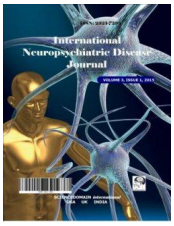

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A General Assessment of the Functional Impact of Acute Disseminated Encephalomyelitis

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Authors' contributions

This work was carried out in collaboration between both authors. Authors IL and OM conceived the study. Author IL designed the experiments and carried out the research. Both authors prepared the first draft of the manuscript and were involved in the revision of the graft manuscript and have agreed to the final content.

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ABSTRACT

Introduction: Long-term disability in patients with acute disseminated encephalomyelitis (ADEM) is caused not only by neurological deficiency, but also by the difficulties with social and psychological adaptation. Together with neurological condition, a very important role in clinical characteristics of the disease belongs to psychosocial disorders, as well as to patients' subjective perception of the disease symptoms that has the impact on their quality of life.
Methods: We have examined 45 patients diagnosed with acute disseminated encephalomyelitis, 10 men and 35 women, aged 15- 53 (average age 32±0.4). All the patients were being treated at the Kiev city centre of multiple sclerosis (Kiev city hospital number 4, Alexandrovskaya City Clinical Hospital, Kiev city, Ukraine) during 3 years. The diagnosis of ADEM was based on neurological examination, MRI of the brain and CSF analysis. The neurological status was assessed by Kurtzke an Expanded Disability Status Scale (EDSS) and Functional Systems Points

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(FSS). In order to assess the impact of the disease on the daily life of patients to the most full extent a survey was conducted with the use of tests: “Functional Limitation Profile” and “Sickness Impact Profile – 68”.

Results: According to the "Functional Limitation Profile" test, patients diagnosed with acute disseminated encephalomyelitis demonstrated functional condition impairment most often in 3 categories: "work" (86% of cases), "leisure and entertainments" (84% of cases), "social interaction" (82 % of cases), the least impaired were the categories "communication" (22% of cases), "emotions" (32% of cases), "food" (32% of cases). According to the "Sickness Impact Profile - 68" test, patients diagnosed with acute disseminated encephalomyelitis showed functional condition impairment most often in the category "social behavior" (84%), "somatic autonomy" (70% of cases), "mental autonomy and communication" (60% of cases). Categories "mobility control" (50%), "emotional stability" (44% of cases), "degree of mobility" (44% of cases) suffered the least. The highest percent in relation to the maximum possible point was noted in the category "social behavior", and the lowest – in the category “somatic autonomy”. Severity of neurologic deficit and increase in the number of demyelination foci on MRI have a negative impact on patients’ self-assessment of their quality of life. Gender of patients and the presence of disseminated encephalomyelitis relapses have the impact on the degree of functional limitation.

Conclusion: We can conclude from the assessments that the emergence of ADEM results in significant changes in the patient’s functional condition. Of the factors observed, the disease has the greatest impact on the patient’s social sphere and associated activities and the smallest impact on their emotional condition. The disease has a significant impact on the emotional state of women and patients with multiphasic course of disseminated encephalomyelitis. It is also reflected in the disorders of their sleep and rest. Social sphere of life is suffering more in men and patients with a first episode of disseminated encephalomyelitis.

Keywords: Acute disseminated encephalomyelitis; quality of life; "Functional Limitation Profile" test; "Sickness Impact Profile - 68" test.

1. INTRODUCTION

Acute disseminated encephalomyelitis (ADEM) is an autoimmune disease characterized by the presence of central nervous system (CNS) inflammation lesions (demyelination) that occur after infection or vaccination [1,2]. ADEM occurs in 1 of 500 cases of rubella, 1,000 cases of measles, 10,000 cases of chicken pox, 4,000 cases of vaccination against smallpox, 100,000 cases of vaccination against measles [3,4]. In 74% of cases, there had been an infectious disease in the medical history of a patient a month before the onset of neurological disorders [5-8]. The following infections may be the triggering factors for ADEM: Viral factors (measles, rubella, mumps, parainfluenza viruses [9-12], hepatitis, influenza A and B [13,14], whooping cough, tetanus [3,15], Epstein- Barr virus, cytomegalovirus [16] and bacterial factors (*Mycoplasma pneumoniae* [17-21], Campylobacter [22-24], *Borrelia Burgdogferi* [4,25], Leptospira, Chlamydia, Legionella, B - hemolytic streptococcus group A [26-28]. However, in most cases there is evidence of a nonspecific upper respiratory tract infection and there is no serologic evidence of pathogen [4,29,30]. Vaccines that may lead to ADEM development include influenza, measles, hepatitis B, rabies, tetanus, chicken pox vaccines [26,31,32]. There are also cases of spontaneous development of the disease [5,7,33].

