

CLINICAL STUDY OF 57 CASES OF NOSOCOMIAL MENINGITIS

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Abstract. Aim. The aim of the present survey was to establish the incidence of the predisposing and risk factors, the clinical features, etiology and evolution of 57 cases of nosocomial meningitis, treated according to their antibiotic resistance patterns. Nosocomial meningitis occurs after neurosurgical interventions for cranio-cerebral trauma or tumors, after invasive explorations of the central nervous system, or after implanting foreign body materials for cerebro-spinal fluid (CSF) drainage. The incidence of nosocomial meningitis varies between 0.34% and 3.1%. **Material and methods.** The data referring to nosocomial meningitis were gathered from the archive of the Clinical Hospital of Infectious Diseases Iași, a referral hospital for Moldova region. (North-East România) We studied 57 cases of nosocomial meningitis (1997-2007). These cases belonged to 56 patients (one of which had two nosocomial meningitis on a ventriculo-peritoneal shunt). **Results.** The predisposing factors were neurosurgical interventions (55.36%), ventriculo-peritoneal shunts (32.14%), rahianesthesia and surgical interventions on the ear and nose areas (10.72%), and mielography (1.18%). The risk factors were: emergency surgery (16.07%), a Glasgow score lower than 10 (12.5%), external drainage of CSF for more than 7days (8.92%) and the presence of post-operative fistulae (7.14%). The registered symptoms were: stiff the neck (80.70%), fever (75.44%), headache (56.14%), encephalitic syndrome (31.58%). The etiological agents were followings: *Staphylococcus* spp 52.63% (*S. aureus* 56.67%, coagulase negative staphylococci for 43.33%), *Enterococcus* spp 8.77%, *Streptococcus pyogenes* and *Pseudomonas* spp. 7.01% each, *Haemophilus influenzae* 1.75%, *Escherichia coli*, *Klebsiella pneumoniae* and mixed etiology 3.51%. The resistance was: 20 strains of Meticillin resistant staphylococci, 12 of which were Meticillin resistant *Staphylococcus aureus* (MRSA); the *Acinetobacter* and *Pseudomonas* strains - sensitivity to Colimycin, Tobramycin and Meropenem; one strain of *Enterococcus* was Vancomycin resistant. Twenty cases of meningitis caused by Meticillin resistant staphylococci were treated with Vancomycin and Rifampin or Ciprofloxacin. Six patients had an unfavorable evolution. The therapeutic strategies for *Acinetobacter* spp, were: Meropenem and Colimycin in 5 cases and Meropenem with Chloramphenicol in 2 cases. Four patients died. The *E. coli* and *K. pneumoniae* meningitis received Meropenem or Ciprofloxacin and Colimistin. The evolution was unfavorable in 2 cases (50%). Two *Enterococcus* spp meningitis received Vancomycin and Meropenem and were cured; 3 cases treated with Pefloxacin and Ceftazydim died (one strain was Vancomycin-resistant). Two patients with *Streptococcus pyogenes* meningitis died within 24 hours of admission. Overall, 25 patients died, with a mortality rate of 44.64%. **Conclusion.** Nosocomial meningitis is a severe infection, with diverse etiology, which rises therapeutic problems due to antibiotic resistance and a high mortality rate.

Key words: nosocomial meningitis, cerebro-spinal fluid, therapy

Rezumat. Scop. Studiul și-a propus sa stabilească: incidența factorilor predispozanți și de risc, manifestările clinice, etiologia și evoluția a 57 meningite nosocomiale, în funcție de schemele terapeutice alese după sensibilitatea la antibiotice a bacteriilor incriminate. Meningita

