

Coagulase-negative staphylococci (CoNS) meningitis: a narrative review of the literature from 2000 to 2020

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Abstract

Coagulase-negative staphylococci (CoNS) are recognized as comprising the main part of human normal microbiota and are rarely associated with severe and intensive infections. However, these organisms can cause a number of infections in humans, especially immunocompromised patients and neonates. Bacterial meningitis, as an important and acute infection in the central nervous system, is still a major global health challenge and a serious infectious disease, causing a high rate of mortality and morbidity. CoNS as causative agents of meningitis are generally related to trauma or direct implantation of foreign bodies and the presence of a cerebrospinal fluid shunt. Numerous epidemiologic and clinical studies have shown that different CoNS isolates such as *Staphylococcus capitis*, *Staphylococcus lugdunensis*, *Staphylococcus hominis*, *Staphylococcus epidermidis*, *Staphylococcus schleiferi*, *Staphylococcus saprophyticus*, *Staphylococcus warneri* and *Staphylococcus haemolyticus* are more frequently associated with meningitis. This study attempts to determine the role of CoNS in meningitis and reviews the reported cases of meningitis induced by CoNS from the year 2000 to 2020 in the literature.

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Introduction

Meningitis, an inflammation of meninges surrounding the spinal cord and the brain, is a significant cause of morbidity and mortality in developing countries and low-income populations [1,2]. Different types of microorganisms such as bacteria, viruses, fungi and parasites can induce meningitis [3]. Bacterial meningitis, an important and acute infection in the central nervous system (CNS), remains a serious infectious disease; it is linked to a high rate of mortality and morbidity all over the

world [4]. The incidence of bacterial meningitis varies different countries; it is estimated that despite the availability of effective treatment regimens, bacterial meningitis continues to be a major global health challenge, with estimated new cases of about 1.2 million and a reported annual mortality rate of 15% to 30% worldwide [5,6].

Despite advances in management, medical care and accessibility of effective antibiotics, bacterial meningitis remains a life-threatening infection among different age groups [4]. However, preterm and very low-birth weight infants are considered to be high-risk groups that require immediate treatment [7]. The aetiologic agents of bacterial meningitis vary with the age of patients, status of vaccination, geographical distribution, surgical conditions, underlying medical conditions, means of contraction and the receipt of different treatments in the community [8]. In total, more than 80% of nosocomial infections and suppurative-inflammatory cases are caused by *Staphylococcus* strains. On the basis of related estimates, the annual mortality rate induced by

TABLE I. Cases of coagulase-negative staphylococci meningitis reported in English-language literature from 2000 to 2020

Organism and study	Published	Country	Age (years)/gender	Abnormality	Underlying condition and clinical manifestation	Treatment	Outcome	Reference	
Staphylococcus capitis (n = 32)	1	2011	USA	65/F	Community-acquired meningitis	DM and cirrhosis	Vancomycin, meropenem	Patient died after 10 days of hospitalization	[14]
	2	2013	Taiwan	41/M	Panspinal epidural abscess concomitant with meningitis	Type 2 DM	NA	Survived	[15]
	3	2007	Taiwan	NA	Bacterial meningitis	DM, Alcoholism	IV vancomycin	Survived	[12]
	4	2013	Turkey	10/F	Meningitis	NA	NA	Unknown	[3]
	5	2012	France	65/M	Meningitis	Subacute tuberculous otitis media complicated by petrositis	NA	Patient died 10 months after disease onset	[16]
	6	2017	Taiwan	71/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	NA	Unknown	[17]
	7	2009	New Zealand	24 weeks/F	Neonatal meningitis	NA	Vancomycin, rifampicin	At developmental evaluation at age 4 years, patient had mild cognitive and motor impairment	[18]
	8	2019	China	(25 cases)>15 to ≤55/—	Meningitis	NA	Vancomycin, teicoplanin, linezolid, TMP/SMX	Unknown	[19]
Staphylococcus lugdunensis (n = 6)	1	2019	UAE	44/M	Meningitis	Native valve endocarditis, polymyositis, dyslipidaemia, asthma	Vancomycin, flucloxacillin, surgery	Survived	[20]
	2	2015	Japan	51/M	Meningitis	Surgery for Rathke cleft cyst	IV vancomycin, surgical treatment	Survived	[21]
	3	2013	USA	2/F	Meningitis	NA	IV ceftriaxone, oxacillin, vancomycin	Patient showed resolution of cystic abscess and no abnormal contrast enhancement	[22]
	4	2002	France	12/M	Congenital obstructive hydrocephalus	Intense headache, vomiting, lethargy	Oxacillin, rifampin, vancomycin/cefotaxime combination	Normal at follow-up 2 months later	[23]
	5	2015	Portugal	59/M	Brain abscess	Psychomotor inhibition, left homonymous haemianopsia	TMP/SMX	Asymptomatic at 6 months' follow-up; neurological exploration unremarkable	[24]
	6	2006	Switzerland	49/F	Brain abscess	Endocarditis	Flucloxacillin supplemented with gentamicin, rifampin, surgical abscess excision	No signs of relapse in next 6 months	[25]
Staphylococcus epidermidis (n = 320)	1	2013	Turkey	1–33/M (3) F (1)	Meningitis	NA	NA	Unknown	[3]
	2	2017	Taiwan	(9 cases) 71/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	NA	Unknown	[17]
	3	2009	New Zealand	25 weeks/F	Neonatal meningitis	NA	Vancomycin, rifampicin	Survived	[18]
	4	2019	Tunisia	51/F	Ventriculitis	Pontocerebellar angle meningioma/extraventricular drainage	Linezolid	Cured	[26]
	5	2019	Tunisia	26/M	Ventriculitis	Craniopharyngioma	Linezolid	Cured	[26]
	6	2019	Tunisia	58/F	Meningitis	Posterior fossa tumour	Linezolid	Cured	[26]
	7	2017	China	(18 cases) 3 days to 12 years/—	Meningitis	Fever, vomiting, meninges irritation, seizure, lethargy, headache, stupor, coma	Vancomycin, linezolid, rifampicin	Unknown	[2]
	8	2016	France	28/M	Healthcare-associated meningitis	Shunt replacement, fever	IV vancomycin, cotrimoxazole, rifampicin	Survived	[27]
	9	2016	France	34/M	Healthcare-associated meningitis	Intermittent headaches, chills, fever	IV vancomycin, cloxacillin, surgery	Survived	[27]
	10	2016	France	56/F	Healthcare-associated meningitis	Hydrocephalus resulting from aneurysmal subarachnoid haemorrhage	IV vancomycin, linezolid	Survived	[27]
	11	2016	France	33/F	Healthcare-associated meningitis	Severe traumatic brain injury	IV vancomycin, linezolid	Survived	[27]
	12	2016	France	64/M	Healthcare-associated meningitis	Acute hydrocephalus resulting from haemorrhagic stroke	IV vancomycin, linezolid	Survived	[27]
	13	2016	France	44/M	Healthcare-associated meningitis	NA	IV vancomycin, linezolid	Survived	[27]

