International Journal of Science and Research Archive
eISSN: 2582-8185
Cross Ref DOI: 10.30574/ijsra
Journal homepage: https://ijsra.net/

(RESEARCH ARTICLE)

Check for updates

HIV-negative encephalitis and meningoencephalitis in the elderly

Nora Righi [1], Warda Boucetta [1], Melissa Doumandji [1], Samy Slimani [1,*], Daniel Floret [2] and Bruno Lina [2]

[1] *Department of Medicine, University of Batna 2, Algeria.*
[2] *Laboratories of the The Redhead Cross, 103 Grande Rue de la Croix Rousse, Lyon, France.*

International Journal of Science and Research Archive, 2023, 10(02), 119–127

Publication history: Received on 11 September 2023; revised on 03 November 2023; accepted on 06 November 2023

Article DOI: https://doi.org/10.30574/ijsra.2023.10.2.0879

Abstract

Introduction. The elderly are at a higher risk of infectious pathologies, which represent the third cause of primary mortality over 65 years and the leading cause of incidental mortality. The aim of a prospective longitudinal study conducted from April 1, 2012 to August 31, 2015 was to compare the epidemiological, clinical, biological, and etiological characteristics of encephalitis and meningoencephalitis in the elderly with those of young adults.

Methods. Patients aged over 28 days with suggestive symptoms of encephalitis were included from three medical departments (resuscitation, infectious diseases, and pediatrics) based on established inclusion and exclusion criteria. Patients seropositive for HIV and children under 15 years of age were excluded. Based on age, two groups were formed: group A (under 65 years old) and group B (65 years old and above), and were compared epidemiologically, clinically, and in terms of evolution.

Results. Out of 141 files that met the inclusion criteria, 38 were excluded (age ≤ 15 years). The average age for groups A and B were 36.27 ± 13.9 years (extremes: 17-64 years) and 72.55 ± 5.6 years (range: 66-83 years), respectively. In group B, progressive onset was the main feature (54.5%), associated with behavioral disorders (81.8%) and focal neurological disorders (81.8%). A significant part of these patients also had respiratory signs (36.8%), while in group A, behavioral disorders, focal and diffuse neurological disorders represented 49.6%, 45.5%, and 29.3% of cases, respectively. Out of 92 (65.2%) patients in group A, 44 (47.8%) had confirmed and/or probable viral etiologies, 31 (33.7%) had confirmed and/or probable bacterial etiologies, 3 (3.3%) had parasitic etiologies, 29 had confirmed co-infections, and 42 (45.7%) were treatable.

Conclusion: The study highlights the frequency of encephalitis and meningoencephalitis of viral origin in the elderly. The diagnosis remains difficult and any neurological sign recent onset and evolving in a febrile context should suggest the diagnosis.

Keywords: Encephalitis; Meningoencephalitis; Elderly; Epidemiology

1. Introduction

Encephalitis and meningoencephalitis are significant health concerns that require accurate etiological diagnosis and long-term support. They are relatively common, with an incidence of 3.5-7.4 per 100,000 inhabitants per year, and have a high mortality rate of 10 to 12% (1-3). The definition of "elderly" remains somewhat vague and disputed in the literature. While the World Health Organization (WHO) defines the elderly as individuals aged 65 and above, other studies suggest that the definition should include only those aged 75 and above (4). The elderly population is at risk for various pathologies, and infectious diseases are the third leading cause of primary mortality and the leading cause of incidental mortality after the age of 65 (4-6). Although encephalitis and meningoencephalitis are less common in the

* Corresponding author: Samy Slimani

elderly compared to other age groups, they are associated with high morbidity, mortality rates of up to 25% (7), and potential sequelae. Diagnostic and therapeutic delays can exacerbate these conditions.

Diagnosing encephalitis and meningoencephalitis in the elderly can be challenging due to differences in epidemiology and clinical presentations, which can sometimes be misleading and lead to inadequate care. The reason for admission is often nonspecific, with symptoms resembling those of a stroke, seizures, or confusion. These clinically deceptive presentations can occur regardless of the etiology and sometimes complicate the diagnostic process (8-10). In the elderly, bacterial infections are more common than viral infections (11-15). Studies have found that S. pneumoniae is the most frequently identified causative agent, accounting for 24% to 65% of cases. There is also an increasing prevalence of multi-resistant bacteria (16). Other pathogens, such as N. meningitidis, L. monocytogenes, and M. tuberculosis, are also found, although less frequently. Herpetic meningoencephalitis accounts for 10% to 35% of cases in the elderly (17-19).