nosocomială survine după intervenții neurochirurgicale pentru traumatisme cranio-cerebrale sau procese tumorale, după explorări invazive ale sistemului nervos central sau consecutiv aplicării de materiale străine organismului pentru drenajul lichidului cefalo-rahidian (LCR). Incidența meningitei nosocomiale variază între 0,34% și 3,1%. **Material și metodă.** Datele statistice referitoare la meningita nosocomială au fost obținut din arhiva Spitalului Clinic de Boli Infecțioase Iași, care primește cazuri din toată Moldova (Nord-Estul României). Astfel, în perioada 1997-2007 s-au investigat 57 de cazuri de meningită nosocomială. Aceste cazuri au provenit de la 56 de pacienți (unul dintre aceștia a prezentat de două ori meningită pe shunt ventriculo-peritoneal). **Rezultate.** Factorii predispozanți au fost intervențiile neurochirurgicale (55,36%), shunt-ul ventriculo-peritoneal (32,14%), rahianestezia și intervenții în sfera ORL (10,72%), mielografia (1,78%). Factorii de risc întâlniți au fost intervenții neurochirurgicale în urgență (16,07%), scorul Glasgow mai mic de 10 (12,5%), drenajul extern mai mult de 7 zile (8,92%) și prezența fistulelor LCR postoperator (7,14%). Simptomele meningitei nu au fost zgomotoase, fiind reprezentate de redoarea cefei (80,70%), febră (75,44%), cefalee (56,14%) și sindrom encefalitic (31,58%). Agenții etiologici incriminați: *Staphylococcus* spp – 52,63% (*S. aureus* 56,67%, stafilococ coagulă negativ 43,33%), *Enterococcus* spp – 8,77%, *Streptococcus pyogenes* – 7,01%, *Acinetobacter baumani* – 12,28%, *Pseudomonas* spp. – 7,01%, *Haemophilus influenzae* – 1,75%, *E. coli*, *Klebsiella pneumoniae* și etiologia mixtă în câte 3,51% din cazuri. Majoritatea bacteriilor au fost rezistente la antibiotice: 20 tulpini de stafilococ dintre care 12 tulpini de *S. aureus* rezistente la oxacilină (SARM), tulpinile de *Acinetobacter* și *Pseudomonas* au fost sensibile la colimicină, tobramicină, meropenem, iar cele din familia *Enterobacteriaceae* și *Enterococcus* au avut rezistență variată (o tulpină de enterococ era vanco-rezistentă). Douăzeci de meningite determinate de stafilococi rezistenți la oxacilină au primit tratament cu vancomicină și rifampicină sau ciprofloxacină. Evoluție nefavorabilă au avut 6 bolnavi. În meningita cu *Acinetobacter* s-au folosit două scheme, meropenem plus colimicină administrată parenteral și intratecal în 5 cazuri și meropenem plus cloramfenicol, la 2 bolnavi. Evoluția a fost nefavorabilă în 4 cazuri. Meningita cu *Pseudomonas* spp a fost tratată cu meropenem sau ciprofloxacină și colimicină intratecal. Evoluția a fost nefavorabilă în 2 cazuri (50%). Meningitele cu *E. coli* și cu *K. pneumoniae* au fost tratate cu meropenem și ciprofloxacină. Toate cazurile au evoluat nefavorabil. Două meningite cu *Enterococcus* spp. au primit terapie cu vancomicină și meropenem, toate vindecându-se, iar alte trei cazuri tratate cu pefloxacină și ceftazidimă au decedat (o tulpină era vanco-rezistentă). Două meningite cu *Streptococcus pyogenes* au decedat în primele 24 de ore de la inițierea terapiei. Per total, au decedat 25 de pacienți, cu o rată a mortalității de 44,64%. **Concluzie.** Meningita nosocomială reprezintă o infecție severă, cu diversitate etiologică, cu probleme terapeutice particulare induse de tulpini rezistente, a cărei evoluție este grevată de o letalitate ridicată.

Cuvinte cheie: meningita nosocomială, lichid cefalo-rahidian, terapie

INTRODUCTION

Nosocomial meningitis occurs after neurosurgical interventions for cranio-cerebral trauma or tumors, after invasive explorations of the central nervous system, or after implanting

foreign body materials for cerebro-spinal fluid (CSF) drainage.