Infectious factor is closely associated with the pathogenesis of ADEM, but it is not localized in the central nervous system or spinal fluid, virus replication in brain cells does not arise. It is not clear how it leads to the development of demyelinating disease that is why there is a hypothesis of molecular mimicry [4]. According to this theory, some infectious agents have peptides similar to immune-dominant epitope of myelin basic protein (MBP). It means that these infectious pathogens can activate T-cells that are autoreactive to MBP in case if phenotype of certain antigens is present in HLA (Human Leukocyte Antigen). It is known that HLA-system has two classes of molecules: I (A, B, C) is expressed on all nuclear cells and II (DR, DQ, DP) is expressed on cells involved in antigen presentation. Currently, ADEM is associated with genotype DRB1*01 and DRB1*03(017). But it is not clear why so many infectious agents can cause one disease. A possible explanation for this is another hypothesis – direct penetration of neurotropic virus in the central nervous system

(CNS) opens brain antigens, previously closed to the immune system, and myelin proteins, causing an inflammatory response that leads to immune-mediated demyelination [3,4].

The development of experimental models, including experimental allergic encephalomyelitis (EAE), has made an important contribution to the understanding of immunopathogenesis of acute disseminated encephalomyelitis [4]. EAE in Theiler's virus model is an autoimmune condition that can be reproduced in animals by administering myelin antigens such as MBP, proteolipid protein and glycoprotein of oligodendrocytes [3], causing primary systemic impulse in autoimmune reaction appearance. Penetrating into peripheral blood, antigen is phagocyted by macrophages that present it on their surface as a part of receptors of main complex of histocompatibility (HLA), after that the antigen is recognized by CD4 + T-cells-helpers. They, in their turn, stimulate the formation of proinflammatory cytokines, resulting in lesion of the blood-brain barrier (BBB), after that autoreactive T-cells with CD4-phenotype to the antigens - myelin basic protein (MBP), proteolipid protein or myelin-oligodendrocyte glycoprotein get into the central nervous system from peripheral blood. In brain tissue they are reactivated by cytotoxic T-cells, B-cells, macrophages and glial cells, and enhance cascade of immunopathological reactions: expression of adhesion molecules and antigen-presenting molecules (HLA-molecules) to the endothelium of the brain vessels and gliocytes; increased production of proinflammatory cytokines – gamma-interferon, tumor-necrosis factor-alpha (TNFα), interleukins (IL-1, SHL-2, IL-12, IL-15), autoantibodies of proteases, chemokines, free radicals, nitric oxide; decreased synthesis of proinflammatory cytokines - IL-4, IL-10, beta-interferon. It leads to violation of BBB permeability, activation of B cells and all components of humoral immunity, complement system and monocytes/macrophages [3]. These autoimmune and pathobiochemical reactions cause formation of disseminated perivascular foci of inflammation, especially around capillary, venous structures (small and medium), causing an inflammatory reaction cascade, destruction of myelin (demyelination), lesion of axons. Thus, the pathogenesis of acute disseminated encephalomyelitis has autoimmune nature and is accompanied by typical pathological changes.

The criteria necessary for the diagnosis of acute disseminated encephalomyelitis are given in the book of Harris C, et al. 2007 [2]. The authors state that for diagnostics of acute disseminated encephalomyelitis it is important to consider the medical history of preceding signs of infectious process, acute onset of the disease with evident disseminated lesion of central nervous system, frequently involving gray matter of the brain, increase of neurological deficit during the short period of time (hours – days), sudden development of encephalopathy and even disorders of consciousness, monophasic course of the disease and absence of metabolic and infectious disorders.