The objective of this study is to investigate the epidemiological, clinical, and etiological features, as well as the long-term prognosis, of encephalitis and meningoencephalitis in the elderly, and compare them to those observed in young adults.

2. Material and methods

A prospective longitudinal and exhaustive study was conducted between 2012 and 2015 on patients aged over 28 days who were admitted to the infectious diseases (PHE), pediatrics (UHC), and medical intensive care (UHC) departments in Batna for encephalitis and meningoencephalitis with negative HIV status. The study followed the inclusion and exclusion criteria recommended by the FLIPS (20). The study primarily focused on epidemiological data, clinical compatibility, and radiology (CT, MRI).

For each patient, a comprehensive study of the cerebrospinal fluid (CSF) was conducted, including cytological analysis, chemical analysis (proteins, glucose, serum/CSF glucose ratio), and microbiological analysis. The microbiological analysis involved direct examination, soluble antigens, and culture for pyogenic germs and **KB**. Additionally, viral culture, polymerase chain reaction (PCR) tests on CSF, serum, and nasopharyngeal samples, and serological tests were performed to further investigate the microbiological aspects. These samples were immediately frozen at -80 °C for subsequent analysis. Blood samples were also collected in EDTA tubes (5 ml) or dry tubes (5 to 10 ml) upon patient discharge. These additional analyses, including real-time PCR/RT-PCR and serological tests, were conducted at the Institute of Infectious Agents (IAI) of Lyon University Hospital, following the standards of IAI microbiology laboratories.

Concurrently with the lumbar puncture, venous blood samples were taken for routine laboratory analysis, including complete blood counts, blood cultures, ionogram, C-reactive protein, and procalcitonin. All these parameters were recorded on a technical sheet. The etiological investigation was conducted in accordance with the recommendations of the FLIPS (20) for the treatment of patients with encephalitis.

The recommended diagnostic procedure for encephalitis and meningoencephalitis is divided into three successive steps, depending on the frequency of infectious agents as a cause of encephalitis and the need to start early treatment for certain pathogens and depending on the outcome. The etiology identified for each case is categorized as confirmed, probable, possible, or unknown. Each case can be affected by more than one etiology. The care measures are decided by the doctors of each department immediately after establishing the diagnosis of encephalitis and/or meningoencephalitis.

Patients who could not exclude a bacterial origin were treated with antibiotics, typically using a third-generation cephalosporin such as cefotaxime or ceftriaxone, along with amoxicillin and/or vancomycin, in accordance with international recommendations (9,21,22). The empirical antibiotic therapy was then adjusted based on the results of microbiological studies and clinical progress. Patients suspected of having herpes simplex meningoencephalitis were treated with acyclovir (15). In this study, two age groups were defined: group A, consisting of patients aged over 15 and under 65, and group B, comprising patients aged 65 and older.

To perform statistical analysis, the study compared various factors, including epidemiological, clinical, radiological, etiological, and therapeutic aspects. An independent factor analysis was also conducted. A p-value of less than 0.05 was considered statistically significant. The Chi-2 test was used to compare quantitative variables, with a risk of error (α) set at 5%.

3. Results

In our study, 141 patients with encephalitis and/or meningoencephalitis were included. Among them, 38 patients under the age of 15 were excluded. The remaining 103 patients met the inclusion and exclusion criteria, and 83 of them (80.6%) had a definite etiology. Of these 83 cases, 50 (48.5%) had a confirmed and/or probable viral etiology, 33 (32%) had a confirmed and/or probable bacterial etiology, and 4 (3.9%) had a parasitic etiology. Among the cases with a definite etiology, 40 (38.8%) had a monomicrobial etiology, while 34 (33%) had a co-infection, with 5% of these cases involving more than two germs. Out of the 103 cases of encephalitis and meningoencephalitis, 11 (7.8%) belonged to the elderly group (Group B), while 92 (65.2%) belonged to the young people group. The age distribution of these 103 patients is shown in Figure 1.