Despite the development of new antibiotics and the improvement of surgical techniques, the infectious complications keep causing significant

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morbidity and mortality in the postoperative period.

The predisposing factors for acquiring nosocomial meningitis are neurosurgical treatment for different conditions, the existence of a ventriculo-peritoneal shunt and interventions on the ear and nose region (1, 2). There have been reports nosocomial meningitis following corticosteroid injections in the epidural space for treating acute lumbar pain (3).

The etiology of nosocomial meningitis is very diverse, varying from Gram positive cocci to Gram negative bacilli.

The incidence of nosocomial meningitis varies between 0.34% and 3.1% according to the literature in the field (4-7).

MATERIAL AND METHODS

The data referring to nosocomial meningitis were gathered from the archive of the Clinical Hospital of Infectious Diseases Iași, a referral hospital for Moldova region (North-East România). We studied 57 cases of nosocomial meningitis (1997-2007). These cases belonged to 56 patients (one of which had two nosocomial meningitis on a ventriculo-peritoneal shunt).

RESULTS

The yearly distribution of the cases shows that the median of hospital admission was 5 cases per year, with important variations, between 2 and 10 cases per year (fig.1).

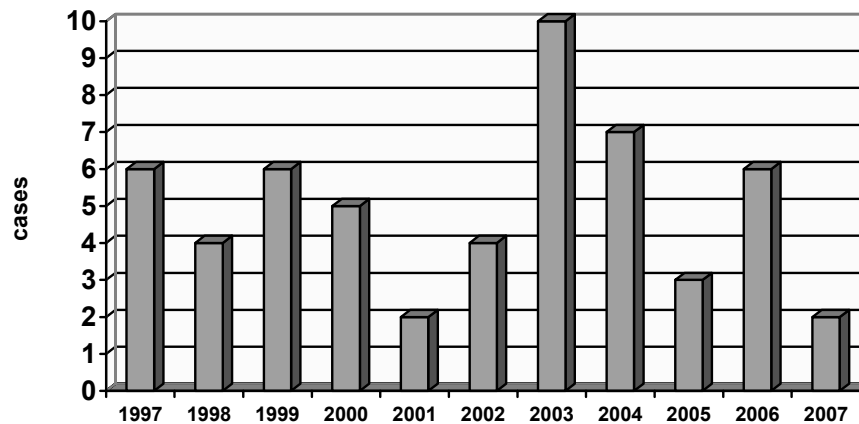


Fig. 1. Nosocomial meningitis – distribution of cases per year

The distribution of cases per sex and provenience shows the predominance

of the masculine sex and of the rural environment (tab. 1).

Table 1. Nosocomial meningitis – distribution of cases per sex and provenience

Provenience/Sex	n	%
Urban	16	28.57
Rural	40	71.43
Masculine	40	71.43
Feminine	16	28.57

The distribution of cases per age groups shows the predominance of adults, but also the presence of

newly born infants (12.5%) and of the children younger than 15 (10.72%) (fig. 2).

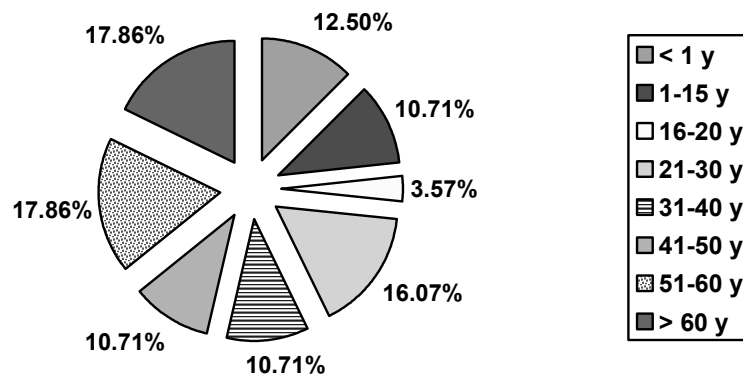


Fig. 2. Nosocomial meningitis – distribution of cases per age groups

The predisposing factors were neurosurgical interventions (55.36), followed by ventriculo-peritoneal shunts, rahianesthesia, interventions on the ear region and mielography. The neurosurgical interventions were made to resolve tumors or expansive cerebral processes (tab. 2).