14	2018	Japan	47/M	Meningitis	Hydrocephalus resulting from aneurysmal subarachnoid haemorrhage	IV vancomycin, surgery	No signs of relapse of meningitis observed; transferred to rehabilitation facility on day 56. Three months later, leukaemia relapsed; he died shortly after	[28]
15	2014	USA	23/M	Ventriculostomy-associated meningitis	Ventriculoperitoneal shunt infection, ventriculitis	IV daptomycin	Discharged to long-term acute-care hospital on day 50 without antibiotics	[29]
16	2019	China	(98 cases)/>15 to <=5/—	Meningitis	NA	Vancomycin, teicoplanin, linezolid, TMP/SMX	Unknown	[19]
17	2013	Italy	48/F	Postneurosurgical meningitis	Subarachnoid haemorrhage resulting from spontaneous rupture of aneurysm located in posterior inferior cerebellar artery	Daptomycin plus cotrimoxazole	Survived	[30]
18	2013	China	32 cases	Bacterial meningitis	NA	Vancomycin	Unknown	[31]
19	2013	Japan	1 day/F	Meningitis	Intraventricular haemorrhage	Linezolid	Healthy and had gained weight 1 month later	[32]
20	2012	Georgia	—/M	Meningitis	Myelograms performed for neck or back pain	Vancomycin, ceftriaxone	Survived	[33]
21	2010	Japan	39/F	Postoperative meningitis	Neck pain, left scapular pain	IV linezolid	Excellent postoperative course; no recurrence of infection or tumour was observed for next 3 years	[34]
22	2008	Japan	67/M	Postneurosurgical meningitis	NA	IV linezolid	Cured	[35]
23	2008	Ireland	—	Device-related meningitis	NA	NA	Unknown	[36]
24	2010	Turkey	3 days/M	Meningitis associated with noninfected cephalohematoma	Indirect hyperbilirubinaemia	Cefotaxime, vancomycin	Discharged from NICU after 2 weeks' therapy and placed on follow-up programme	[37]
25	2006	Netherlands	43/F	Meningitis	Epidermoid tumour of left pontine angle; underwent suboccipital craniotomy with near-total tumour resection	IV vancomycin, linezolid	In good clinical condition, with no signs of meningitis	[38]
26	2005	Taiwan	(10 cases) 37.5/—	Meningitis	Neurosurgical devices, alcoholism, SLE	IV vancomycin	Survived	[39]
27	2004	Sweden	55/M	Inflammatory meningitis	Massive subarachnoid haemorrhage, acute hydrocephalus	Fusidic acid, rifampicin	Survived	[40]
28	2004	Germany	18/F	Meningitis	Severe cerebral trauma	Linezolid	Survived	[41]
29	2002	USA	23/F	Ventriculoperitoneal shunt infection	Pseudo tumour cerebri with fever and headache	IV linezolid, surgery	No further episodes of shunt meningitis during 1 year of follow-up	[42]
30	2000	Germany	3 months	Ventriculoperitoneal shunt	Congenital hydrocephalus with poor feeding and fever	IV vancomycin, netilmicin, rifampicin, surgery	Patient remained free of infection during 2-year follow-up	[43]
31	2000	Canada	19/M	Pump-associated meningitis	Undefined degenerative motor neuron disorder with irritability and fever	IV vancomycin, rifampin, gentamicin	Patient had no recurrence of infection and showed good therapeutic reduction in his spasticity	[44]
32	2020	Iran	(15 cases)/—	Meningitis	NA	NA	Unknown	[45]
33	2020	China	(49 cases) 3.7/—	Paediatric refractory purulent meningitis	NA	NA	Unknown	[46]
34	2016	China	(11 cases) 18–77/—	Nosocomial meningitis and ventriculitis	NA	Vancomycin, gentamicin	Cured	[47]
35	2016	USA	44 days	Neonatal meningitis	Neurosurgery	NA	Unknown	[48]
36	2015	China	(32 cases) 37.5/—	Postneurosurgical meningitis	NA	Sulfamethoxazole, vancomycin	Cured	[8]
37	2011	Taiwan	(10 cases) 18–87/—	Postneurosurgical bacterial meningitis	DM, liver cirrhosis, alcoholism	Vancomycin plus 3G or 4G cephalosporin	Unknown	[7]
38	2019	China	(4 cases) 12.1/—	Late-onset meningitis, early-onset meningitis	Irritability, lethargy, seizures	3G cephalosporin	Unknown	[4]
39	2013	Korea	(2 cases) 52/—	Postoperative bacterial meningitis	Neurosurgery, CSF pleocytosis	NA	Unknown	[49]
Staphylococcus hominis (n = 66)								
1	2013	Turkey	5–33/F (1) M (1)	Meningitis	NA	NA	Unknown	[3]
2	2017	Taiwan	71/—			NA	Unknown	[17]