According to the recent studies of International Pediatric Multiple Sclerosis Study Group (IPMS), ADEM is regarded as polysymptomatic disease with multifocal lesion of CNS. Encephalopathy and disorders of consciousness are part of the presentation [34].

Some authors consider ADEM as polysymptomatic demyelinating inflammatory disease which is characterized by acute or subacute onset, no data about preceding lesion of CNS, significant improvement of patient's condition after the treatment [34,35]. ADEM is also characterized by the signs of systemic inflammatory response (headache, dizziness, nausea, fever, myalgia), appearing a few days – weeks after the infectious disease (so-called latent period) [36].

In most cases ADEM is characterized by the monophasic course accompanied by considerable variations concerning the duration of the disease and period of convalescence of the patient. However, there are also possible relapses of ADEM that have already been known since 1932, as described by van Bogaert, who published the paper "ADEM with relapses" [37]. ADEM relapses can be considered as a multiphasic course of this disease or its transformation into multiple sclerosis (according to the McDonald Criteria) (see, e.g., the works [38-44].

Appearance of new clinic symptoms three months after initial signs of this disease is considered as a relapse of ADEM. In the case of this disease relapse, the pathological process comprises new parts of brain and/or spinal cord (which is usually confirmed by clinical investigations and neuro visual methods).

If the relapse appears in a short time interval after initial signs and is combined with further infection or cancelled hormonal therapy, the term multiphasic disseminated encephalomyelitis (MDEM) should be used [45,46].

MDEM is characterized by poly-symptomatic manifestations of this disease, availability of demyelination foci in Magnetic resonance imaging (MRI) data, mainly in subcortical parts of brain, to a lesser extent located periventricularly, with total or partial disappearance of foci during the convalescent period [47]. The multiphasic course of disseminated encephalomyelitis can be diagnosed in the case of disease relapse appearance at least 3 months after its initial presentation [46-49]. Appearance of new clinic symptoms and new foci in MRI data 12 to 18 months after the primary episode of the disease is indicative of its possible transformation into multiple sclerosis (according to the McDonald Criteria) [44,50].

Long-term disability in patients with acute disseminated encephalomyelitis is caused not only by neurological deficiency, but also by the difficulties with social and psychological adaptation [1,4,10,51,52]. Together with neurological condition, a very important role in clinical characteristics of the disease belongs to psychosocial disorders, as well as to patients' subjective perception of the disease symptoms that has the impact on their quality of life. Quality of life is impaired in ADEM in part due to physical disability. ADEM can diminish quality of life by interfering with the ability to work, pursue leisure activities, and carry on usual life roles. Symptoms that affect quality of life in patients with ADEM may include impaired mobility, fatigue, depression, pain, spasticity, cognitive impairment, sexual dysfunction, bowel and bladder dysfunction, vision and hearing problems, seizures. Polymorphic clinical features of ADEM significantly affect the quality of life of patients with this diagnosis – that was the main reason of carrying out this research.

The purpose of our work was to assess the degree of psychosocial and physical function impairment in patients diagnosed with acute disseminated encephalomyelitis and to identify the spheres of life affected by the disease the most.

2. METHODS

We have examined 45 patients diagnosed with acute disseminated encephalomyelitis, 10 men and 35 women, aged 15- 53 (average age 32 ± 0.4). All the patients were being treated at the Kiev city centre of multiple sclerosis (Kiev city hospital number 4, Alexandrovskaya City Clinical Hospital, Kiev city, Ukraine) during 3 years. The diagnosis of ADEM was based on neurological examination, MRI of the brain and CSF analysis. All ADEM patients met the recently published diagnostic criteria [2]. The onset of disease in all patients was acute with evident disseminated lesion of central nervous system, increase of neurological deficit was observed during the short period of time (hours – days) and sudden development of encephalopathy. All patients underwent magnetic resonance imaging (MRI) studies of the brain and/or of the spinal cord to detect the location of the lesions of demyelination, lesion-load and size. The inclusion criteria were the absence of the other medical conditions that could affect their quality of life, normal results of fundosopic and transcranial doppler ultrasound exam, age not older than 55 years old. The neurological status was assessed by Kurtzke an Expanded Disability Status Scale (EDSS) and Functional Systems Points (FSS) [41]. Based on a standard neurological examination, the 7 functional systems (plus "other") are rated. These ratings are then used in conjunction with observations and information concerning gait and use of assistive devices to rate the EDSS. Each of the FSS is an ordinal clinical rating scale ranging from 0 to 5 or 6. The EDSS is an ordinal clinical rating scale ranging from 0 (normal neurologic examination) to 10 (death due to MS) in half-point increments. The FSS include pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral (or mental), and other. The average point according to EDSS scale in patients with acute disseminated encephalomyelitis was 2.5±0.8 points. All patients were treated with hormonal pulse-therapy, using methylprednisolone in the dose of 500-1000 mg daily in 200 ml of isotonic sodium chloride solution (within 5 days).