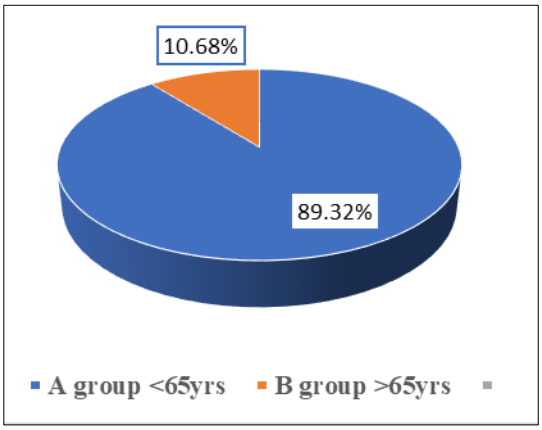

Figure 1 Distribution of patients by group

Among the 11 patients (7.8%) in Group B, 9 (81.8%) received a diagnosis. Of these, 8 (72.7%) cases had a confirmed and/or probable viral etiology, including 8 cases of coronaviruses, 4 cases of CMV, 3 cases of HSV, 1 case of EBV, 1 case of Adenovirus, 1 case of HHV6, 1 case of VZV, and 1 case of KB virus. Two (18.2%) cases had a confirmed and/or probable bacterial etiology (KB), and 1 (19.1%) case had a possible bacterial etiology (KB). One (19.1%) case had a parasitic etiology (PF). Among the patients with a parasitic etiology, 4 (36.4%) had a monomicrobial parasitic etiology, and 5 (45.5%) had co-infections, including 2 cases of "2 confirmed-probable," 2 cases of "probable-probable," and 1 case of "probable-possible." Eight cases (72.7%) were treatable.

Among the 92 patients (65.2%) in Group A, 74 (80.4%) received a diagnosis. Of these, 44 (47.8%) had a confirmed and/or probable viral etiology, including 12 cases of EBV, 10 cases of HSV, 10 cases of coronaviruses, 4 cases of Enterovirus, 4 cases of CMV, 3 cases of HHV6, 1 case of adenovirus, 1 case of mumps, 1 case of rubella, 1 case of Rhinovirus, 1 case of VZV, and 2 cases with a possible viral etiology (1 West Nile, 1 VZV). Additionally, 31 cases (33.7%) had a confirmed and/or probable bacterial etiology, including 18 cases of BK, 5 cases of Listeria, 4 cases of Streptococcus pneumoniae, 3 cases of Chlamydae, 1 case of Streptococcus D, 1 case of BGN, and 1 case of Lyme. Furthermore, 19 cases (20.7%) had a possible bacterial etiology, including 6 cases of BK, 4 cases of Coxiella Burnetii, 3 cases of Rickettsia Typhi, 2 cases of Mycoplasma, 1 case of Chlamydae, 2 cases of Rickettsia Conorrii, and 1 case of Rickettsii Rickettsii. Three cases (3.3%) had a parasitic etiology (PF). Among the patients with a parasitic etiology, 36 (39.1%) had a monomicrobial etiology, and 29 cases had coinfections, including "2 confirmed-confirmed," 12 "confirmed-probable," 13 "probable-probable" and/or "probable-possible," and 2 "possible-possible." Forty-two cases (45.7%) were treatable. The pathogens involved in the 103 patients with encephalitis and meningoencephalitis are listed in Table 1.

Table 1 Identified etiologies of encephalitis and meningoencephalitis

Etiologies	A Group n= 92%	B Group n= 11%
EBV	12	01
HSV1	10	03
Coronavirus	10	08
Enterovirus	04	00

CMV	04	04
HHV6	3	1
VZV	2	01
Adenovirus	1	1
Rubella	1	0
Mumps	1	0
West Nile	1	0
Rhinovirus	1	0
KB virus	0	1
KB	24	3
B Dorgferi	1	0
Listeria	5	0
Chlamydiae	4	0
Mycoplasma	2	0
Tweezers	2	0
S pneumonia	4	0
Streptococcus D	1	0
N meningitidis	0	0
Klebsiella	1	0
Coxiella burnetti	4	0
Rickettsii typhi	3	0
Rickettsii Conorii	2	0
Rickettsii rickettsie	1	0
Plasmodium Falciparum	3	1