The risk factors that have been registered in these patients were: emergency surgery in 9 cases, a Glasgow score less than 10 in 7 cases, external CSF drainage over 7 days in 5 cases, and post-operative fistulae in 4 cases (tab. 3).

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Table 2. Nosocomial meningitis – predisposing factors

Predisposing factors	n	%
Neurosurgical interventions	31	55.36
Ventriculo-peritoneal shunt	18	32.14
Rah anesthesia and ear interventions	6	10.72
Mielography	1	1.78

Table 3. Nosocomial meningitis – risk factors.

Risk factors	n	%
Emergency surgery	9	16.07
Glasgow score <10	7	12.5
External drainage >7 days	5	8.92
Post-operative fistulae	4	7.14

The patient PD, female from the rural environment, developed two nosocomial meningitis on a ventriculo-peritoneal shunt, one caused by *Staphylococcus epidermidis* (which evolved favorably) and another caused by *Enterococcus* spp., represented the cause of death.

In the beginning period of the meningitis, the symptoms were less striking, while in the state period they were more obvious, with stiff neck in 46 cases, fever in 43 cases, headache in 32 cases, encephalitic syndrome in 18 cases, vomiting in 16 cases and nausea in 10 cases (fig. 3).

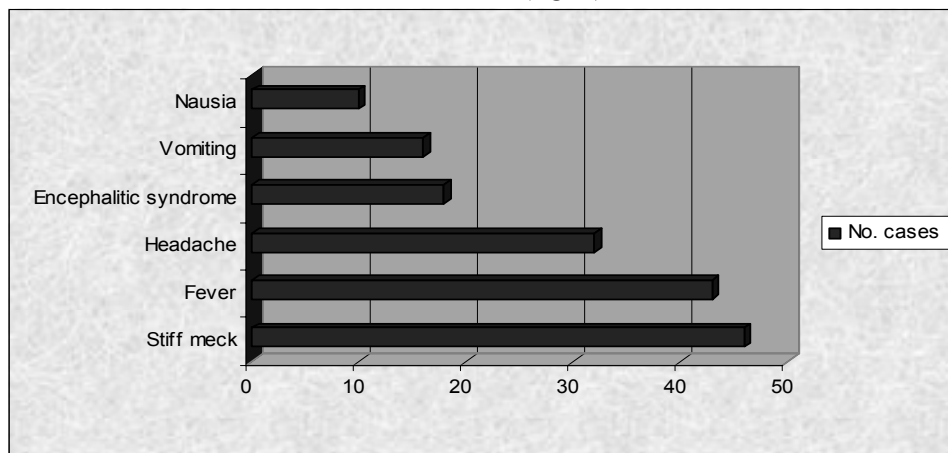


Fig. 3. The frequency of clinical symptoms of nosocomial meningitis

The diagnosis suspected on the clinical data and the presence of predisposing and risk factors, was confirmed by the laboratory analysis of the cerebro-spinal fluid.

The CSF extracted on lumbar puncture was turbid in 40 cases, yellow and clear in 6 cases each, and hemorrhagic in 5 cases (tab. 4).

Table 4. The frequency of CSF aspect in nosocomial meningitis

Aspect	n	%
Turbid	40	70.17
Yellow	6	10.53
Clear	6	10.53
Hemorrhagic	5	8.77

The neutrophile count in the sediment of the CSF was helpful for the diagnosis in the cases where the CSF was clear, yellow or hemorrhagic . It varied between 30 and 100% (fig. 4).

The albumin in the CSF was constantly high, varying from 0.5g% to over 20 g% (tab. 5).

