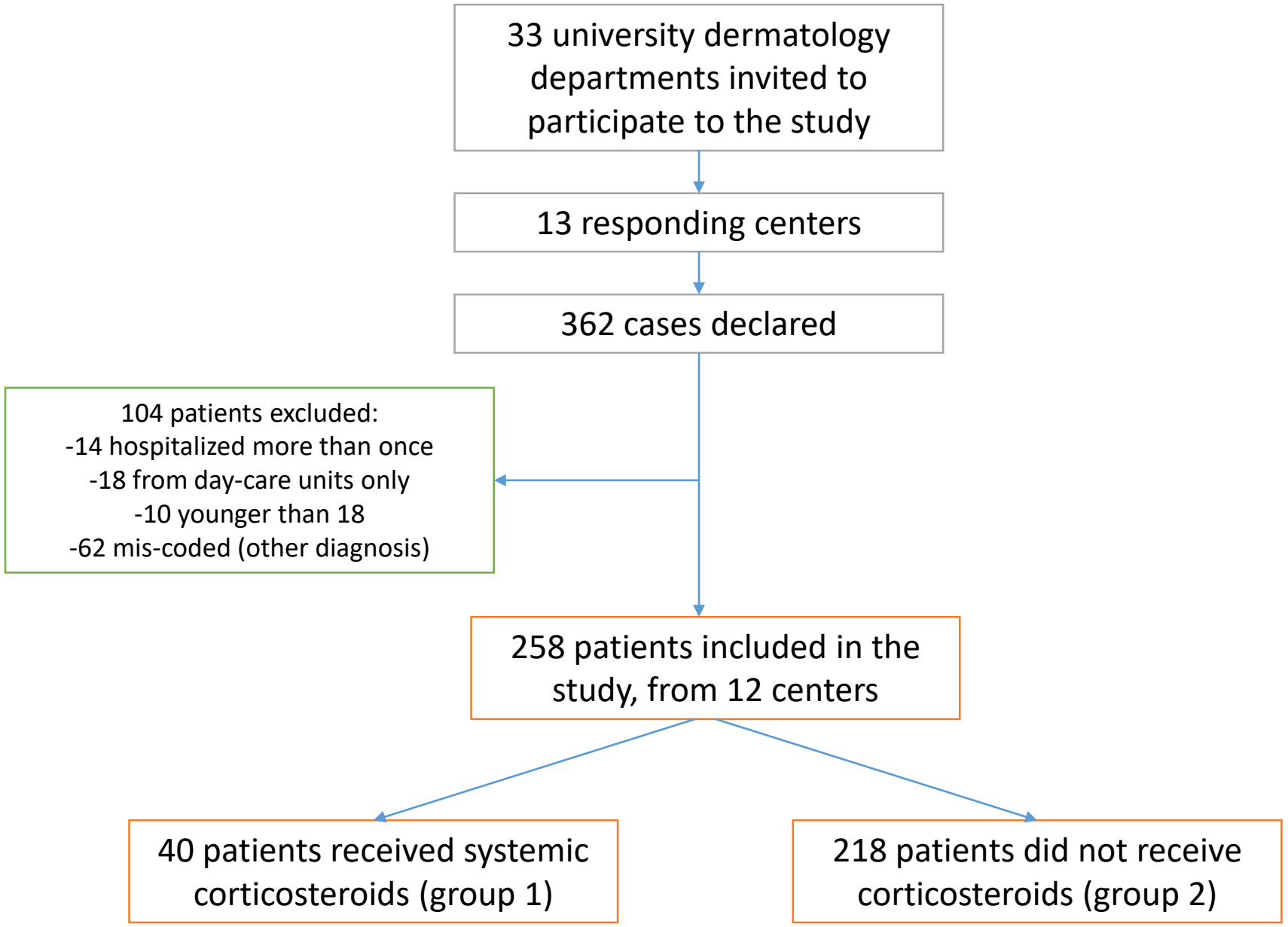

Figure 1. Flow chart of patient inclusion

Table 1. Characteristics of patients with and without systemic corticosteroids (SCS) treatment for erythema multiforme (EM)					
	Total n=258	With SCS n=40	Without SCS n=218	OR (95% CI)	p value*
Males, no. (%)	158 (61.2)	22 (53.7)	136 (62.4)	1.1 (0.56–2.14)	0.6
Age, mean (SD)	36.9 (16.9)	30.2 (12.9)	38.2 (17.3)	Not applicable	<0.01
Comorbidities[$], no. (%)	96 (37.2)	11 (26.8)	86 (39.4)	0.76 (0.36–1.59)	0.11
Previous EM episode, no. (%)	94 (36.4)	27 (65.9)	67 (30.7)	5.92 (2.89–12.14)	<0.01
EM requiring multiple hospitalizations, no. (%)	38 (147)	13 (31.7)	25 (11.5)	4.49 (2.06–9.79)	<0.01
Duration of symptoms before hospital admission, days, median (range)	6 (0-60)	7 (0-60)	6 (1-32)	Not applicable	0.73

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Cause, no. (%)	Total n=258	With SCS n=40	Without SCS n=218	OR (95% CI)	p value*
Herpes simplex virus 1 or 2 infection	108 (41.9)	16 (39)	92 (42.2)	1.2 (0.61–2.38)	0.86
Mycoplasma pneumoniae infection	54 (20.9)	4 (9.8)	50 (22.9)	0.36 (0.12–1.05)	0.09