All the patients were under observation for 3 years. If during this period (3 years) no relapse of demyelination disease was detected, we interpreted it as the monophasic type of the ADEM course. In the case when disease relapses appeared, having the signs of disseminated encephalomyelitis from the clinical viewpoint and after neuro-visual patient examination, it was considered as the multiphasic option of the disease course (MDEM). In the case of clinically confirmed

multiple sclerosis (in accord with the McDonald criteria [44]), we interpreted it as transition of ADEM into multiple sclerosis. We assessed the functional limitations of patients with ADEM depending on the clinical course of ADEM (in patients with a first episode of disseminated encephalomyelitis (the disease was diagnosed for the first time) and its multiphasic course.

In order to assess the impact of the disease on the daily life of patients to the most full extent a survey was conducted with the use of tests: "Functional Limitation Profile" and "Sickness Impact Profile – 68" [10,35,38-41]. All the patients were interrogated according to these tests after the acute period of disease – disappearance of encephalopathy phenomenon, i.e. disappearance of acute manifestations of the disease.

"Functional Limitation Profile" test helped to assess the change of patient's behavior in case of acute disseminated encephalomyelitis in 12 categories of life activity: "walk", "body care and motion", "movement", "household activity", "leisure and entertainments", "social interaction", "emotions", "clarity of mind", "sleep and rest", "food", "communication", "work". While carrying out "Sickness Impact Profile - 68" test, functional condition of patients was assessed in 6 categories of life activity. "Somatic autonomy" category reflected the extent of help that the patient requires when performing everyday activities (dressing up, standing, walking, eating etc). "Mobility control" category characterized the degree of control of motion functions, including walking and actions with hands. "Psychic autonomy and communication" category described behavior, connected with mental functions and verbal communication. "Mobility degree" category included the ways the disease limits household and professional activity."Social Behavior" category reflects social sphere of activity. "Emotional stability" category reflects disease impact on the emotional sphere. All items are scored dichotomously (no=0, yes =1). Points then were summed. A higher point meant a worse quality of life.

There were no control subjects (without systemic or neurological diseases), because according to the "Functional Limitation Profile" and "Sickness Impact Profile – 68" tests no values are considered "normal", and these tests are used only in subjects with certain diseases, not in healthy individuals.

Statistical analysis of the results was made with the use of Stata 12. Generalized characteristic of the investigated indices is represented by the arithmetic mean (X). Variability of parameters was assessed by standard deviation. The correlation between the degree of functional limitation in patients with ADEM according to the results of the "Functional Limitation Profile" and "Sickness Impact Profile – 68" tests and the size of demyelination foci on MRI was evaluated with Pearson coefficient correlation analysis. For comparative analysis there was used t-test (five percent for two tailed tests was chosen as the level of significance) and χ^2 test (α=0.05, two sided).

According to the decision of the Ethics Committee of the O.O. Bogomolets National Medical University (Kyiv city, Ukraine), the investigations described in these articles have been carried out according to modern scientific standards. All patients signed informed consent form. There have been provided the measures ensuring safety of the patients, respect of their rights and dignity as well as moral and ethical standards in accordance with the human rights principles of the Declaration of Helsinki. Ethics Committee does not have any objections against publishing these articles (protocol number 48 dated 29.09.2010.)

3. RESULTS

Demographic and clinical data are shown in Table 1 and Table 2.