The sex distribution was similar in both groups, with 51 men and 41 women in group A, resulting in a sex ratio of 1.24. The average age of group A was 36.27 ± 13.9 years, ranging from 17 to 64 years. In group B, there were 7 men and 4 women, resulting in a sex ratio of 1.75. The average age of group B was 72.55 ± 5.6 years, ranging from 66 to 83 years. Regarding comorbidities, diabetes was observed in 36.4% of group B patients, compared to 8.7% in group A. Cancer was present in 18.2% of group B patients, while only 1.1% of group A patients had cancer. Additionally, 18.2% of group B patients were diagnosed with epilepsy, and 9.1% had psychiatric disorders. In contrast, 6.5% of group A patients had underlying respiratory problems, and 4.4% were diagnosed with psychiatric disorders.

In group B, the elderly population, the following clinical characteristics were observed: gradual onset was mostly observed in 54.5% of cases, signs of tuberculous impregnation were present in 45.5% of cases, headaches were reported by 72.7% of patients, neck stiffness was observed in 45.5% of cases, often associated with behavioral disorders (81.8%), focal neurological disorders were present in 81.8% of cases, psychiatric disorders and hallucinations were reported in 18.2% of cases, respiratory signs were observed in 54.5% of patients. In contrast, group A, the young adult population, had lower rates of behavioral disorders (55.4%) and focal neurological disorders (56.5%). Respiratory impairment was observed in only 29.3% of cases.

Table 2 Comparison of the 2 groups according to the epidemiological parameters

Epidemiological parameters	A Group n= 92	B Group n=11	P
Underlying pathology	25(27.2)	8(72.7)	**0.002**
Diabetes	8 (8.7)	4(36.4)	**0.007**
Cancer	1(1.1)	2(18.2)	NS (0.069)
Cardiovascular pathology	7(7.6)	2(18.2)	0.009
Immunosuppressive Therapy	3(3.3)	1(9.1)	NS (0.069)
Prior psychiatric history.	4(4.4)	1(9.1)	NS 0.8
Head trauma	11(12)	0	NS 0.225
Epilepsy	1(1.1)	2(18.2)	NS 0.806

For the population belonging to Group B, the following clinical characteristics were observed: gradual onset was mostly observed in 54.5% of cases, 45.5% had shown signs of tuberculous impregnation, 72.7% complained of headaches, 45.5% had neck stiffness associated with behavior disorders in 81.8% of cases, focal neurological disorders were observed in 81.8% of cases, 18.2% of cases were accused of having psychiatric disorders and hallucinations, many patients also had respiratory signs (54.5%). In Group A, the following clinical characteristics were observed: behavioral disorders represented only 55.4%, focal neurological disorders represented only 56.5%, respiratory impairment represented only 29.3%. The clinical characteristics of the 11 elderly people belonging to Group B and the 92 young patients belonging to Group A are listed in Table 3.

Table 3 Comparison of the 2 groups according to clinical parameters

Clinical parameters	A Group n=92%	B Group n=1%	P
Gradual Start	54(58.7)	6(54.5)	0.792 NS
Fever >38.5	67(72.8)	7(63.6)	NS 0.522
The altered general condition	62(67.4)	9(81.8)	NS 0.543
ENT signs	18(19.6)	0	NS 0.106
Respiratory impairment	27(29.3)	6(54.5)	NS 0.091
Headache	83(90.2)	8(72.7)	**0.087**
Meningeal stiffness	47(51,1)	5(45.5)	NS 0.724
Consciousness disorders	53(57.6)	9(81.8)	NS (0.121)
Confusion	12(13)	2(18.2)	NS 0.630
Glasgow 8-11	20(21.7)	4(36.4)	NS 0.278
Behavioral problems	51(55.4)	9(81.8)	NS 0.535
Neurological disorders focal points	52(56.5)	9(81.8)	NS 0.469

For Group B, the following biological characteristics were observed: pleiocytosis was present in 45.5% of cases, 63.6% had normal glycorrhachia, 45.5% had hyperproteinorachia, 81.8% had hyponatremia. For Group A, the following biological characteristics were observed: pleiocytosis was present in 78.8% of cases, 61.1% had normoglycorachia, 60% had hyperproteinorachia and 45.7% had hyponatremia. Biological characteristics of the 11 elderly people belonging to Group B and the 92 young patients belonging to Group A are listed in Table 4.