Other	23 (8.9)	3 (7.5)	20 (7.7)	0.96 (0.27–3.41)	0.43
Idiopathic	67 (26)	17 (41.5)	50 (22.9)	3.07 (1.53–6.18)	<0.01
Previous herpes virus infection	110 (42.6)	17 (41.5)	93(42.7)	1.31 (0.67–2.58)	1
Symptoms (%)					
Fever	85 (32.9)	16 (39)	69 (31.7)	1.83 (0.92–3.64)	0.27
Weight loss	26 (10.1)	8 (19.5)	18 (8.3)	3.33 (1.34–8.29)	0.04
Fatigue	199 (76.4)	30 (73.2)	69 (31.7)	8.22 (3.82–17.69)	<0.01
Decreased oral food intake	165 (64)	27 (65.9)	138 (63.3)	1.81 (0.89–3.66)	0.71
Cough and/or shortness of breath	61 (23.6)	7 (17.1)	55 (25.2)	0.78 (0.33–1.87)	0.39

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Type of EM[$], no. (%)					
Minor	85 (32.9)	11 (26.8)	74 (33.9)	0.94 (0.45–1.99)	0.31
Major	171 (66.3)	28 (68.3)	143 (65.6)	1.88 (0.91–3.85)	
Treatment used, no. (%)					
Acyclovir	119 (46.1)	19 (46.3)	100 (45.9)	1.43 (0.73–2.79)	0.06
Macrolide antibiotic	52 (20.2)	4 (9.8)	48 (22)	0.49 (0.17–1.43)	0.03
Length of hospital stay, days, median (range)	5 (1-45)	6 (1-19)	5 (1-45)	Not applicable	0.15

Qui a beneficié des cortiocoïdes?

- ATCD EP
- ATCD hospitalisation pour EP
- Perte de poids et fatigue
- Utilisation de Macrolide