Continued

TABLE I. Continued

Organism and study	Published	Country	Age (years)/gender	Abnormality	Underlying condition and clinical manifestation	Treatment	Outcome	Reference
	3	China	(27 cases) > 15 to <55/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	Vancomycin, teicoplanin, linezolid, TMP/SMX	Unknown	[19]
	4	China	(5 cases) 3 days to 12 years/—	Meningitis	Fever, vomiting, meninges irritation, seizure, lethargy, headache, stupor, coma	Vancomycin, linezolid, rifampicin	Unknown	[2]
	5	Republic of Korea	51/F	Meningitis	Cauda equina syndrome	IV vancomycin	Discharged	[50]
	6	Bulgaria	60/M	Meningitis	Fever, headache, photophobia, hyperacusis, hyperaesthesia	Ceftazidime, vancomycin, amikacin, metronidazole, meropenem ceftriaxone, gentamycin	Successfully recovered and discharged without sequelae	[51]
	7	Nepal	(12 cases) 1–60 months/—	Meningitis	NA	NA	Unknown	[52]
	8	China	(2 cases) 18–77/—	Nosocomial meningitis and ventriculitis	NA	Vancomycin, gentamicin	Cured	[47]
	9	China	(13 cases) 37.5/—	Postneurosurgical meningitis	NA	Sulfamethoxazole, vancomycin	Cured	[8]
	10	China	(1 cases) 12.1/—	Late-onset meningitis	Irritability, lethargy, seizures	3G cephalosporin	Unknown	[4]
	11	Korea	(2 cases) 52/—	Postoperative bacterial meningitis	Neurosurgery, CSF pleocytosis	NA	Unknown	[49]
<i>Staphylococcus schleiferi</i> (n = 4)	1	Spain	19/F	Meningitis ventriculitis	Hydrocephalus multiple cholesteatoma	Vancomycin	Survived	[11]
	2	Spain	77/M	Ventriculitis meningitis	Meningioma hydrocephalus	Vancomycin	Survived	[11]
	3	China	2 month/M	Meningitis/meningoencephalitis with septic shock	Coma, tonic-clonic seizure, tachycardia	Vancomycin, meropenem, ceftriaxone, chloramphenicol	At 1 month's follow-up examination, infant was in good spirits with mild residual weakness of right upper and lower limbs	[53]
	4	China	6/F	Meningitis/meningoencephalitis with raised intracranial pressure	NA	IV cloxacillin	At 3 months' follow-up, she was walking without assistance, with mild residual weakness of left upper and lower limbs	[54]
<i>Staphylococcus saprophyticus</i> (n = 11)	1	Taiwan	(3 cases) 71/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	NA	Unknown	[17]
	2	Iran	(5 cases) 32.4/—	Postneurosurgical bacterial meningitis	Neurosurgical procedures, followed by fever, headache, loss of consciousness, meningismus	NA	Two patients died	[55]
	3	Taiwan	71/—	Postneurosurgical bacterial meningitis	DM, liver cirrhosis, alcoholism	Vancomycin plus 3G or 4G cephalosporin	Unknown	[7]
	4	China	(2 cases) 12.1/—	Late-onset meningitis	Irritability, lethargy, seizures	3G cephalosporin	Unknown	[4]
<i>Staphylococcus haemolyticus</i> (n = 117)	1	Turkey	19/F	Meningitis	NA	NA	Unknown	[3]
	2	Taiwan	71/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	NA	Unknown	[17]
	3	China	(40 cases) > 15 to <55/—	Meningitis	NA	Vancomycin, teicoplanin, linezolid, TMP/SMX	Unknown	[19]
	4	China	(8 cases) 3 days to 12 years/—	Meningitis	Fever, vomiting, meninges irritation, seizure, lethargy, headache, stupor, coma	Vancomycin, linezolid, rifampicin	Unknown	[2]
	5	China	(9 cases) —/—	Bacterial meningitis	NA	Vancomycin	Unknown	[31]
	6	Taiwan	(4 cases) 37.5/—	Meningitis	Neurosurgical devices, alcoholism, SLE	IV vancomycin	Survived	[39]
	7	China	(27 cases) 3.7/—	Paediatric refractory purulent meningitis	NA	NA	Unknown	[8]

8	2014	Bulgaria	60/M	Meningitis	Fever, headache, photophobia, hyperacusis, hyperaesthesia	Ceftazidime, vancomycin, amikacin, metronidazole, meropenem	Successfully recovered and discharged without sequelae	[51]
9	2016	China	(5 cases) 18–77/—	Nosocomial meningitis, ventriculitis	NA	Ceftriaxone, gentamycin	Cured	[47]
10	2015	China	(11 cases) 37.5/—	Postneurosurgical meningitis	NA	Sulfamethoxazole, vancomycin	Cured	[8]
11	2011	Taiwan	(2 cases) 18–87/—	Postneurosurgical bacterial meningitis	DM, liver cirrhosis, alcoholism	Vancomycin plus 3G or 4G cephalosporin	Unknown	[7]
12	2019	China	(5 cases) 12.1/—	Late-onset meningitis, early-onset meningitis	Irritability, lethargy, seizures	3G cephalosporin	Unknown	[4]
13	2019	India	28/F	Device-associated meningitis	Pituitary macroadenoma	Linezolid, cotrimoxazole	Survived	[10]
14	2000	Taiwan	53/F	Nosocomially acquired meningitis	Altered consciousness, fever, hydrocephalus	Vancomycin	Vegetative state	[56]
15	2013	Korea	52/—	Postoperative bacterial meningitis	Neurosurgery, CSF pleocytosis	NA	Unknown	[49]
Staphylococcus warneri (n = 5)								
1	2013	Turkey	(2 cases) 8–19/M	Meningitis	NA	NA	Unknown	[3]
2	2009	New Zealand	24 weeks/F	Neonatal meningitis	NA	Vancomycin, rifampicin	At developmental evaluation at age 4 years, patient had mild cognitive and motor impairment	[18]
3	2016	USA	21 days	Neonatal meningitis	NA	NA	Unknown	[48]
4	2010	Spain	59/F	Meningitis	Fever and productive cough, <i>Strongyloides stercoralis</i> hyperinfection, lymphoma	IV vancomycin	Survived	[57]
Staphylococcus capitis (n = 32)								
1	2011	USA	65/F	Community-acquired meningitis	DM, cirrhosis	Vancomycin, meropenem	Patient died after 10 days of hospitalization	[14]
2	2013	Taiwan	41/M	Panspinal epidural abscess concomitant with meningitis	Type 2 DM	IV antibiotic treatment	Survived	[15]
3	2007	Taiwan	—	Adult bacterial meningitis	DM, alcoholism	IV vancomycin	Survived	[12]
4	2013	Turkey	10/F	Meningitis	NA	NA	Unknown	[3]
5	2012	France	65/M	Meningitis	Subacute tuberculous otitis media complicated by petrositis	NA	Patient died 10 months after disease onset	[16]
6	2017	Taiwan	71/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	NA	Unknown	[17]
7	2009	New Zealand	24 weeks/F	Neonatal meningitis	NA	Vancomycin, rifampicin	At developmental evaluation at age 4 years, patient had mild cognitive and motor impairment	[18]
8	2019	China	(25 cases) >15–≤55/—	Meningitis	NA	Vancomycin, teicoplanin, linezolid, TMP/SMX	Unknown	[19]
Staphylococcus lugdunensis (n = 6)								
1	2019	UAE	44/M	Meningitis	Native valve endocarditis, polymyositis, dyslipidaemia, asthma	Vancomycin, flucloxacillin, surgery	Survived	[20]
2	2015	Japan	51/M	Meningitis	Surgery for Rathke cleft cyst	IV vancomycin, surgical treatment	Survived	[21]
3	2013	USA	2/F	Meningitis	NA	IV ceftriaxone, oxacillin, vancomycin	Patient showed resolution of cystic abscess and no abnormal contrast enhancement	[22]
4	2002	France	12/M	Congenital obstructive hydrocephalus	Intense headache, vomiting, lethargy	Oxacillin, rifampin, vancomycin/cefotaxime combination	Normal at follow-up 2 months later	[23]
5	2015	Portugal	59/M	Brain abscess	Psychomotor inhibition, left homonymous haemianopsia	TMP/SMX	Asymptomatic at 6 months' follow-up; neurological exploration unremarkable	[24]
6	2006	Switzerland	49/F	Brain abscess	Endocarditis	Flucloxacillin supplemented with gentamicin, rifampin, surgical abscess excision	No signs of relapse during next 6 months	[25]
Staphylococcus epidermidis (n = 320)								
1	2013	Turkey	1–33/M (3) F (1)	Meningitis	NA	NA	Unknown	[3]