Table 4 Comparison of the 2 groups according to the Biological Parameters

Biological Parameters	A Group n=92	B Group n=11	P
Pleocytosis	67(78.8)	5(45.5)	NS (0.075)
Hypoglycorachia	32(38.1)	2(18.2)	NS (0.347)
hyperalbuminorachia	48(60)	5(45.5)	NS (0.797)
Hyperleukocytosis	42(45.7)	6(54.5)	NS (0.576)
Strongly Positive CRP	24(26.1)	6(54.5)	NS (0.061)
Positive Pro calcitonin	54(58.7)	7(63.7)	NS (0.685)
Hyponatremia	42(45.7)	9(81.8)	NS (0.091)

For Group B, the following radiological and evolutionary characteristics were observed: pathological imaging was observed in 90.9% of cases, with parietal lobe involvement in 45.5% and hydrocephalus in 36.4%. The pathological EEG was observed in 9.1% of cases. Admission to intensive care was required for 36.4% of cases. 72.7% of patients in Group B passed away. For Group A, the following radiological and evolutionary characteristics were observed: pathological imaging was observed in 62% of cases, with hydrocephalus in 23.3% and frontal lobe involvement in 16.7%, the pathological EEG was observed in 14.1% of cases, admission to intensive care was required for 18.5% of cases. 28.3% of patients in Group A passed away. Radiological and evolutionary characteristics of the 11 elderly people belonging to Group B and the 92 young patients belonging to Group A are listed in Table 5.

Table 5 Comparison of the 2 groups according to radiological and progressive parameters

Radiological and progressive parameters	A Group n=92	B Group n=11	P
Pathological Imaging	57(62)	10(90.9)	NS 0.232
Hydrocephalus	21(23.3)	4(36.4)	NS 0.345
Parietal lobe involvement	14(15.6)	5(45.5)	**0.017**
Bilateral involvement	12(13,3)	4(36.4)	**0.048**
ECG	13(14.1%)	1(9.1%)	**0.005**
Intensive care Admission	17 (18.5)	4(36.4%)	**0.000**
Death	28.3%	72.7%	**0.003**

4. Discussion

Previous studies have primarily focused on meningitis in adults (23-26). However, there are fewer studies on the particularities of infectious meningitis in the elderly (27). In your study, the frequency of involvement in the elderly population was found to be 7.8%. Among the elderly patients, 72.8% had comorbidity, and 9.1% had immunosuppression. These results indicate a lower frequency of infection in the elderly compared to other studies. For instance, a study conducted in France over a 10-year period (January 1988 to June 1998) reported an involvement rate of 27.6% among the elderly (42 out of 152 cases). The presence of comorbidity was observed in 51% of cases, and immunosuppression was present in 30% (28). Similarly, a study conducted in the United States from 1998 to 2007 showed a frequency of 20% among elderly patients. Another study conducted in Taiwan reported that the elderly group accounted for 34.8% (87 out of 261 cases) (6,29).

In your study, 72.7% of viral attacks were reported, including CMV, HSV, and Echovirus. This is quite different from viral meningitis, where elderly subjects seem to be less affected (24). Your result is significantly higher than what was reported in other studies, such as 23.8%, 11%, 10.5%, and 11.6% (30-32). In the study by Gorse et al. (32), viral etiologies were reported to be 47.8% for young subjects, compared to 72.4%.

In the elderly, most published works find that the first pathogenic agent is Streptococcus pneumoniae in 24% to 65% of cases (30). Other studies have reported that Streptococcus pneumoniae, Neisseria meningitidis, and Listeria monocytogenes were common pathogens (33,34). However, your results are different, highlighting a significant

proportion of tuberculous etiology (27.3%). This difference in the pathogens involved may reflect several factors, including geographic distribution, which can influence the epidemiological trend of meningoencephalitis (25,35).

In their work on meningoencephalitis, most authors have highlighted several predisposing factors, including ENT infectious pathologies, diabetes, immunosuppression, and head trauma (25,27). However, the results of your study did not align with these findings, except for diabetes (36.4%) and cancer (18.2%), which were like what was reported in a study conducted in Taiwan (29). The significance of the underlying pathology was found to be objective when compared to encephalitis and meningoencephalitis in young subjects. The same was observed for diabetes and cardiovascular pathology, with respective p-values of 0.007 and 0.002. The higher incidence of diabetes in Group B (elderly) can be attributed to the fact that the prevalence of diabetes increases with age (36). The presence of epilepsy (18.2%) was considered a serious risk factor in this age category (33,35,37).