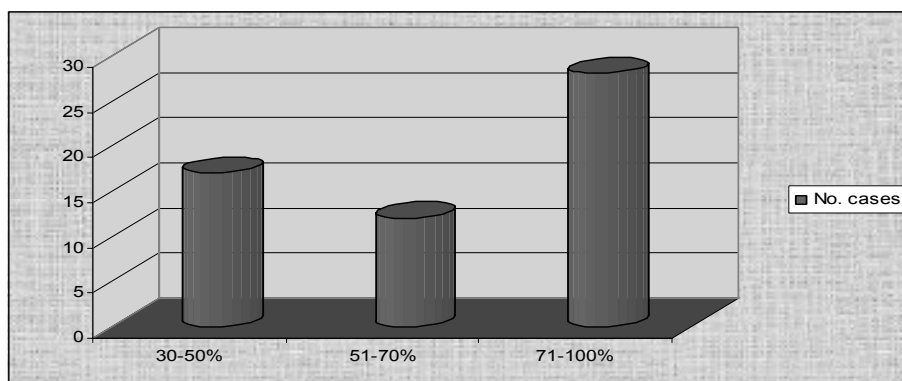


Fig. 4. Nosocomial meningitis – sediment

Table 5. The frequency of CSF albumin in nosocomial meningitis

Albumin g%	n	%
0.5-1	7	12.28
1.01-2	21	36.84
2.01-3	11	19.30
>3	18	31.58

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The etiological agents were *Staphylococcus* spp - 52.63% (*S. aureus* 56.67%, coagulase negative staphylococci for 43.33%), *Enterococcus* spp 8.77%, *Streptococcus pyogenes* and *Pseudomonas* spp. - 7.01% respectively, *Haemophilus influenzae* 1.75%,

Escherichia coli, *Klebsiella pneumoniae* and mixed etiology 3,51% respectively. Mixed etiology consisted of *E. coli* and *Peptococcus* spp. in one case and *Enterococcus* with *Pseudomonas aeruginosa* in the other (fig. 5).

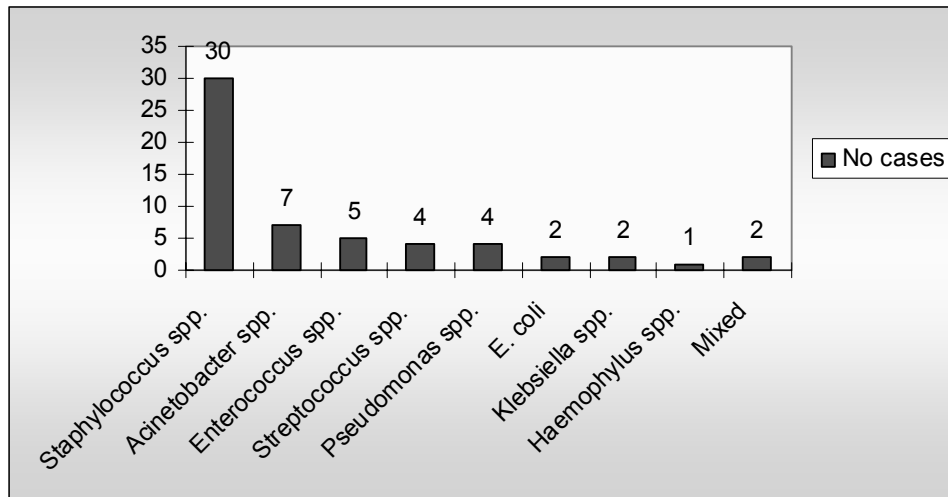


Fig. 5. The frequency of etiological agents in nosocomial meningitis

The susceptibility test results: 20 strains of *Staphylococcus* were methicillin resistant, 12 of which were methicillin resistant *Staphylococcus aureus* (MRSA); the *Acinetobacter* and *Pseudomonas* strains were sensitive to Colimycin, Tobramycin and Meropenem; the *Enterobacter* and *Enterococcus* strains had variable sensitivity (one strain of *Enterococcus* was Vancomycin resistant) (tab. 6).