Continued

TABLE I. Continued

Organism and study	Published	Country	Age (years)/gender	Abnormality	Underlying condition and clinical manifestation	Treatment	Outcome	Reference
2	2017	Taiwan	(9 cases) 71/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	NA	Unknown	[17]
3	2009	New Zealand	25 weeks/F	Neonatal meningitis	NA	Vancomycin, rifampicin	Survived	[18]
4	2019	Tunisia	51/F	Ventriculitis	Pontocerebellar angle meningioma/extraventricular drainage	Linezolid	Cured	[26]
5	2019	Tunisia.	26/M	Ventriculitis	Craniopharyngioma	Linezolid	Cured	[26]
6	2019	Tunisia.	58/F	Meningitis	Posterior fossa tumour	Linezolid	Cured	[26]
7	2017	China	(18 cases) 3 days to 12 years/—	Meningitis	Fever, vomiting, meninges irritation, seizure, lethargy, headache, stupor, coma	Vancomycin, linezolid, rifampicin	Unknown	[2]
8	2016	France	28/M	Healthcare-associated meningitis	Shunt replacement, fever	IV vancomycin, cotrimoxazole, rifampicin	Survived	[27]
9	2016	France	34/M	Healthcare-associated meningitis	Intermittent headaches, chills, fever	IV vancomycin, cloxacillin, surgery	Survived	[27]
10	2016	France	56/F	Healthcare-associated meningitis	Hydrocephalus resulting from aneurysmal subarachnoid haemorrhage	IV vancomycin, linezolid	Survived	[27]
11	2016	France	33/F	Healthcare-associated meningitis	Severe traumatic brain injury	IV vancomycin, linezolid	Survived	[27]
12	2016	France	64/M	Healthcare-associated meningitis	Acute hydrocephalus resulting from a haemorrhagic stroke	IV vancomycin, linezolid	Survived	[27]
13	2016	France	44/M	Healthcare-associated meningitis	Hydrocephalus resulting from aneurysmal subarachnoid haemorrhage	IV vancomycin, linezolid	Survived	[27]
14	2018	Japan	47/M	Meningitis	Acute myeloid leukaemia, catheter-related bloodstream infection	IV vancomycin, surgery	No signs of relapse of meningitis observed; transferred to rehabilitation facility on day 56. Three months later, leukaemia relapsed; he died shortly after He was discharged to a long-term acute care hospital on day 50 without antibiotics	[28]
15	2014	USA	23/M	Ventriculostomy-associated meningitis	Ventriculoperitoneal shunt infection, ventriculitis	IV daptomycin	Unknown	[29]
16	2019	China	(98 cases) > 15 to ≤55/—	Meningitis	NA	Vancomycin, teicoplanin, linezolid, TMP/SMX	Unknown	[19]
17	2013	Italy	48/F	Postneurosurgical meningitis	Subarachnoid haemorrhage resulting from spontaneous rupture of an aneurysm located in posterior inferior cerebellar artery	Daptomycin plus cotrimoxazole	Survived	[30]
18	2013	China	32 case	Bacterial meningitis	NA	Vancomycin	Unknown	[31]
19	2013	Japan	1 day/F	Meningitis	Intraventricular haemorrhage	Linezolid	Healthy and had gained weight 1 month later	[32]
20	2012	Georgia	—/M	Meningitis	Myelograms performed for neck or back pain	Vancomycin, ceftriaxone	Survived	[33]
21	2010	Japan	39/F	Postoperative meningitis	Neck pain, left scapular pain	IV linezolid	Excellent postoperative course; no recurrence of infection or tumour was observed for next 3 years	[34]
22	2008	Japan	67/M	Postneurosurgical meningitis	NA	IV linezolid	Cured	[35]
23	2008	Ireland	NA	Device-related meningitis	NA	NA	Unknown	[36]
24	2010	Turkey	3 days/M	Meningitis associated with noninfected cephalohematoma	Indirect hyperbilirubinaemia	Cefotaxime, vancomycin	Discharged from NICU after 2 weeks' therapy and placed on follow-up programme	[37]
25	2006	Netherlands	43/F	Meningitis	Epidermoid tumour of left pontine angle underwent a suboccipital craniotomy with near total resection of tumour	IV vancomycin, linezolid	She was in good clinical condition, with no signs of meningitis	[38]
26	2005	Taiwan	(10 cases) 37.5/—	Meningitis	Neurosurgical devices, alcoholism, SLE	IV vancomycin	Survived	[39]
27	2004	Sweden	55/M	Inflammatory meningitis	Massive subarachnoid haemorrhage, acute hydrocephalus	Fusidic acid, rifampicin	Survived	[40]
28	2004	Germany	18/F	Meningitis	Severe cerebral trauma	Linezolid	Survived	[41]