In the elderly, the typical presentation of encephalitis and meningoencephalitis is an association of fever, impaired consciousness (from confusion to coma), and possibly irritation meningitis but without frank meningeal syndrome (38), contrasting with the classic presentation of children or young adults (39). Although stiffness of the neck, a sign that is not very specific and not very sensitive in the elderly to be considered (12), in your study, it was observed in 45.5% of cases. Confusion, which is the main sign of meningoencephalitis in the elderly and should alert the clinician (40), was observed in 18.5% of the population studied.

In your series, 81.8% of cases experienced disorders of consciousness, and 36.4% of cases had comitial crises. These values are consistent with previously published data (30). On the other hand, 81.8% of your cases exhibited neurological signs associated with cerebral locations, compared to only 31% in the other study (30). This suggests that the diagnosis of encephalitis and meningoencephalitis in the elderly is difficult, as the neurological presentation accounts for a greater share than with any other germ. In a study on herpetic meningoencephalitis in elderly subjects, similar conclusions were drawn based on the results, including disordered consciousness (77.3%), convulsions (31.8%), and focal signs (54.5%). All patients in that study also presented neurological signs (16).

According to your results, there are no more abnormalities highlighted in the elderly compared to the young subjects. The frequency of anomalies of cerebral tomography in your series was close to that reported in the literature (90%) (25,27,40), except for parietal lobe involvement (p=0.007), bilateral involvement (p=0.048), and electrical abnormalities (p=<0.001).

The prognosis of meningoencephalitis has been the subject of several studies. Mortality in bacterial infection is estimated in the literature at 7.3% to 27% in young adults compared to 35% to 57% in elderly persons (10,11). From your point of view, you also deplored a higher rate of mortality in Group B (72.7%) compared to 28.3% in young persons, because age is a serious prognostic factor. This death rate in Group B was much higher than what was reported in the Taiwan study (43%) (29).

5. Conclusion

This study has successfully highlighted the frequency of encephalitis and meningoencephalitis in elderly subjects. The diagnosis of these conditions remains challenging due to the prevalence of confusion and comitial crises, which lack specificity. However, any recent neurological sign that evolves in a febrile context should raise suspicion for these conditions. It is important to note that performing a brain CT scan should not be done systematically and should not delay treatment. Initial treatment should consider these epidemiological considerations. Furthermore, the relative frequency of pathogens involved in encephalitis and meningoencephalitis in the elderly is similar to that observed in young subjects.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The study was carried out in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the University of Batna. Before enrollment, all patients received information on the aims and procedures of the study, and were included only after they expressed their willingness to participate.

Statement of Informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Raschilas F, Wolff M, Delatour F, Chaffaut C, De Broucker T, Chevret S, et al. Outcome of and prognostic factors for herpes simplex encephalitis in adult patients: results of a multicenter study. Clinical Infectious Diseases. 2002, 35(3):254-60.

[2] Whitley RJ, Alford CA, Hirsch MS, Schooley RT, Luby JP, Aoki FY, et al. Vidarabine versus acyclovir therapy in herpes simplex encephalitis. New England Journal of Medicine. 1986, 314(3):144-9.

[3] Sarrazin JL, Bonneville F, Martin-Blondel G. Brain infections. Diagn Interv Imaging. 2012 Jun;93(6):473-90. doi: 10.1016/j.diii.2012.04.020.

[4] Le Moal G, Roblot F, Paccalin M, Pasdeloup T, Roblot P, Becq-Giraudon B. Particularités des méningites du sujet âgé [Details of meningitis in the elderly]. Rev Med Interne. 2000 Oct;21(10):844-53. French. doi: 10.1016/s0248-8663(00)00235-6.

[5] Yoshikawa TT. Perspective: aging and infectious diseases: past, present, and future. Journal of Infectious Diseases. 1997, 176(4):1053-7.

[6] Dayaramani C, De Leon J, Reiss AB. Cardiovascular Disease Complicating COVID-19 in the Elderly. Medicina (Kaunas). 2021 Aug 17;57(8):833. doi: 10.3390/medicina57080833.