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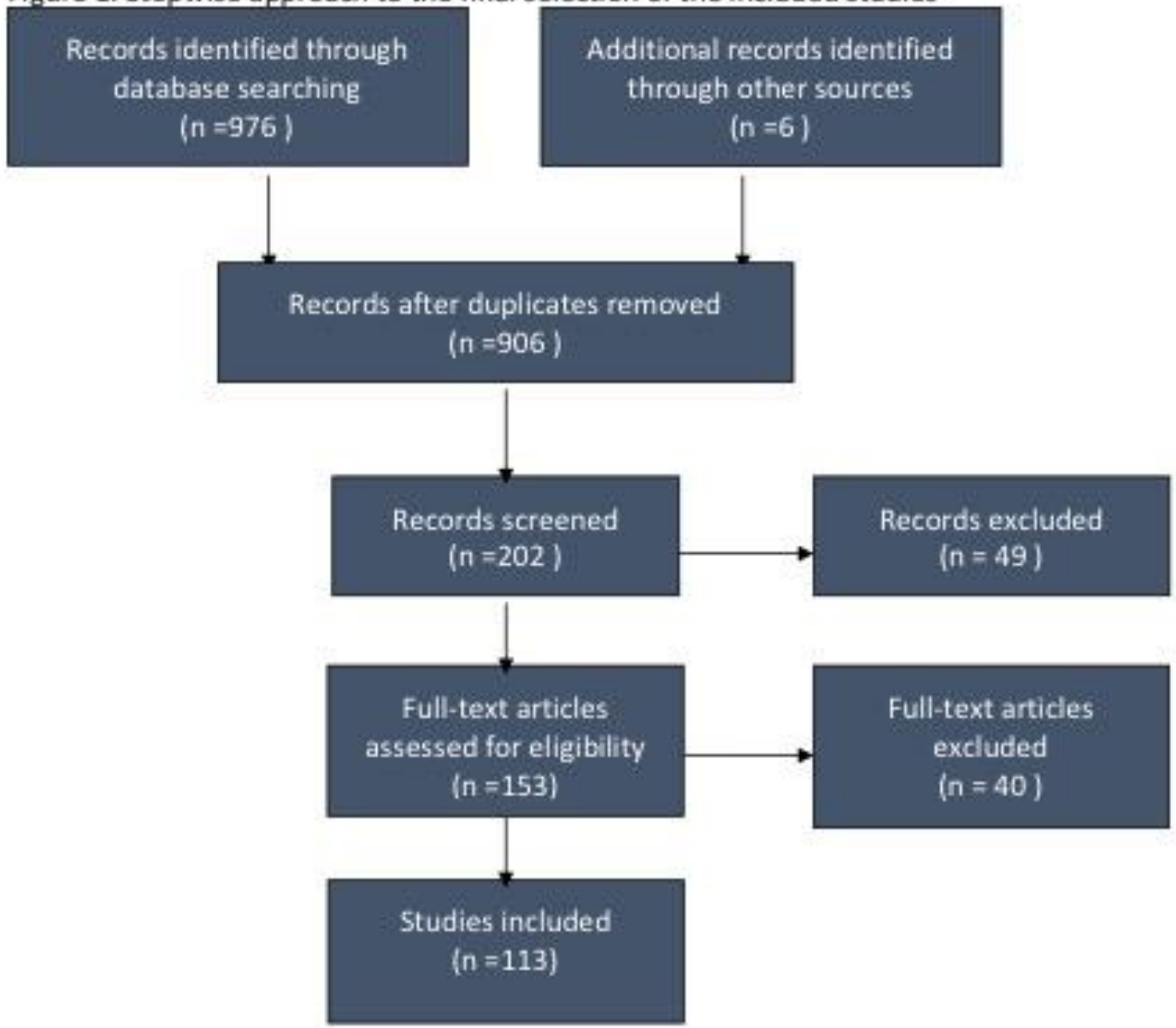