29	2002	USA	23/F	Ventriculoperitoneal shunt infection	Pseudo tumour cerebri with fever and headache	IV linezolid, surgery	No further episodes of shunt meningitis during 1 year's follow-up	[42]
30	2000	Germany	3 months	Ventriculoperitoneal shunt	Inborn hydrocephalus presented with poor feeding and fever	IV vancomycin, netilmicin, rifampicin, surgery	Patient remained free of infection during 2 years' follow-up	[43]
31	2000	Canada	19/M	Pump associated meningitis	Undefined degenerative motor neuron disorder with irritability and fever	IV vancomycin, rifampin, gentamicin	Patient had no recurrence of infection and showed good therapeutic reduction in his spasticity	[44]
32	2020	Iran	(15 cases)/—	Meningitis	NA	NA	Unknown	[45]
33	2020	China	(49 cases) 3.7/—	Paediatric refractory purulent meningitis	NA	NA	Unknown	[46]
34	2016	China	(11 cases) 18–77/—	Nosocomial meningitis, ventriculitis	NA	Vancomycin, gentamicin	Cured	[47]
35	2016	USA	44 days	Neonatal meningitis	Neurosurgery	NA	Unknown	[48]
36	2015	China	(32 cases) 37.5/—	Postneurosurgical meningitis	NA	Sulfamethoxazole, vancomycin	Cured	[8]
37	2011	Taiwan	(10 cases) 18–87/—	Postneurosurgical bacterial meningitis	DM, liver cirrhosis, alcoholism	Vancomycin plus 3G or 4G cephalosporin	Unknown	[7]
38	2019	China	(4 cases) 12.1/—	Late-onset meningitis, early-onset meningitis	Irritability, lethargy, seizures	3G cephalosporin	Unknown	[4]
39	2013	Korea	(2 cases) 52/—	Postoperative bacterial meningitis	Neurosurgery, CSF pleocytosis	NA	Unknown	[49]
Staphylococcus hominis (n = 66)								
1	2013	Turkey	5–33/F (1) M (1)	Meningitis	NA	NA	Unknown	[3]
2	2017	Taiwan	71/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	NA	Unknown	[17]
3	2019	China	(27 cases) >15 to ≤55/—	Meningitis	NA	Vancomycin, teicoplanin, linezolid, TMP/SMX	Unknown	[19]
4	2017	China	(5 cases) 3 days to 12 years/—	Meningitis	Fever, vomiting, meninges irritation, seizure, lethargy, headache, stupor, coma	Vancomycin, linezolid, rifampicin	Unknown	[2]
5	2019	Republic of Korea	51/F	Meningitis	Cauda equina syndrome	IV vancomycin	Discharged	[50]
6	2014	Bulgaria	60/M	Meningitis	Fever, headache, photophobia, hyperacusis, hyperaesthesia	Ceftazidime, vancomycin, amikacin, metronidazole, meropenem ceftriaxone, gentamycin	Successfully recovered and were discharged without sequelae	[51]
7	2016	Nepal	(12 cases) 1–60 months/—	Meningitis	NA	NA	Unknown	[52]
8	2016	China	(2 cases) 18–77/—	Nosocomial meningitis, ventriculitis	NA	Vancomycin, gentamicin	Cured	[47]
9	2015	China	(13 cases) 37.5/—	Postneurosurgical meningitis	NA	Sulfamethoxazole, vancomycin	Cured	[8]
10	2019	China	(1 cases) 12.1/—	Late-onset meningitis	Irritability, lethargy, seizures	3G cephalosporin	Unknown	[4]
11	2013	Korea	(2 cases) 52/—	Postoperative bacterial meningitis	Neurosurgery, CSF pleocytosis	NA	Unknown	[49]
Staphylococcus schleiferi (n = 4)								
1	2001	Spain	19/F	Meningitis ventriculitis	Hydrocephalus multiple cholesteatoma	Vancomycin	Survived	[11]
2	2001	Spain	77/M	Ventriculitis meningitis	Meningioma hydrocephalus	Vancomycin	Survived	[11]
3	2017	China	2 month/M	Meningitis/ meningoencephalitis with septic shock	Coma, tonic-clonic seizure, tachycardia	Vancomycin, meropenem, ceftriaxone, chloramphenicol	At 1-month follow-up examination, infant was in good spirits with mild residual weakness of right upper and lower limbs	[53]
4	2015	China	6/F	Meningitis/ meningoencephalitis with raised intracranial pressure	NA	IV cloxacillin	At 3-month follow-up examination, she was walking without assistance with mild residual weakness of left upper and lower limbs	[54]
Staphylococcus saprophyticus (n = 11)								
1	2017	Taiwan	(3 cases) 71/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	NA	Unknown	[17]
2	2014	Iran	(5 cases) 32.4/—	Postneurosurgical bacterial meningitis	NA	NA	Two patients died	[55]

Continued

TABLE I. Continued

Organism and study	Published	Country	Age (years)/gender	Abnormality	Underlying condition and clinical manifestation	Treatment	Outcome	Reference
Staphylococcus haemolyticus (n = 117)	3	Taiwan	71/—	Postneurosurgical bacterial meningitis	Neurosurgical procedures, followed by fever, headache, loss of consciousness, meningismus DM, liver cirrhosis, alcoholism	Vancomycin plus 3G or 4G cephalosporin	Unknown	[7]
	4	China	(2 cases) 12.1/—	Late-onset meningitis	Irritability, lethargy, seizures	3G cephalosporin	Unknown	[4]
	1	Turkey	19/F	Meningitis	NA	NA	Unknown	[3]
	2	Taiwan	71/—	Postneurosurgical bacterial meningitis	Hydrocephalus, liver cirrhosis, brain tumours	NA	Unknown	[17]
	3	China	(40 cases)/>15 to <55/—	Meningitis	NA	Vancomycin, teicoplanin, linezolid, TMP/SMX	Unknown	[19]
	4	China	(8 cases) 3 days to 12 years/—	Meningitis	Fever, vomiting, meninges irritation, seizure, lethargy, Headache, stupor, coma	Vancomycin, linezolid, rifampicin	Unknown	[2]
	5	China	(9 cases) —/—	Bacterial meningitis	NA	Vancomycin	Unknown	[31]
	6	Taiwan	(4 cases) 37.5/—	Meningitis	Neurosurgical devices, alcoholism, SLE	IV vancomycin	Survived	[39]
	7	China	(27 cases) 3.7/—	Paediatric refractory purulent meningitis	NA	NA	Unknown	[8]
	8	Bulgaria	60/M	Meningitis	Fever, headache, photophobia, hyperacusis, hyperaesthesia	Ceftazidime, vancomycin, amikacin, metronidazole, meropenem ceftriaxone, gentamycin	Successfully recovered and discharged without sequelae	[51]
	9	China	(5 cases) 18–77/—	Nosocomial meningitis, ventriculitis	NA	Vancomycin, gentamicin	Cured	[47]
	10	China	(11 cases) 37.5/—	Postneurosurgical meningitis	NA	Sulfamethoxazole, vancomycin	Cured	[8]
	11	Taiwan	(2 cases) 18–87/—	Postneurosurgical bacterial meningitis	DM, liver cirrhosis, alcoholism	Vancomycin plus 3G or 4G cephalosporin	Unknown	[7]
	12	China	(5 cases) 12.1/—	Late-onset meningitis, early-onset meningitis	Irritability, lethargy, seizures	3G cephalosporin	Unknown	[4]
	13	India	28/F	Device-associated meningitis	Pituitary macroadenoma	Linezolid, cotrimoxazole	Survived	[10]
14	Taiwan	53/F	Nosocomially acquired meningitis	Altered consciousness, fever, hydrocephalus	Vancomycin	Vegetative state	[56]	
15	Korea	52/—	Postoperative bacterial meningitis	Neurosurgery, CSF pleocytosis	NA	Unknown	[49]	
Staphylococcus warneri (n = 5)	1	Turkey	(2 cases) 8–19/M	Meningitis	NA	NA	Unknown	[3]
	2	New Zealand	24 weeks/F	Neonatal meningitis	NA	Vancomycin, rifampicin	At developmental evaluation at age 4 years, patient had mild cognitive and motor impairment	[18]
	3	USA	21 days	Neonatal meningitis	NA	NA	Unknown	[48]
	4	Spain	59/F	Meningitis	Fever and productive cough, <i>Strongyloides stercoralis</i> hyperinfection, lymphoma	IV vancomycin	Survived	[57]

3G, third generation; 4G, fourth generation; CSF, cerebrospinal fluid; DM, diabetes mellitus; IV, intravenous; NA, not available; NICU, neonatal intensive care unit; SLE, systemic lupus erythematosus; TMP/SMX, trimethoprim/sulfamethoxazole.

staphylococcal meningitis varies from 31% to 56% worldwide [9]. Among *Staphylococcus* strains, coagulase-negative staphylococci (CoNS) as causative agents of meningitis are the main components of the normal flora of the skin and mucous membranes [10,11]. CoNS meningitis is generally found in immunocompromised patients and is usually related to trauma or direct implantation of foreign bodies and the presence of a cerebrospinal fluid (CSF) shunt [12].