In all the patients, MRI detected foci of demyelination – hyperintensities on T2-weighted image and hypointensities on T1-weighted image (the size of 7±0.6 mm). Localization and frequency of lesions of the brain areas was the following: periventricular area – 72%, frontal lobes of hemispheres – 33.6%, parietal lobes – 28.8%, cerebellum – 28.8%, subcortical area – 25.6%, pons – 25.6%, thalamus – 20% , semioval centers –19.2%, internal capsule – 18%, temporal lobes – 14.4%, corona radiate – 14.4%, basal ganglia – 12.8%, brainstem – 6.4%, cerebral peduncle – 6.4%, medulla oblongata – 6.4%, occipital lobes – 3.2%.

Therefore, in patients with ADEM demyelination foci were located mostly periventricularly, less frequently they were detected in frontal and parietal lobes of the brain hemispheres and cerebellum. Brainstem, cerebral peduncle, medulla oblongata and occipital lobe were least

commonly impaired. Perifocal edema around foci of demyelination was present in 27 patients (60% of cases). We found no statistically significant link between the degree of functional limitation in patients with ADEM according to the results of the "Functional Limitation Profile" and "Sickness Impact Profile - 68" tests and the size of demyelination foci on MRI (correlation coefficient r = 0.01; P> 0.05). However, we detected statistically significant relationship between the degree of functional limitation in patients with ADEM according to the results of the "Functional Limitation Profile" and "Sickness Impact Profile - 68" tests and the number of demyelination foci according to MRI data (correlation coefficient r = 0,5; P <0.05) and the degree of disability on the EDSS (correlation coefficient r = 0,7; P <0.05). Severity of neurologic deficit (assessed on the EDSS) and an increase in the number of demyelination foci on MRI have a negative impact on patients' self-assessment of their quality of life.

Table 1. Demographic and clinical profile of participants

Variables	Number of patients (%)
Overall numbers (%)	45 (100%)
Baseline age, (mean±SD) years	32 ± 0.4
Gender	
• Men	10 (22%)
• Women	35 (78%)
Race	
• White	45 (100%)
Educational attainment (years)	16.1±0.24
>=12 years	42 (93%)
<12 years	3 (7%)
Medical comorbidities	
• Depression	-
• Other psychiatric disorders	-
• Hypertension	3
• Diabetes mellitus	-
• Hyperlipidemia	-
• Atrial fibrillation	-
• Cigarette smoking	5
Immuno suppressing states	-
Immunodeficiency states	-
Immunosuppressive therapy prior to disease onset	-
Socioeconomic state	middle-income
Disability level according to the EDSS scale, points	2.5±0.8 points.

Table 2. Clinical presentation of patients with ADEM

Variables	Number of patients (%)
Prior infection	2(4.4%)
Prior immunization	2(4.4%)
Polysymptomatic presentation	40(8.9%)
Monosymptomatic presentation	5(11.1%)
Motor disturbances	32(71.1%)
Numbness/abnormal sensation	18(40.0%)
Brain stem symptoms	8(17.8%)
Unilateral optic neuritis	4(8.9%0
Bilateral optic neuritis	1(2.2%)
Cerebellar symptoms	27(60.0%)
Encefalitis	3(6.7%)
Myelitis	2(4.4%)
Encephalopathy	43(95.6%)
Seizures	13(28.9%)

3.1 Assessment of the Functional Impact of Acute Disseminated Encephalomyelitis According to the "Functional Limitation Profile" Test Data

While conducting the "Functional Limitation Profile" test the functional condition changes were present in all the patients. The frequency of functional limitations is shown in Table 3 and Fig. 1. Patients with a diagnosis of acute disseminated encephalomyelitis showed the impairment of functional condition most often in 4 categories: "work", "leisure and entertainment", "social interaction" and "household activity".

3.2 Assessment of the Functional Impact of Acute Disseminated Encephalomyelitis According to the "Sickness Impact Profile – 68" test data

The frequency of functional limitations according to the "Sickness Impact Profile – 68" test is shown in Fig. 2.

General assessment of the impact of the disease on the functional condition of patients is presented in Table 4 and Fig. 3.