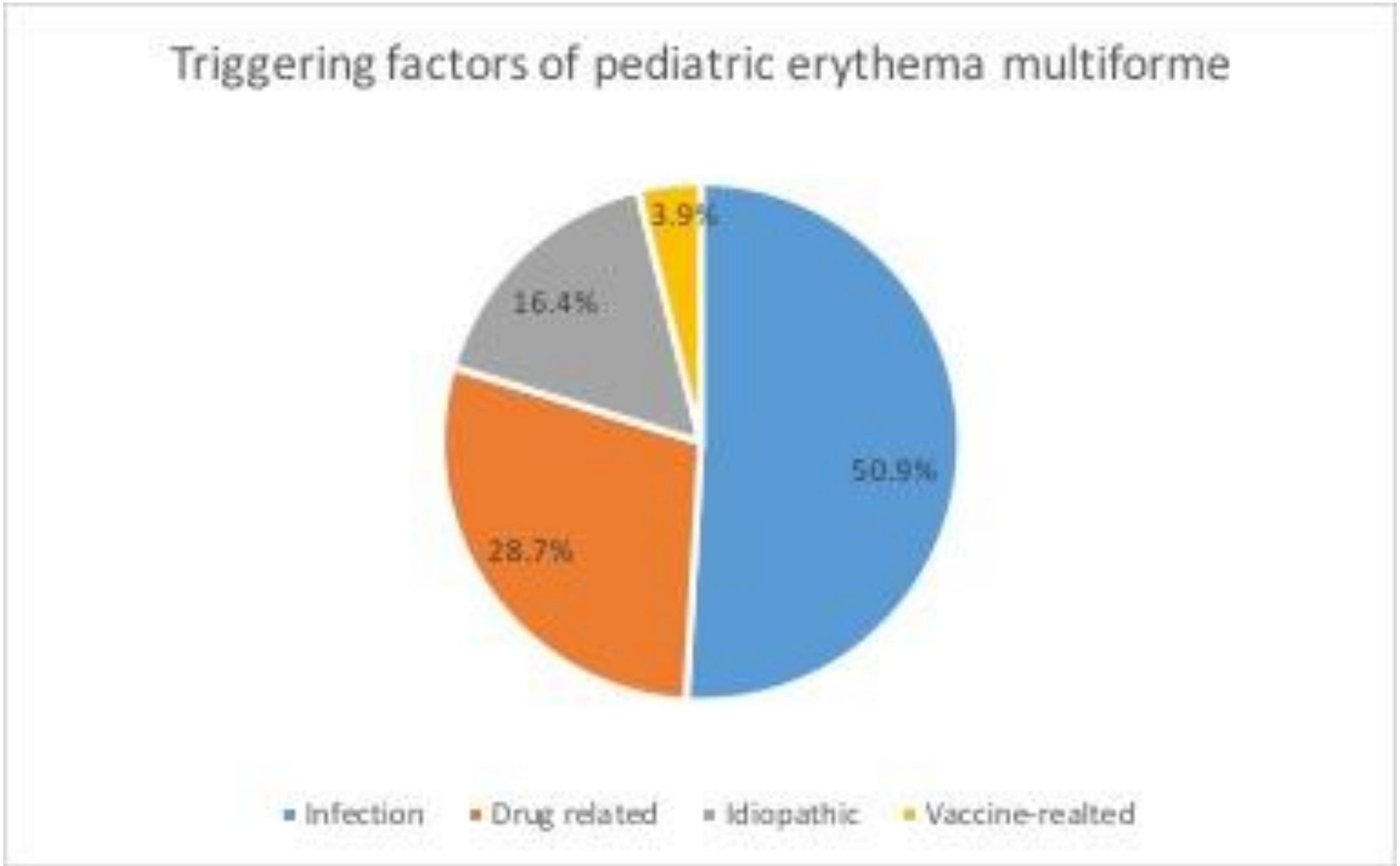
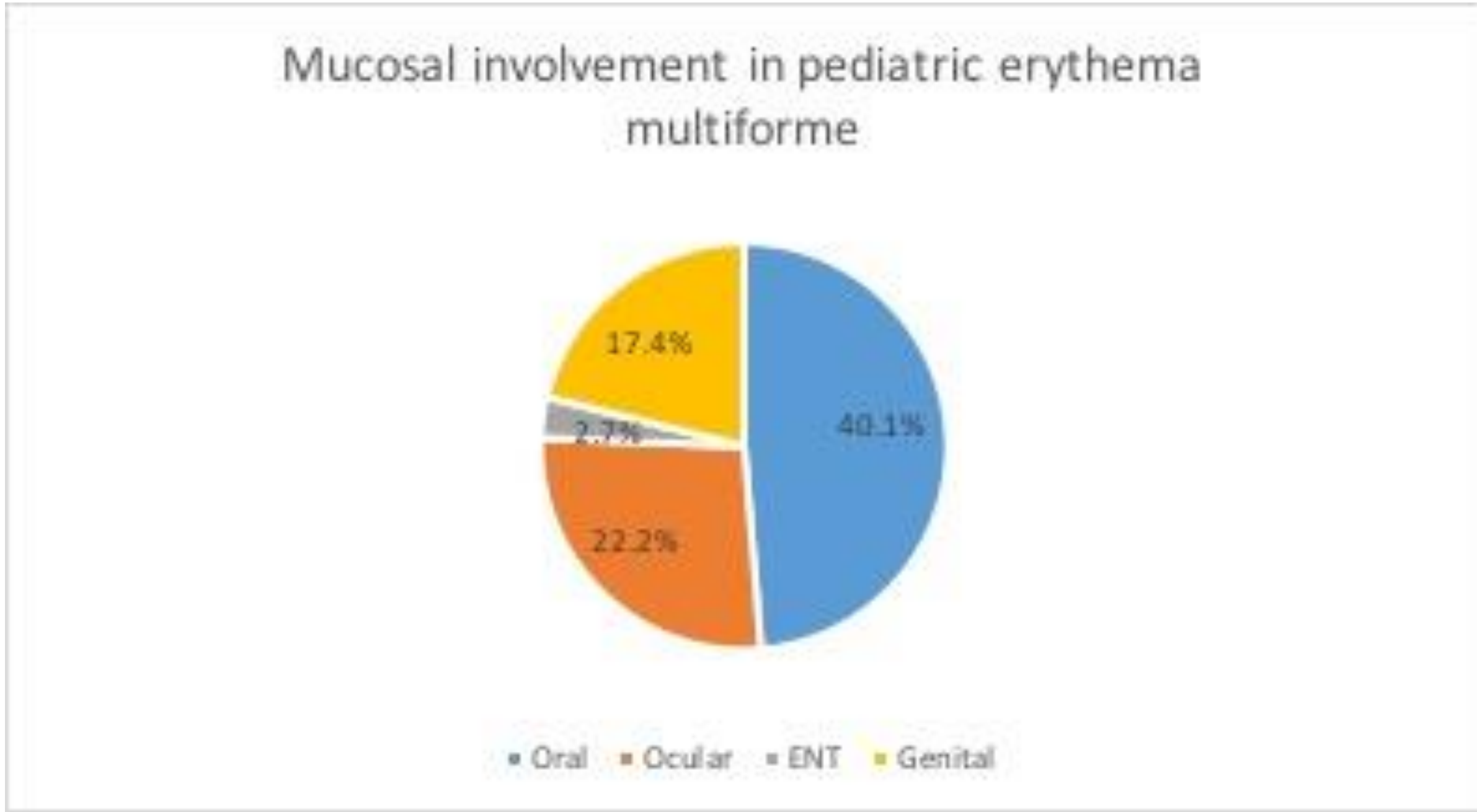
Key words: diagnosis; erythema multiforme; etiology; pediatric; treatment.

