The Diverse Spectrum of Invasive Meningococcal Disease in Pediatric and Adolescent Patients: Narrative Review of Cases and Case Series

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Supplementary Table S1 Sample sites for *Neisseria meningitidis* isolation and identification in 184 IMD cases

Sample site	***n* (%)**	**References**
Blood	111 (60.3)	[1-64]
CSF	49 (26.6)	[3, 4, 8-10, 12, 13, 16, 17, 19, 20, 22, 26, 30, 31, 36, 39, 42, 43, 51-53, 55, 60, 62, 63, 65-77]
Blood and CSF	26 (14.1)	[3, 4, 8-10, 12, 13, 16, 17, 19, 26, 30, 31, 36, 39, 42, 43, 51, 52, 55, 60, 62, 63]
Blood and/or CSF	12 (6.5)	[78]
Synovial fluid	19 (10.3)	[34, 52, 79-85]
Conjunctival swab	3 (1.6)	[52, 86, 87]
Aqueous or vitreous humor	3 (1.6)	[17, 39, 88]
Punch biopsy from a purpuric lesion of the skin	1 (0.5)	[89]
Cerebral tissue	1 (0.5)	[3]
Not reported	10 (5.4)	[63, 90-94]

Multiple sample site may be reported for each patient
CSF cerebrospinal fluid, *IMD* invasive meningococcal disease

Supplementary Table S2 Clinical presentations in 133 IMD cases

Clinical presentation	***n* (%)**	**References**
Meningitis	62 (46.6)	[1, 3, 4, 8-13, 16, 17, 19, 22, 26, 30, 32, 36, 39, 40, 42-44, 51-53, 57, 58, 60, 62-64, 68, 70, 72-78, 95]
Sepsis	49 (36.8)	[3, 7, 8, 10, 14, 17, 19, 22-24, 26, 32, 35, 38-42, 44, 46, 47, 49, 51, 53, 54, 57, 59, 65, 68, 78, 80, 90, 91, 95]
Septic arthritis	23 (17.3)	[22, 34, 52, 55, 56, 62, 79-85, 96]
Shock	19 (14.3)	[5, 19, 30, 33, 38, 41, 46, 47, 51, 64, 72, 78, 90, 91, 95, 97]
Purpura fulminans	16 (12.0)	[5, 6, 24, 28, 31-33, 41, 45, 52, 54, 61, 64, 78, 89, 97]
Pneumonia	6 (4.5)	[22, 44, 52, 55]

Multiple clinical presentations may be reported for each patient

IMD invasive meningococcal disease

Supplementary Table S3 Clinical symptoms by age group in 137 IMD cases

By age group	**Neonate (*n* = 4)**	**Infant (*n* = 23)**	**Child aged 1–5 years (*n* = 34)**	**Child aged 6–12 years (*n* = 20)**	**Adolescent (*n* = 48)**	**Age N/R (*n* = 7)**	**Total (*N* = 137)**
Symptom	***n* (%)**						
Fever	2 (50.0)	19 (82.6)	31 (91.2)	15 (75.0)	34 (70.8)	6 (85.7)	94 (68.6)
Vomiting	0 (0.0)	7 (30.4)	9 (26.5)	8 (40.0)	24 (50.0)	2 (28.6)	50 (36.5)
Rash	3 (75.0)	7 (30.4)	12 (35.3)	3 (15.0)	11 (22.9)	6 (85.7)	30 (21.9)
Headache	0 (0.0)	0 (0.0)	1 (2.9)	5 (25.0)	26 (54.2)	0 (0.0)	32 (23.4)
Petechiae	0 (0.0)	5 (21.7)	5 (14.7)	3 (15.0)	7 (14.6)	0 (0.0)	8 (5.8)
Joint stiffness or pain	0 (0.0)	0 (0.0)	3 (8.8)	4 (20.0)	13 (27.1)	0 (0.0)	20 (14.6)
Neck stiffness or pain	0 (0.0)	3 (13.0)	3 (8.8)	4 (20.0)	8 (16.7)	0 (0.0)	18 (13.1)
Lethargy or fatigue	2 (50.0)	2 (8.7)	5 (14.7)	0 (0.0)	7 (14.6)	2 (28.6)	17 (12.4)
Diarrhea	0 (0.0)	3 (13.0)	1 (2.9)	0 (0.0)	10 (20.8)	0 (0.0)	14 (10.2)
Tachycardia	0 (0.0)	3 (13.0)	3 (8.8)	3 (15.0)	4 (8.3)	0 (0.0)	13 (9.5)
Myalgia	0 (0.0)	0 (0.0)	0 (0.0)	2 (10.0)	10 (20.8)	0 (0.0)	11 (8.0)
Irritability	0 (0.0)	5 (21.7)	2 (5.9)	0 (0.0)	0 (0.0)	1 (14.3)	8 (5.8)
Refusal to eat/drink or reduced appetite	2 (50.0)	1 (4.3)	3 (8.8)	0 (0.0)	0 (0.0)	1 (14.3)	7 (5.1)
Sore throat	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (14.6)	0 (0.0)	7 (5.1)