Thus, the patients with a diagnosis of acute disseminated encephalomyelitis showed functional condition impairment most often in the categories "social behavior", less frequently there were observed changes in the categories "somatic autonomy" and "psychic autonomy and communication." The categories "mobility control", "emotional stability," "degree of mobility" suffered the least frequently. The highest percent in relation to the maximum possible point was observed in the category "social behavior", and the lowest - in the category "somatic autonomy".

3.3 Assessment of the Functional Limitations of Patients with ADEM According to the "Functional Limitation Profile" Test data Depending on Gender and on the Clinical Course of ADEM

Correlation analysis revealed a statistically significant direct relationship between the degree of functional limitations in patients with ADEM and age of the patients (correlation coefficient r = 0.44; P <0.001), so the older the age is, the higher the degree of functional limitations caused by the emergence of the disease is. Thus, the age factor significantly affects the quality of life of patients with ADEM, as manifested by the presence of more pronounced limitations in the spheres of patients' life connected with the disease emergence. Statistical analysis of the results, obtained using the $\chi 2$ test, showed the relationship between gender and the degree of functional limitations in patients with ADEM. The results of survey of patients, diagnosed with acute disseminated encephalomyelitis according to the test "Functional Limitation Profile", that was confirmed statistically using Student's criteria for two independent selections, showed that compared to women men demonstrate greater changes associated with disease progression in category "social interaction" and "communication" (respectively 423.6±9.5 points (men) and 263.8±28.9 points (women), P <0.001 and 145.5±2.8 points (men) and 82.6±5.3 points (women), P <0.001).

Thus, the presence of the disease more affects the social activity of men. However, women perceive the presence of disease more emotionally (average indices of the changes in the category "emotion" are 81.5±1.1 points (men) and 151±9 points (women), P <0.001). Women also demonstrate more pronounced changes in the category "sleep and rest" (12±5.9 points (men) and 128.6±8.1 points (women), P <0.001) (Table 5).

There is also a statistically significant relationship between the clinical course of disseminated encephalomyelitis (a first episode of acute encephalomyelitis or its multiphasic course) and the degree of functional limitation of patients ($\chi 2$ - 374, P <0.001). The use of Student's test for two independent selections (Table 6) also found differences in functional limitations according to the "Functional Limitation Profile" test in patients with a first episode of disseminated encephalomyelitis and its multiphasic course. Changes in emotional state associated with presence of the disease, were more pronounced in the patients with multiphasic course, compared to patients with a first episode of disseminated encephalomyelitis (243 points and 135.6±7.6 points respectively, P <0.001). Patients with multiphasic course of disseminated encephalomyelitis, compared to patients with a first episode of its onset, had more pronounced changes in the category "sleep and rest" and less pronounced – in the category "communication" (122.3±6.1 points (patients with

a first episode of onset of disseminated encephalomyelitis) and 181.5±40.4 points respectively (patients with multiphasic course of disseminated encephalomyelitis), P <0/01 and 104±4.6 points (patients with a first episode of onset of disseminated encephalomyelitis) and 48.5±0.7 points (patients with multiphasic course of disseminated encephalomyelitis), P <0.001).

Table 3. Assessment (in points) of the disease impact on the functional condition of patients according to the "Functional Limitation Profile" test data

Behavior categories	Average point	Total point	Maximum possible point	% in relation to the maximum possible point
Walk	208±18	7700	45270	17
Body care and motion	282±42	11014	86715	13
Movement	186±14	4081	37715	11
Household activity	224±23	8965	30825	29
Leisure and entertainments	186±10	7813	17235	45
Social interaction	295±31	12093	58005	21
Emotions	142±7	2277	31185	7
Clarity of mind	273±20	9826	26595	37
Sleep and rest	129±6	2242	31770	7
Food	34	544	30825	2
Communication	94±4	1034	23400	4
Work	186±13	7987	26000	31

Table 4. Assessment (in points) of the disease impact on the functional condition of patients according to the "Sickness Impact Profile – 68" test data

Behavior categories	Average point	Total point	Maximum possible point	% in relation to the maximum possible point
Social behavior	6.4±0.5	277	540	51
Degree of mobility	4.3±0.4	98	450	22
Psychic autonomy and communication	4±0.2	122	495	25
Mobility control	3.5±0.3	89	540	16
Emotional stability	3±0.2	70	270	26
Somatic autonomy	2.2±0.4	80	765	10