Figure 1. Stepwise approach to the final selection of the included studies




Triggering factors of pediatric erythema multiforme
3.9%
16.4%
50.9%
28.7%
Infection
Drug related
Idiopathic
Vaccine-realted


Mucosal involvement in pediatric erythema multiforme
17.4%
40.1%
2.7%
22.2%
Oral
Ocular
ENT
Genital

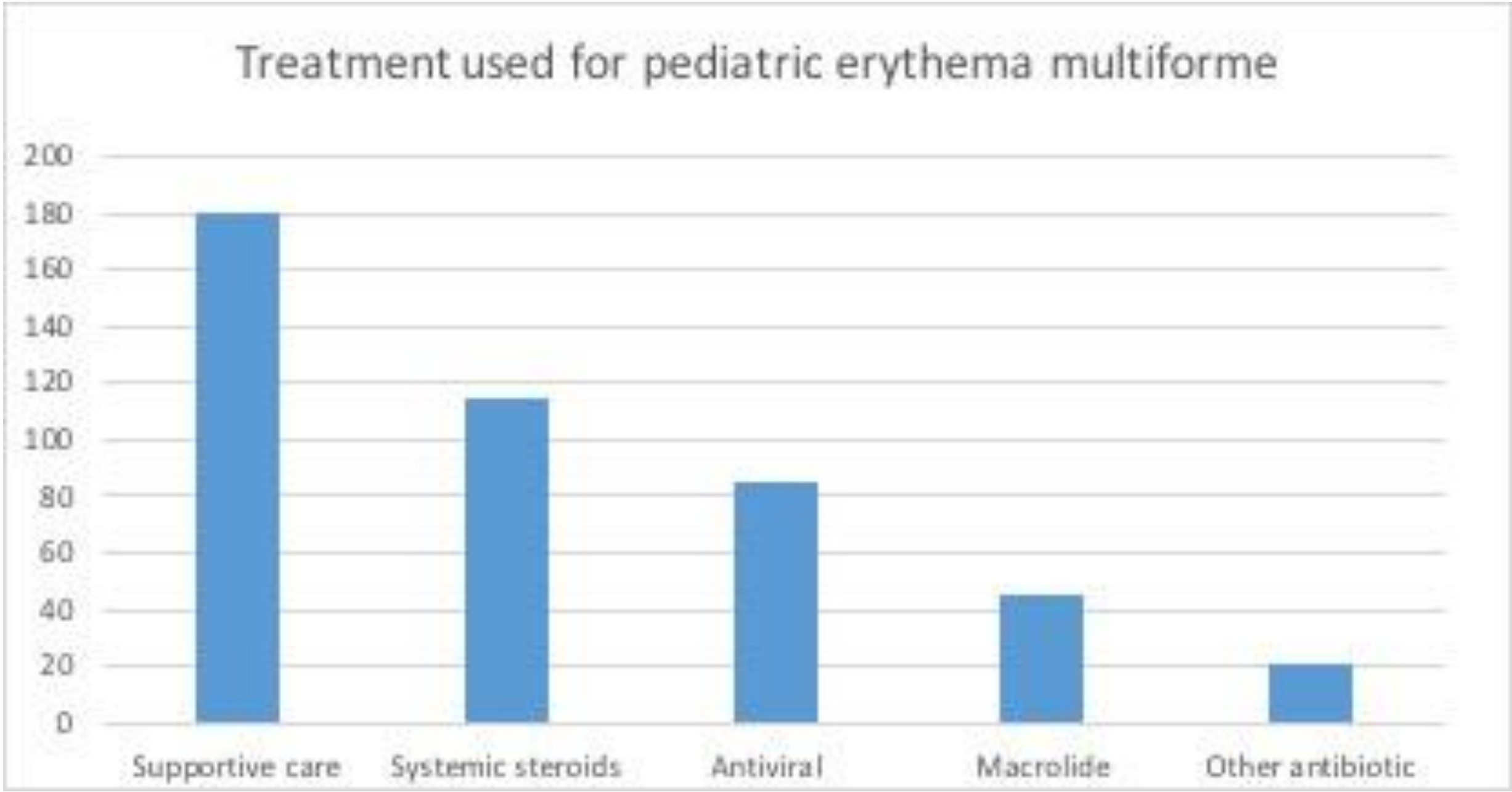

Treatment used for pediatric erythema multiforme
200
180
160
140
120
100
80
60
40
20
0
Supportive care
Systemic steroids
Antiviral
Macrolide
Other antibiotic