Hypotension	1 (25.0)	1 (4.3)	2 (5.9)	0 (0.0)	2 (4.2)	0 (0.0)	6 (4.4)
Nausea	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)	5 (10.4)	0 (0.0)	6 (4.4)
Respiratory difficulties	1 (25.0)	1 (4.3)	0 (0.0)	0 (0.0)	4 (8.3)	0 (0.0)	6 (4.4)
Bulging fontanel	1 (25.0)	4 (17.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (14.3)	6 (4.4)
Chills	0 (0.0)	0 (0.0)	2 (5.9)	0 (0.0)	3 (6.3)	0 (0.0)	5 (3.6)
Purpuric lesions	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)	4 (8.3)	0 (0.0)	5 (3.6)
Cough	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.2)	2 (28.6)	4 (2.9)
Photophobia	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	3 (6.3)	0 (0.0)	4 (2.9)
Malaise	0 (0.0)	0 (0.0)	1 (2.9)	1 (5.0)	2 (4.2)	0 (0.0)	4 (2.9)
Abdominal pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.0)	3 (6.3)	0 (0.0)	3 (2.2)
Dyspnea	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)	2 (4.2)	0 (0.0)	3 (2.2)
Hypoglycemia	0 (0.0)	2 (8.7)	1 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)

Multiple symptoms may be reported for each patient. References: [1, 4-32, 34-37, 39-47, 49-51, 53-85, 87-91, 93, 95-98]

IMD invasive meningococcal disease, *N/R* not reported

Supplementary Table S4 Treatment for IMD

Antibiotic treatment (*n* = 138)	***n* (%)**	**References**
Ceftriaxone	88 (63.8)	[4, 6, 7, 9, 10, 17, 18, 23, 24, 26, 27, 29-33, 35-38, 45-47, 50, 52-56, 58-64, 70, 75, 77, 78, 80, 81, 85, 86, 88, 89, 95, 96]
Cefotaxime	27 (19.6)	[1, 8, 9, 11, 14, 19, 25, 48, 51, 66, 67, 72, 78, 79, 82, 88, 90]
Piperacillin/tazobactam	2 (1.4)	[68, 97]
Meropenem	2 (1.4)	[40, 44]
Penicillin	2 (1.4)	[16]
Amikacin	1 (0.7)	[64]
Non-specified cephalosporine	1 (0.7)	[73]
Not specified	15 (10.9)	[12, 15, 22, 28, 76, 84]
Died before treatment initiation	4 (2.9)	[39, 42, 65, 71]
Non-antibiotic treatment (*n* = 66)	***n* (%)**	**References**
Vasopressors and/or inotropes	14 (21.2)	[6, 14, 23, 29, 30, 33, 35, 41, 44, 54, 64, 78, 98]
Corticosteroids	13 (19.7)	[10, 24, 29, 35, 51, 54, 63, 70, 75, 77, 78, 89]
Mechanical ventilation	13 (19.7)	[14, 23, 41, 44, 51, 54, 63, 64, 72, 78]

Fresh frozen plasma infusion	10 (15.2)	[14, 78, 89]
Platelet transfusion	7 (10.6)	[78]
Antiepileptics	2 (3.0)	[63, 91]
Immunoglobulins	2 (3.0)	[14, 23]
Continuous venovenous hemodiafiltration	2 (3.0)	[78]
Volume exchange transfusion	1 (1.5)	[67]
Therapeutic plasma exchange	1 (1.5)	[78]
Hemoadsorption for cytokine removal therapy	1 (1.5)	[54]
Surgery (*n* = 21)	***n* (%)**	**References**
Limb amputation	9 (42.9)	[3, 24, 33, 64, 91-93, 97, 99]
Craniotomy	4 (19.0)	[26, 43, 66, 70]
Joint drainage	4 (19.0)	[79-81, 85]
Insertion of a ventricular drain and decompression of the foramen magnum	1 (4.8)	[69]