The CoNS, especially methicillin-resistant *Staphylococcus*, are the most frequent pathogens involved in postneurosurgical infection [13]. Numerous epidemiologic and clinical studies have shown that different CoNS isolates can cause meningitis. Moreover, some species such as *Staphylococcus capitis*, *Staphylococcus lugdunensis*, *Staphylococcus hominis*, *Staphylococcus epidermidis*, *Staphylococcus schleiferi*, *Staphylococcus saprophyticus*, *Staphylococcus warneri* and *Staphylococcus haemolyticus* are associated with definite clinical infection more frequently, especially postneurosurgical meningitis (Table 1, Fig. 1).

By considering the association of CoNS with meningitis, we attempt to shed light on the role of CoNS and review the related epidemiologic results. CoNS isolates in meningitis facilitate the task of determining the role of CoNS in the process of meningitis.

subspecies and acts as normal flora of human ears, neck, face and scalp. This bacterium comprises 5% of all CoNS bacteria and has the ability to induce numerous severe infections such as otitis externa, infective endocarditis (prosthetic and native valve endocarditis), cellulitis, primary chronic osteomyelitis, urinary tract infection, late- and early-onset sepsis, orthopaedic peri-prosthetic infections, pneumonia and catheter-associated bloodstream infections [60,61]. Patients with a suppressed immune system or underlying cardiac disease are considered to be highly susceptible to these infections, so they are therefore categorized into the high-risk groups [62]. *S. capitis* is generally reported in premature neonates and is occasionally identified in neonatal intensive care unit outbreaks [63].

However, studies have revealed that *S. capitis* is a causative agent of adult meningitis [14]. An overview of the published studies from 2000 to 2020 reveals that *S. capitis* may cause several cases of meningitis including community-acquired meningitis, pansominal epidural abscess concomitant with meningitis, postneurosurgical bacterial meningitis and neonatal meningitis (Table 1). Underlying conditions and clinical manifestations in patients with *S. capitis* meningitis are alcohol consumption, type 2 diabetes mellitus (DM), liver cirrhosis, subacute tuberculous otitis media complicated by petrositis, fever, nuchal rigidity, hydrocephalus and brain tumours [14]. Intravenous antibiotic treatments such as vancomycin, meropenem, rifampicin, teicoplanin, linezolid and trimethoprim/sulfamethoxazole have been used for *S. capitis* meningitis [15,18,19]. However, the mechanism of *S. capitis* meningitis is not well understood, and more study is required to explain the meningitis mechanism in *S. capitis* cases.

CoNS in meningitis

Staphylococcus capitis

Staphylococcus capitis is a member of CoNS and was first identified by Kloos and Schleifer in 1975 [58,59]. *S. capitis* has two

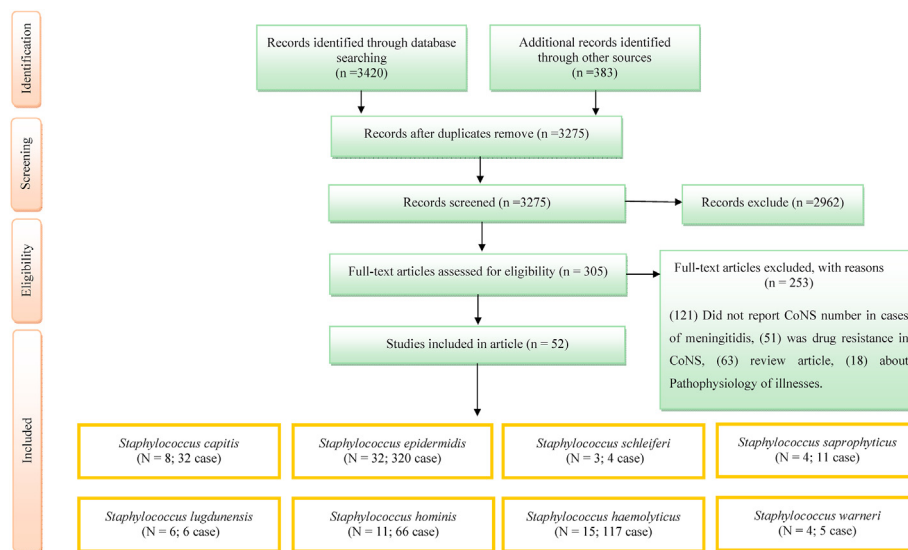


FIG. 1. Flowchart of study selection for inclusion.

Staphylococcus lugdunensis

Staphylococcus lugdunensis is a Gram-positive bacterium considered as a CoNS, as first described by Freney et al. in 1988 [76]. *S. lugdunensis* colonizes 30% to 50% of patients, and similar to other CoNS isolates, it constitutes the microbiota of the skin of healthy individuals [60]. Cutaneous infections, dental abscesses, cardiac pacemakers and infected vascular devices are breeding grounds for *S. lugdunensis* infections in the community [64]. However, this organism behaves similarly to *Staphylococcus aureus* and causes both nosocomial and community-acquired infections including ventriculoperitoneal shunt infection, catheter-related bacteraemia, osteomyelitis, infective endocarditis, aggressive valve destruction with abscess formation, brain abscess and meningitis [65].

According to reports, *S. lugdunensis* can cause meningitis after dental infection, embolic native valve endocarditis and ventriculostomy [22,66]. Biofilm formation in *S. lugdunensis* is an important means to adhere to native tissues and prosthetic materials [60]. On the basis of published studies from 2000 to 2020, the underlying conditions and clinical manifestations in patients with *S. lugdunensis* meningitis include native valve endocarditis, polymyositis, dyslipidaemia, asthma surgery for Rathke cleft cyst, intense headache, vomiting, lethargy, psychomotor inhibition and left homonymous haemianopsia [20,23,24]. Most patients with *S. lugdunensis* meningitis have been treated with intravenous vancomycin, flucloxacillin, ceftriaxone, oxacillin, rifampin and surgery. Patients with brain abscess have received treatments with trimethoprim/sulfamethoxazole, flucloxacillin supplemented with gentamicin, rifampin and surgical abscess excision [24,25]. Moreover, combination therapy has been applied to the case of patients with congenital obstructive hydrocephalus, oxacillin, rifampin and vancomycin/cefotaxime [22] (Table 1).