Table 5. Assessment (in points) of the functional limitations of patients with ADEM according to the "Functional Limitation Profile" test data depending on gender

Behavior categories	Men (n=20)	Women (n=25)
Social interaction	423.6±9.5	263.8±28.9*
Clarity of mind	338±31.8	257.2±24.2
Body care and motion	273±93	284.4±49.2
Household activity	255±37	217.4±29.6
Leisure and entertainments	194.5±28	184±10.9
Walk	179±40	213.7±21.7
Movement	171±18	188.7±18.5
Work	152.1±13.6	194.6±17
Communication	145.5±2.8	82.6±5.3*
Emotions	81.5±1.1	151±9*
Sleep and rest	12±5.9	128.6±8.1*
Food	34	34

*Note. * – reliability of the difference of indices between groups of patients is P <0.001.*

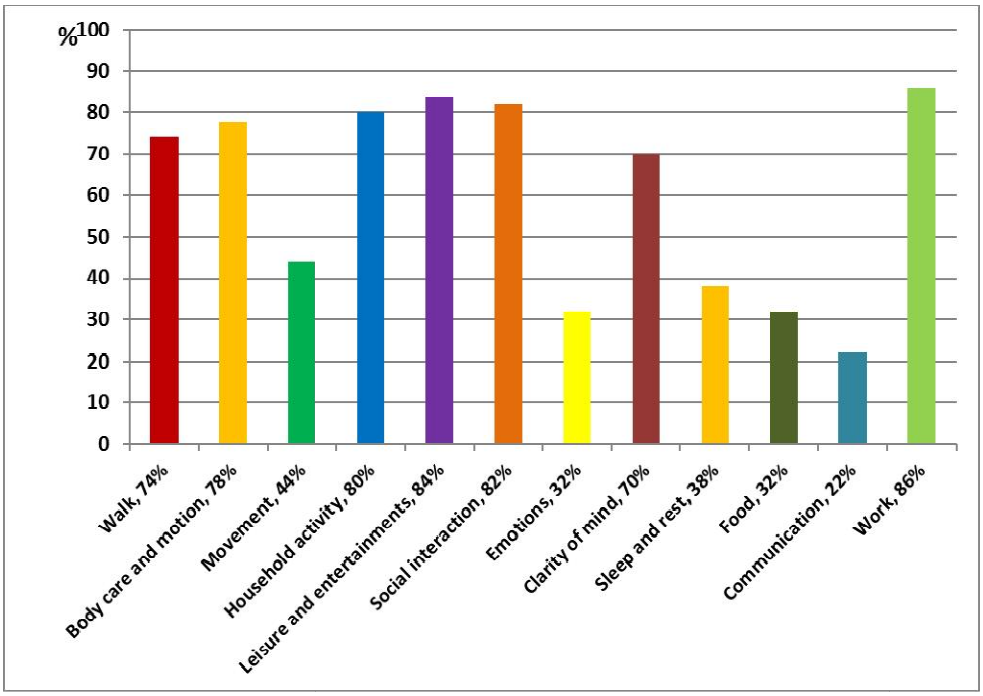

Fig. 1. The structure of functional limitations in patients with acute disseminated encephalomyelitis according to the "Functional Limitation Profile" test data