Placement of a ventriculo-peritoneal shunt for hydrocephalus	1 (4.8)	[67]
Plastic surgery for cutaneous sequelae	1 (4.8)	[41]
Ocular enucleation	1 (4.8)	[88]

Multiple treatments may be reported for each patient

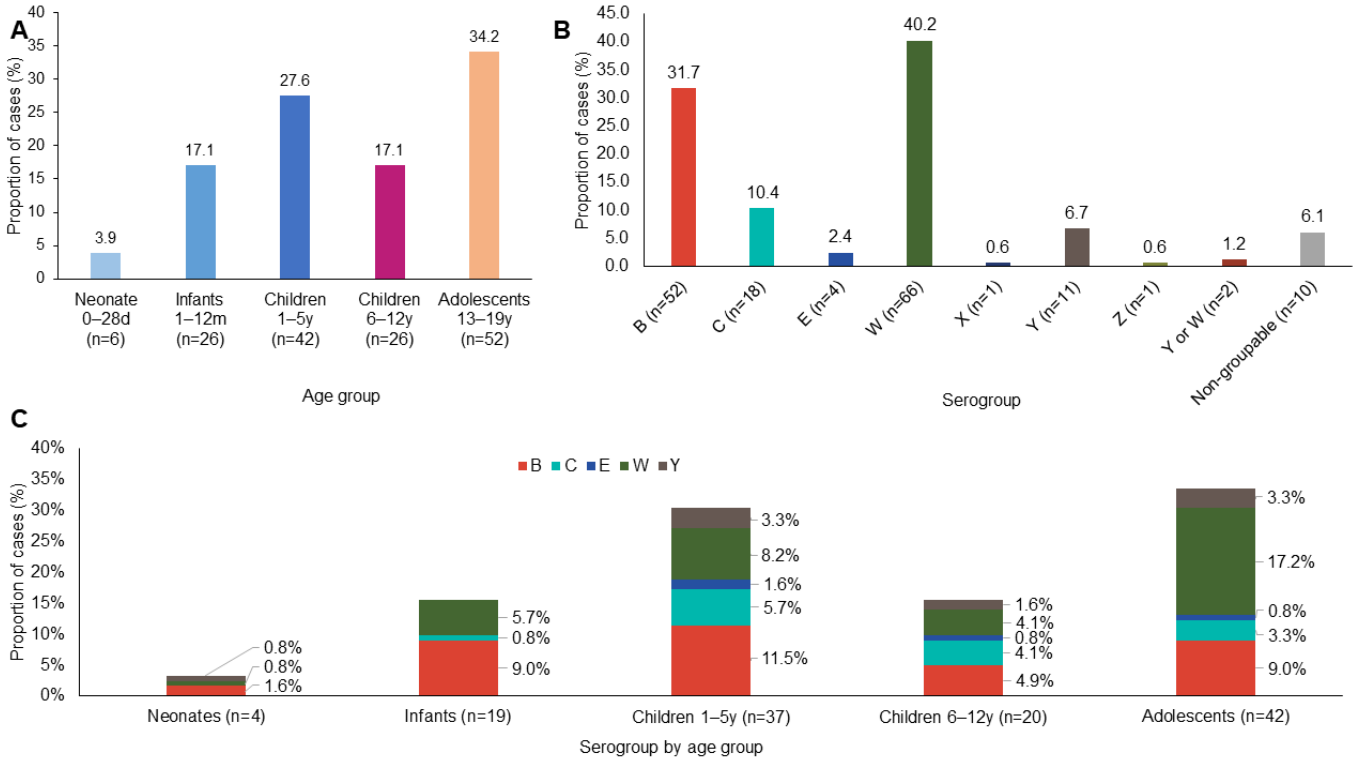
IMD invasive meningococcal disease

Supplementary Fig. S1 Geographic distribution of 184 IMD case reports.

IMD invasive meningococcal disease

Supplementary Fig. 2 (A) Age distribution in 152 IMD cases; age was reported as a range for 24 patients in one case series (3 months to 14 years) [52] and eight patients in another series (5 months to 46 months) [20]; **(B)** *Neisseria meningitidis* serogroup in 164 IMD cases; **(C)** *Neisseria meningitidis* serogroup by age group in 122 IMD cases; patients with non-groupable *N. meningitidis* (*n* = 10) and patients from two case series reporting age as a range (*n* = 32) were not included.

d days, *IMD* invasive meningococcal disease, *m* months, *y* years



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