Staphylococcus epidermidis

Staphylococcus epidermidis is a member of the human microbiota often considered to be a culture contaminant in clinical laboratory and hospital environments [60]. Unlike other CoNS isolates, genes encoding enterotoxins and toxic shock syndrome toxin I (TSST-I) have not been found among *S. epidermidis* strains [67]. *S. epidermidis* is considered to be the main pathogen in hospital-acquired infections, and it causes a number of severe infections such as surgical site infections, intravenous catheter-related bloodstream infections, peritoneal dialysis-related infections, CNS shunt infections, ophthalmologic infections, urinary tract infection and infections of indwelling prosthetic devices in the healthcare setting [68]. In recent years, *S. epidermidis* has been isolated frequently from immunocompromised patients. Among

CoNS isolates, most cases of CNS infections such as meningitis are induced by *S. epidermidis* and are generally linked to neurosurgical devices (ventriculoperitoneal shunts) [32]. Therefore, in the absence of neurosurgical devices, *S. epidermidis* meningitis is quite infrequent [28].

In general, *S. epidermidis* causes postneurosurgical meningitis, neonatal meningitis, ventriculitis, healthcare-associated meningitis, ventriculostomy-associated meningitis and paediatric refractory purulent meningitis [29]. According to the published studies listed in Table 1, the most prevalent underlying conditions in patients with *S. epidermidis* meningitis include hydrocephalus caused by aneurysm, liver cirrhosis, brain tumours, shunt replacement and ventriculoperitoneal shunt infection, pontocerebellar angle meningioma/extraventricular drainage, craniopharyngioma, subarachnoid haemorrhage, acute myeloid leukaemia, catheter-related bloodstream infection, systemic lupus erythematosus, neurosurgery, CSF pleocytosis and DM. Moreover, fever, vomiting, meninges irritation, seizure, lethargy, headache, stupor, chills, poor feeding, neck pain and left scapular pain are the most frequently reported clinical manifestations in patients [28,29,32].

S. epidermidis has different virulence factors such as cysteine protease, serine protease, lipase, metalloprotease with elastase activity, resistance to antibiotics, ability to produce delta toxin and ability to adhere to and form biofilm on the surface of foreign bodies such as implanted devices [69,70]. The ability to form biofilm on the surface of foreign bodies leads to the emergence of antibiotic-resistant *S. epidermidis* isolates, and the infections induced by these organisms have become increasingly difficult to eradicate. *S. epidermidis* isolates form biofilm, express resistance genes and form various cell layers, which lead to the inhibition of antibiotic penetration into CSF [71]. In most cases of methicillin-resistant *S. epidermidis* meningitis, intravenous vancomycin, rifampicin and linezolid have been used to treat patients [18,26,27]. However, in a rare case, physicians used daptomycin plus cotrimoxazole and fusidic acid plus rifampicin for the treatment of meningitis [30,40].

The penetration of intravenous vancomycin into CSF is low. In such cases, some clinical information suggests that the removal of the prosthetic device and combination therapy through anti-inflammatory drugs such as steroids are required [41]. In contrast, linezolid has excellent CSF penetration [34]. Daptomycin as a lipopeptide antibiotic has bactericidal activity against *S. epidermidis* strains. In *S. epidermidis* infections that do not respond to vancomycin, intraventricular daptomycin is a better treatment [30]. However, only 5% to 6% of the intravenously administered daptomycin enters the CSF. Therefore,

intrathecal administration of daptomycin is an appropriate choice in meningitis cases [72].

Staphylococcus hominis

Similar to other CoNS isolates, *Staphylococcus hominis* is a common member of the healthy human skin microbiome. In addition, in contrast to *S. epidermidis*, this organism produces acid from trehalose, and it is rarely resistant to novobiocin [60]. Among *Staphylococcus* species, two species, *S. hominis* and *Staphylococcus warneri*, constitute 14% of all CoNS isolates in body fluids such as urine, prostatic secretions and semen [73]. *S. hominis* has the ability to form biofilm on the surface of smooth devices in human body, and it is considered to be a potential pathogen, which can cause different infections such as infective endocarditis and meningitis in immunocompromised patients [51,60]. Several studies have revealed that besides *S. aureus* and *S. haemolyticus*, *S. hominis* is a causative agent of bacterial meningitis in humans [48,52]. Results of a study indicated that *S. hominis* penetrated the epidural, subdural or sub-arachnoid space and caused meningitis during transsacral epiduroscopic laser decompression in patients with catheter, epiduroscope or laser device [50].

In general, an overview of the reported meningitis cases due to *S. hominis* revealed that this organism can cause post-neurosurgical meningitis, nosocomial meningitis, ventriculitis and late-onset meningitis. Fever, vomiting, seizure, lethargy, headache, stupor, photophobia and seizures are the most frequently reported clinical manifestations in patients with *S. hominis* meningitis [8,47]. The most prevalent underlying conditions in these patients are hydrocephalus, liver cirrhosis, brain tumours, meninges irritation, cauda equina syndrome, hyperacusis, hyperaesthesia, neurosurgery and CSF pleocytosis. Intravenous vancomycin and linezolid are the main antibiotics that are usually used for the treatment of *S. hominis* meningitis (Table 1).

Staphylococcus schleiferi

Staphylococcus schleiferi was first described by Freney et al. in 1988 [76]. However, the first report of *S. schleiferi* isolated from humans was presented in 1994 [74]. This organism has the ability to create several invasive infections among adults such as wound infection, bacteraemia, meningitis and prosthetic infections [11,75]. In most cases, invasive infections caused by this organism result from contact with dogs [76]. *S. lugdunensis* subsp. *schleiferi* behaves similarly to *S. aureus* and expresses heat-stable DNase and clumping factor. *S. lugdunensis* subsp. *schleiferi* can produce a pseudo coagulase, so it is therefore occasionally identified as a coagulase-positive staphylococcus [11]. However, the coagulase tube test result of this organism is negative. In contrast, *Staphylococcus schleiferi* subsp. *coagulans* do not express clumping factor yet produce coagulase [74]. The

organism has several virulence factors including β -haemolysin, lipase, adherence, protease and esterase [77].