Table II. Characteristics of the pediatric erythema multiforme patients

Variable	Overall	Infants*	Children*	*P* value
Patients, n	580	19	270	
Age, y, mean ± standard deviation (range)	6.1 ± 5.6 (0.1-17)	0.37 ± 0.3 (0.06-0.99)	7.5 ± 5 (1-17)	
Male sex (%)	335 (57.8)	10 (52.6)	164 (60.7)	.4
Comorbidities† (%)	41 (7)			
Recurrent erythema multiforme, n (%)	83 (14.3)	1 (5.3)	41 (15.2)	.3
Trigger, n (%)				
Herpes simplex virus	104 (17.9)	1 (5.3)	49 (18.1)	.2
Mycoplasma pneumoniae	91 (15.7)	0	53 (19.6)	.02
Other infection	84 (14.5)	6 (31.5)	69 (25.6)	.5
Drug	140 (24.1)	0	38 (14.1)	.14
Vaccine	19 (3.2)	9 (47.3)	10 (3.7)	<.01
Other cause	70 (12)			
Idiopathic	80 (13.8)	3 (15.8)	48 (17.8)	1
Erythema multiforme major, n (%)	229 (39.5)	2 (10.5)	141 (52.2)	<.01
Mucosa, n (%)				
Average affected per patient	1	0.15	0.99	.009
Oral		2 (10.5)	127 (47)	<.01
Ocular		0	78 (28.9)	<.01
Ears, nose, and throat		0	9 (3.3)	<.01
Nose		0	4	
Pharynx		0	4	
Ear		0	1	
Genital		0	60 (22.2)	<.01
Skin biopsy done, n (%)	58 (10)	12 (62.3)	46 (17.0)	<.01
Abnormal blood test, n (%)	136 (23.4)	9 (47.4)	75 (27.8)	.11
Treatment used, n (%)				
Only supportive care	180 (31.0)			
Systemic corticosteroids	115 (19.8)	2 (10.5)	80 (29.6)	.11
Antiviral	85 (14.6)	1 (5.3)	39 (14.4)	.48
Macrolide	45 (7.7)	0	41 (15.2)	.08
Other antibiotic	21 (3.6)	2 (10.5)	19 (7)	.63
Topical corticosteroids	12 (2)			
Sequelae, n (%)	8 (1.3)	0	8 (3.0)	1
Duration, d, median (range)	12.4 (5-14)	14 (7-14)	12.4 (7-14)	.4

*The studies that included both infants and older children altogether without specifying the disease characteristics in each age category were excluded from this table to make the comparison possible between the 2 age groups.

†The comorbidities were convulsive disorders, psychiatric disorders such as generalized anxiety disorder, cryoglobulinemia (in a minority of cases), and atopic dermatitis.