[7] Schuchat A, Robinson K, Wenger JD, Harrison LH, Farley M, Reingold AL, et al. Bacterial meningitis in the United States in 1995. New England journal of medicine. 1997, 337(14):970-6.

[8] Behrman RE, Meyers BR, Mendelson MH, Sacks HS, Hirschman SZ. Central nervous system infections in the elderly. Archives of internal medicine. 1989, 149(7):1596-9.

[9] Newman DH. Clinical assessment of meningitis in adults. Annals of Emergency Medicine. 2004, 44(1):71-3.

[10] Gorse GJ, Thrupp LD, Nudleman KL, Wyle FA, Hawkins B, Cesario TC. Bacterial meningitis in the elderly. Archives of Internal Medicine. 1984, 144(8):1603-7.

[11] Miller LG, Choi C. Meningitis in older patients: how to diagnose and treat a deadly infection. Geriatrics. 1997, 52(8):43-4, 7-50, 5.

[12] Miller L, Choi C. Meningitis in older patients: how to diagnose and treat a deadly infection. Geriatrics (Basel, Switzerland). 1997, 52(8):43-4, 7.

[13] Hausfater P, Fillet AM, Rozenberg F, Arthaud M, Trystram D, Huraux JM, et al. Prevalence of viral infection markers by polymerase chain reaction amplification and interferon-alpha measurements among patients undergoing lumbar puncture in an emergency department. Journal of medical virology. 2004, 73(1):137-46.

[14] Koskiniemi M, Piiparinen H, Mannonen L, Rantalaiho T, Vaheri A. Herpes encephalitis is a disease of middle aged and elderly people: polymerase chain reaction for detection of herpes simplex virus in the CSF of 516 patients with encephalitis. The Study Group. Journal of Neurology, Neurosurgery &amp, Psychiatry. 1996, 60(2):174-8.

[15] Kupila L, Vuorinen T, Vainionpää R, Hukkanen V, Marttila R, Kotilainen P. Etiology of aseptic meningitis and encephalitis in an adult population. Neurology. 2006, 66(1):75-80.

[16] Pasdeloup T, Roblot F, Aucher P, Fauchère JL, Becq-Giraudon B. Infections à pneumocoques observées au CHU de Poitiers dans la population adulte. Etude épidémiologique et clinique [Pneumococcal infections in the adult population observed at the Poitiers University Hospital. Epidemiologic and clinical study]. Presse Med. 1998 Apr 11;27(14):653-7.

[17] Van Vliet K, Glimåker M, Lebon P, Klapper P, Taylor C, Ciardi M, et al. Multicenter evaluation of the Amplicor enterovirus PCR test with cerebrospinal fluid from patients with aseptic meningitis. Journal of Clinical Microbiology. 1998, 36(9):2652-7.

[18] Jouanny P, Vespignani H, Gérard A, Jeandel C, Ducrocq X, Penin F, Weber M, Dureux JB, Cuny G, Canton P. Méningoencéphalite herpétique du sujet âgé. A propos de 13 observations [Herpetic meningoencephalitis in the elderly. Apropos of 13 cases]. Rev Med Interne. 1994;15(8):504-9. French. doi: 10.1016/s0248-8663(05)81479-1.

[19] Jouanny P, Vespignani H, Gerard A, Jeandel C, Ducrocq X, Penin F, et al. Herpetic meningoencephalitis in the elderly. Apropos of 13 cases. La Revue de Medecine Interne. 1994, 15(8):504-9.

[20] Mailles A, Stahl J-P, Committee botS, Group tI. Infectious encephalitis in France in 2007: a national prospective study. Clinical Infectious Diseases. 2009, 49(12):1838-47.

[21] Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, et al. Practice guidelines for the management of bacterial meningitis. Clinical infectious diseases. 2004, 39(9):1267-84.

[22] Van de Beek D, De Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M. Clinical features and prognostic factors in adults with bacterial meningitis. New England Journal of Medicine. 2004, 351(18):1849-59.

[23] Wenger JD, Hightower AW, Facklam RR, Gaventa S, Broome CV, Group BMS. Bacterial meningitis in the United States, 1986: report of a multistate surveillance study. Journal of infectious diseases. 1990, 162(6):1316-23.