In the studies published from 2000 to 2020, several rare cases of *S. schleiferi* meningitis have been reported. The abnormalities and the patient outcomes are described in Table 1. The aforementioned studies have reported meningioma and hydrocephalus multiple cholesteatoma as underlying conditions. Among patients with *S. schleiferi* meningitis, the most frequent clinical manifestations are tonic-clonic seizure and tachycardia. Intravenous vancomycin, cloxacillin, meropenem, ceftriaxone and chloramphenicol have been used for the treatment of these patients [11,53,54].

Staphylococcus saprophyticus

Staphylococcus saprophyticus is a member of the human microbiota that causes several rare infections such as pyelonephritis, infective endocarditis (native valve endocarditis and prosthetic valve endocarditis) and meningitis as well as urinary tract infection, endophthalmitis and uncomplicated cystitis among young women [60]. In general, from 2000 to 2019, several cases of meningitis due to *S. saprophyticus* were reported (Table 1). Hydrocephalus, liver cirrhosis, brain tumours and DM were the most prevalent underlying conditions associated with these cases [4]. Moreover, the most frequent clinical manifestations among these patients were fever, headache, loss of consciousness, meningismus, irritability, lethargy or seizures. Vancomycin plus a third- or fourth-generation cephalosporin was used for the treatment of patients with *S. saprophyticus* meningitis [4,7,55].

Staphylococcus haemolyticus

Staphylococcus haemolyticus is considered to be a member of methicillin-resistant staphylococci that induces several infections in a healthcare setting. This organism is the main pathogen among patients admitted to intensive care units [60,78]. *S. haemolyticus* is the second most common cause of CoNS bacteraemia and accounts for approximately 22% to 24% of CNS infections [10]. This organism, like most CoNS isolates, can cause several infections such as sepsis, bacteraemia, native and prosthetic valve endocarditis, prosthetic joint infections, soft tissue or skin infections and meningitis [10,49].

S. haemolyticus is the main pathogen in patients with neurosurgical procedures or head trauma, and it can cause adult meningitis and device-related infections in these patients [56]. Numerous reports of *S. haemolyticus* meningitis from around the world are summarized in Table 1. This organism can cause postneurosurgical bacterial meningitis, paediatric refractory purulent meningitis, nosocomial meningitis, ventriculitis, late- and early-onset meningitis and device-associated meningitis [8,17,47]. Hydrocephalus, liver cirrhosis, brain tumours,

systemic lupus erythematosus, hyperacusis and hyperaesthesia, DM, pituitary macroadenoma, neurosurgery and CSF pleocytosis as an underlying condition have been detected in patients with *S. haemolyticus* meningitis. Furthermore, the most frequent clinical manifestations among these patients include fever, vomiting, meninges irritation, photophobia, seizure, lethargy, headache, stupor and coma [2,7,49,56].

S. haemolyticus has the ability to produce biofilm, which in turn leads to biofilm-mediated infections. These infections are resistant to antibiotic therapy and the host immune system [10]. *S. haemolyticus* strains have several important resistance genes and act as the main reservoir for the distribution of antimicrobial resistance to other CoNS isolates, leading to the emergence of multidrug-resistant bacteria [78]. Vancomycin, linezolid, rifampicin and third-generation cephalosporins have frequently been used for the treatment of patients with *S. haemolyticus* meningitis (Table 1).

Staphylococcus warneri

Staphylococcus warneri is a member of CoNS isolates and is normally found on the skin of healthy individuals, in the nasal cavities and in the mouths of animals. This organism is not usually considered pathogenic, but it has been isolated from several infections such as native and prosthetic valve endocarditis, canine meningoencephalitis, septicaemia, osteomyelitis, bovine abortion, subdural empyema, urinary tract infection and discitis in immunocompromised patients [60,79]. Like *S. epidermidis*, *S. warneri* produces biofilm on the surface of various materials. Moreover, this bacterium produces acid from trehalose, and it has different virulence factors such as attachment to polymer surfaces and metabolic changes in various situations [80]. The ability to form biofilm in foreign bodies and medical devices allows this bacterium to be resistant to the antimicrobials used to treat infections [81]. An overview of published studies reveals that this organism can cause meningitis (especially in neonates). Intravenous vancomycin has been used in most cases for the treatment of *S. warneri* meningitis [57]. More studies are required to understand the mechanism of *S. warneri* pathogenesis in meningitis.

Discussion and conclusion

Globally, different microorganisms such as bacteria, viruses, fungi and parasites can cause meningitis [82,83]. Bacterial meningitis occurs among all age groups, especially during childhood [84]. Acute bacterial meningitis is related to high rates of mortality and morbidity. Hence, precise diagnosis and suitable prescription of antimicrobials for its treatment are necessary [85]. Among bacterial agents, the most cases of meningitis are caused by *Haemophilus influenzae* type b, *Neisseria meningitidis* and *Streptococcus*

pneumoniae [2,86]. However, in recent years, numerous cases of CoNS meningitis have been reported.

CoNS isolates constitute the main part of the human normal microbiota population. Immunocompromised patients and individuals who insert foreign objects or medical devices into their bodies are considered to be in a high-risk group of patients susceptible to meningitis [13]. Among CoNS isolates, *S. epidermidis* and *S. haemolyticus* account for the majority of meningitis cases. In general, our analysis found that DM, liver cirrhosis, native valve endocarditis, hydrocephalus, alcoholism and brain tumours are the main underlying conditions in patients with CoNS meningitis. DM is the main underlying condition in patients with *S. capitis* meningitis. Among CoNS isolates, *S. capitis* is related to mortality, and two patients with *S. capitis* meningitis died 10 days after disease onset and hospitalization. In most cases, *S. lugdunensis* meningitis was created after native valve endocarditis and brain abscess. As shown in Table 1, most cases of *S. epidermidis* meningitis are related to neurosurgical intervention and ventriculoperitoneal shunt infection. *S. epidermidis* leads to the inflammation of the ventricles in the brain of patients. Similar to *S. epidermidis*, most cases of meningitis caused by *S. hominis* and *S. saprophyticus* are postneurosurgical meningitis.

Moreover, our analysis of the included articles found that *S. warneri* is one of the main organisms in neonatal meningitis. The bacteria in the CoNS genus form biofilm, which facilitates resistance to different classes of antibiotics and makes their eradication difficult at infection sites. In most cases, vancomycin and linezolid have been used for the treatment of CoNS meningitis. Vancomycin has inadequate penetration into the CSF, which depends on both the inflammatory meningeal status and the integrity of the blood–brain barrier. Linezolid exhibited a highly potent activity against methicillin-resistant staphylococci and penetrated CSF readily. Moreover, linezolid was well tolerated by patients and was characterized by a very low rate of side effects [27,32]. In total, patients outcomes in the published studies indicate that CoNS meningitis has been treated by using antibiotic therapy in most cases.

Conflict of interest

None declared.

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