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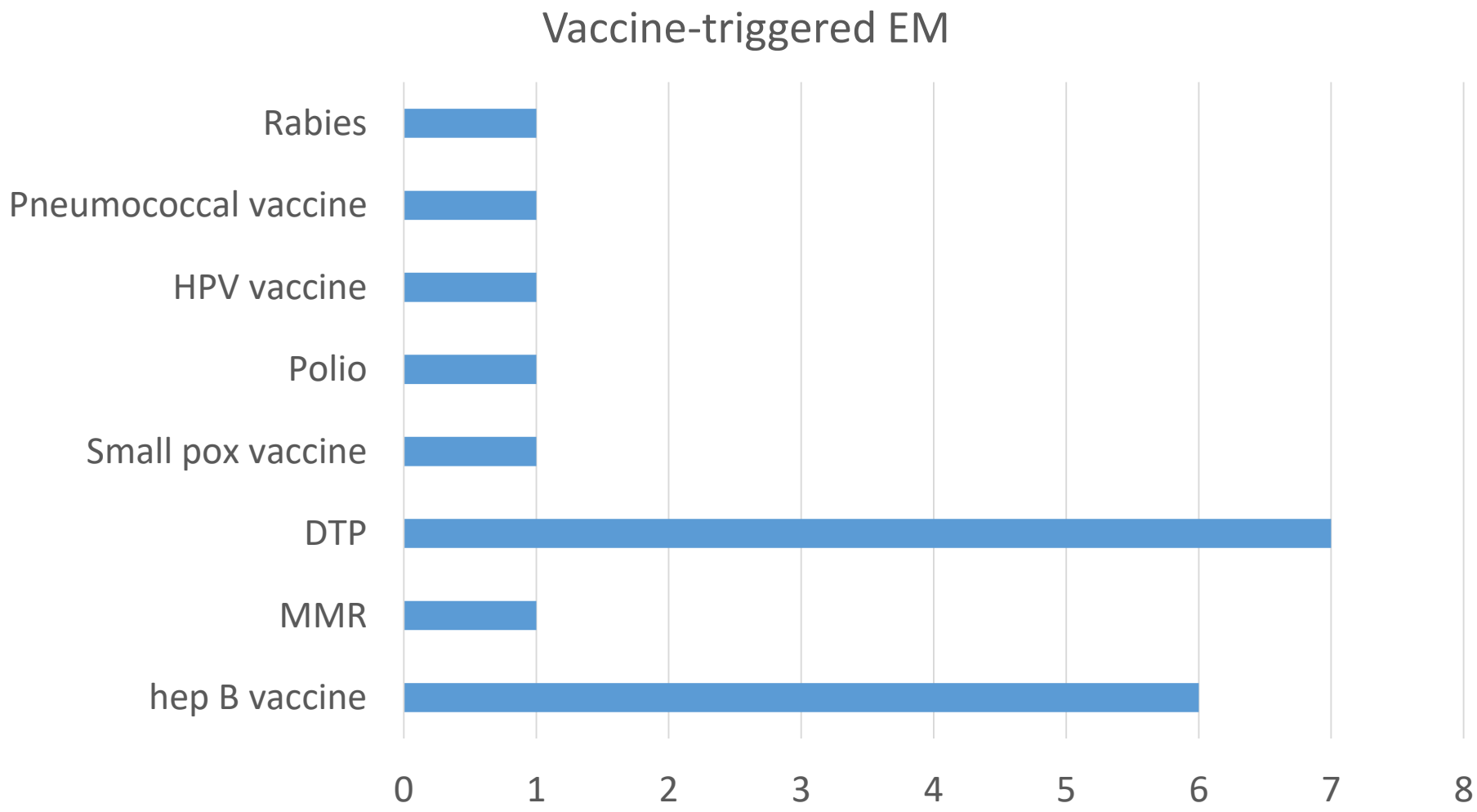
Vaccine-triggered EM
Rabies
Pneumococcal vaccine
HPV vaccine
Polio
Small pox vaccine
DTP
MMR
hep B vaccine
0
1
2
3
4
5
6
7
8

Table III. Characteristics of recurrent and nonrecurrent pediatric EM cases

Characteristic	Recurrent EM	Nonrecurrent EM	*P* value
Patients, n	59	398	
Age, y, mean ± SD (range)	9.1 ± 3.5 (0.1-14)	5.9 ± 4.8	.01
Male sex, n (%)	45 (76.3)	217 (54.7)	.001
Trigger, n (%)			
Herpes simplex virus	36 (61)	50 (12.6)	<.001
Mycoplasma pneumoniae	7 (11.9)	62 (15.6)	.5
Other infection	0	58 (14.6)	<.001
Drug	0	113 (28.4)	<.001
Other cause	0	1 (0.3)	<.001
Idiopathic	15 (25.4)	34 (8.5)	<.001
EM major, n (%)	33 (55.9)	111 (27.9)	<.001
Mucosa, n (%)			
Average affected per patient	0.89	0.55	.02
Oral	36 (61)	54 (13.6)	<.001
Ocular	10 (16.9)	29 (7.3)	.02
Ears, nose, and throat	2 (3.4)	9 (2.3)	.6
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Treatment used, n (%)			
Antiviral	51 (86.4)	19 (4.8)	<.001
Macrolide	7 (11.9)	38 (9.5)	.6
Other antibiotic	5 (8.5)	16 (4)	.12
Systemic corticosteroids	29 (49.2)	51 (12.8)	<.001
Sequelae, n (%)	2 (3.4)	6 (1.5)	.3

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- L’EP chez les enfants → herpes simplex virus et *Mycoplasma pneumonia*
- L’EP chez les nourrissons → vaccins
- Diagnostic clinique sauf chez les nourrissons et dans les cas récurrents
- PEC symptomatique + agents anti-infectieux selon le tableau clinique
- Corticoïdes dans les cas récurrents ou sévères