[24] Aronson S, DeBuono B, Buechner J. Acute bacterial meningitis in Rhode Island: a survey of the years 1976 to 1985. Rhode Island Medical Journal. 1991, 74(1):33-6.

[25] Durand ML, Calderwood SB, Weber DJ, Miller SI, Southwick FS, Caviness Jr VS, et al. Acute bacterial meningitis in adults--A review of 493 episodes. New England Journal of Medicine. 1993, 328(1):21-8.

[26] Geiseler PJ, Nelson KE, Levin S, Reddi K, Moses VK. Community-acquired purulent meningitis: a review of 1,316 cases during the antibiotic era, 1954-1976. Reviews of infectious diseases. 1980, 2(5):725-45.

[27] Chan Y, Wilder-Smith A, Ong B, Kumarasinghe G, Wilder-Smith E. Adult Community Acquired Bacterial Meningitis in a Singaporean Teaching Hospital. A Seven-Year Overview. Singapore Med J.2002, 43(12):632-6.

[28] Owen JC, Moore FR, Williams AJ, Stark L, Miller EA, Morley VJ, et al. Test of recrudescence hypothesis for overwintering of eastern equine encephalomyelitis virus in gray catbirds. Journal of medical entomology. 2011, 48(4):896-903.

[29] Lai W-A, Chen S-F, Tsai N-W, Chang C-C, Chang W-N, Lu C-H, et al. Clinical characteristics and prognosis of acute bacterial meningitis in elderly patients over 65: a hospital-based study. BMC geriatrics. 2011, 11(1):1-6.

[30] Le Moal G, Roblot F, Paccalin M, Pasdeloup T, Roblot P, Becq-Giraudon B. [Details of meningitis in the elderly]. Rev Med Interne. 2000, 21(10):844-53.

[31] RASMUSSEN HH, SØRENSEN HT, MØLLER-PETERSEN J, MORTENSEN FV, NIELSEN B. Bacterial meningitis in elderly patients: clinical picture and course. Age and ageing. 1992, 21(3):216-20.

[32] Domingo P, Barquet N, Alvarez M, Coll P, Nava J, Garau J. Group B streptococcal meningitis in adults: report of twelve cases and review. Clinical infectious diseases. 1997, 25(5):1180-7.

[33] Cabellos C, Verdaguer R, Olmo M, Fernández-Sabé N, Cisnal M, Ariza J, et al. Community-acquired bacterial meningitis in elderly patients: experience over 30 years. Medicine. 2009, 88(2):115-9.

[34] Erdem H, Kilic S, Coskun O, Ersoy Y, Cagatay A, Onguru P, et al. Community-acquired acute bacterial meningitis in the elderly in Turkey. Clinical microbiology and infection. 2010, 16(8):1223-9.

[35] Chang W-N, Lu C-H, Huang C-R, Tsai N-W, Chuang Y-C, Chang C-C, et al. Changing epidemiology of adult bacterial meningitis in southern Taiwan: a hospital-based study. Infection. 2008, 36(1):15-22.

[36] Foo N-P, Chen K-T, Lin H-J, Guo H-R. Characteristics of pyogenic liver abscess patients with and without diabetes mellitus. Official journal of the American College of Gastroenterology| ACG. 2010, 105(2):328-35.

[37] Zoons E, Weisfelt M, De Gans J, Spanjaard L, Koelman J, Reitsma J, et al. Seizures in adults with bacterial meningitis. Neurology. 2008, 70(22 Part 2):2109-15.

[38] Roos KL. Meningitis as it presents in the elderly: diagnosis and care. Geriatrics (Basel, Switzerland). 1990, 45(8):63-4, 9.

[39] Tunkel AR, Scheld WM. Acute bacterial meningitis. The Lancet. 1995, 346(8991-8992):1675-80.

[40] Kirkpatrick B, Reeves D, MacGowan A. A review of the clinical presentation, laboratory features,antimicrobial therapy and outcome of 77 episodes of pneumococcal meningitis occurring in children and adults.Journal of Infection. 1994, 29(2):171-82.

[41] Thigpen MC, Whitney CG, Messonnier NE, Zell ER, Lynfield R, Hadler JL, et al. Bacterial meningitis in the United States, 1998–2007. New England Journal of Medicine. 2011, 364(21):2016-25.