Twenty cases of meningitis caused by MRSA were treated with Vancomycin and Rifampin or Ciprofloxacin. Six patients had an unfavorable evolution. The cases of meningitis caused by

MRSA were treated with Chloramphenicol, Ceftazidim, Ciprofloxacin and Pefloxacin in various combinations. Of these, two evolved unfavorably.

The therapeutic strategies for *Acinetobacter* spp, were: Meropenem and Colimycin in 5 cases and Meropenem with Chloramphenicol in 2 cases. Four patients died.

Pseudomonas spp. meningitis was treated with Meropenem or Ciprofloxacin and Colimycin. Out of four patients, two died.

The *E. coli* and *K. pneumoniae* meningitis received Meropenem and Ciprofloxacin. All four patients died.

Two *Enterococcus* spp meningitis received Vancomycin and Meropenem and were cured; 3 cases treated with Pefloxacin and Ceftazidim died (one strain was vancomycin-resistant).

Two patients with *Streptococcus pyogenes* meningitis died within 24 hours of admission, while two other cases had a favorable evolution. Overall, 25 patients died, with a mortality rate of 44.64%.

Table 6. The frequency of etiological agents by evolution of nosocomial meningitis

Etiological agent	Favorable evolution		Unfavorable evolution		Total	
	n	%	n	%	n	%
<i>Staphylococcus</i>	22	38.60	8	14.03	30	52.63
<i>Acinetobacter</i>	3	5.26	4	7.01	7	12.28
<i>Enterococcus</i>	2	3.51	3	5.26	5	8.77
<i>Streptococcus</i>	2	3.51	2	3.51	4	7.01
<i>Pseudomonas</i>	2	3.51	2	3.51	4	7.01
<i>Escherihia</i>	0	-	2	3.51	2	3.51
<i>Klebsiella</i>	0	-	2	3.51	2	3.51
<i>Haemophyllus</i>	1	1.75	0	-	1	1.75
Mixed etiology	0	-	2	3.51	2	3.51
Total	32	56.14	25	43.86	57	100

DISCUSSION

Most of the authors noticed the rise in the incidence of nosocomial meningitis. Its incidence vary between 0.34% and 3.1% (4-7)

The literature referring to the etiology of nosocomial meningitis showed different results: some studies suggested that 76% of the cases are caused by Gram positive cocci, while other studies noticed that the most important group of pathogens was that of the Gram negative bacilli (61%) (4). In our study, the predominant etiological agents were Gram positive cocci, as they were responsible for 34 cases out of 57 (59.65%).

According with Huang and Pintado, at the beginning of the nosocomial meningitis the symptoms are not striking, and the most important clue for diagnosis is the persistence or fever

after the neurosurgical intervention, sometimes accompanied by headache, stiff neck, vomiting or encephalitic syndrome (8, 9).

Leib et al. showed the value of CSF lactate is a quick test with good sensibility and specificity for identifying post neurosurgical bacterial meningitis. When this test is not possible, the laboratory analysis of the CSF (aspect, neutrophile count and sediment) are very useful (10).

Although authors like Hong Nguyen, Geers and Montero reported the existence of nosocomial meningitis caused by *Candida* species, especially *Candida albicans*, we noticed the lack of these etiological agents in our study. The cases admitted to the Clinical Hospital of Infectious Diseases Iași had a diverse etiology, which was

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in concordance with other published data (4, 13, 14).

CONCLUSIONS

1. The presence of fever in a post neurosurgical patient must make us consider a cerebral or meningeal infection.
2. Persistent fever, headache, stiff neck and encephalitic syndrome are the characteristic symptoms/signs of meningeal infection.
3. As the first clinical manifestations are usually minor, experienced neurosurgeons are needed in order to suspect nosocomial meningitis. The infectious diseases specialist must be contacted for a better prognosis of cases.
4. Any suspicion of meningeal infection should be followed by a lumbar puncture and the analysis of CSF before administering antibiotics which penetrate the CSF, in order to determine its etiology.
5. Nosocomial meningitis is a severe infection, with diverse etiology, which rise therapeutic problems due to antibiotic resistance and a high mortality rate.

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