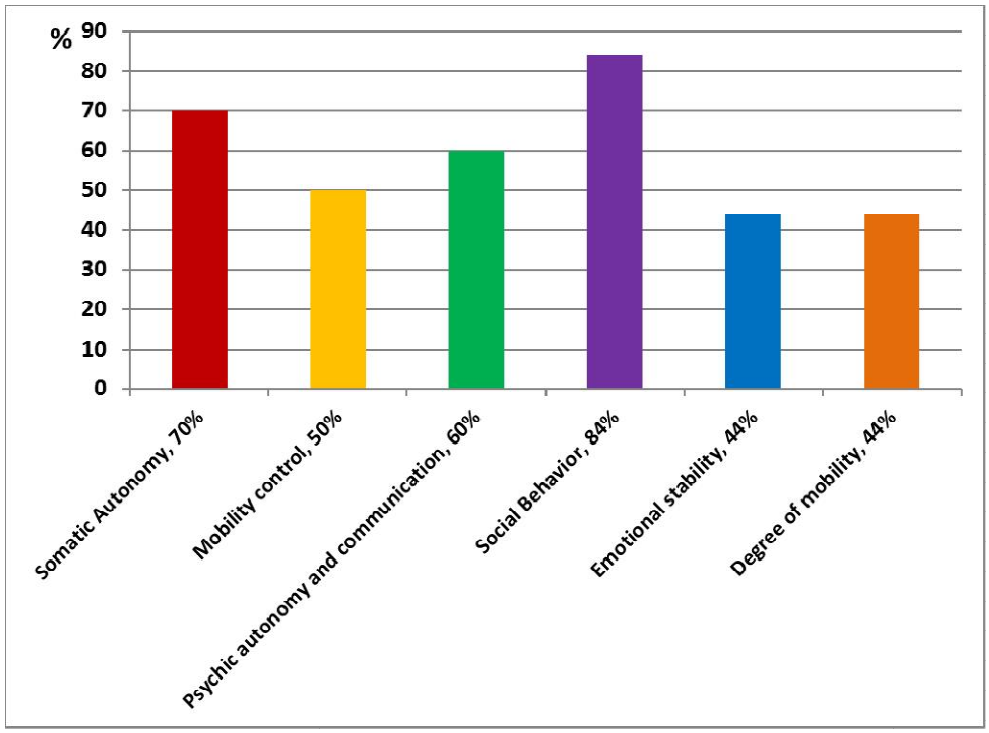

Fig. 2. The structure of functional limitations in patients with acute disseminated encephalomyelitis according to the "Sickness Impact Profile – 68" test data

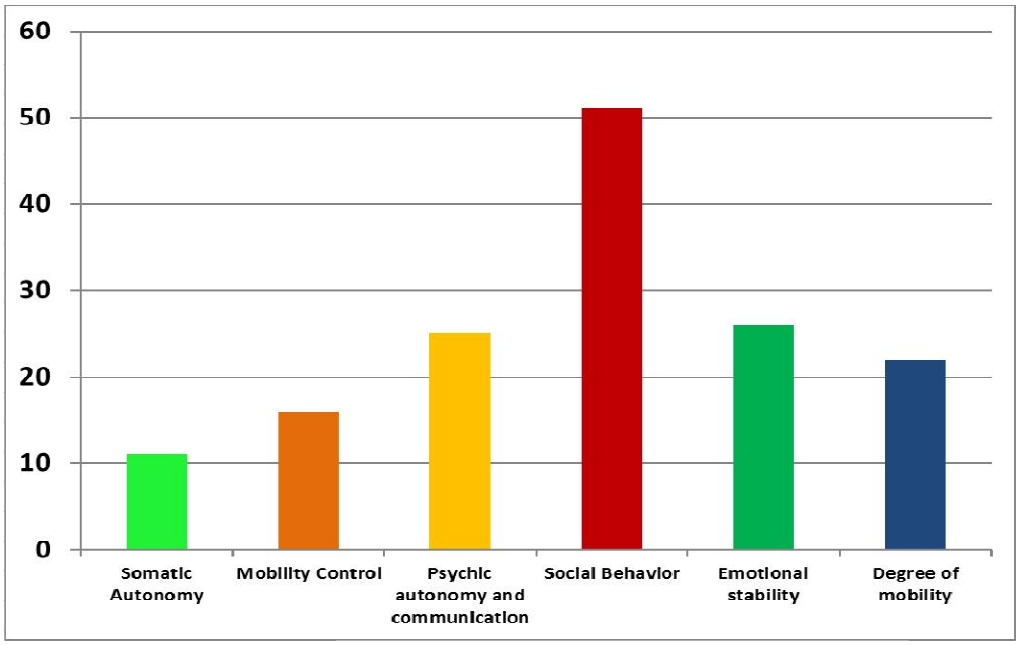

Fig. 3. Assessment in points of functional limitations in patients with acute disseminated encephalomyelitis according to the "Sickness Impact Profile – 68" test data (% in relation to the maximum possible point)

Table 6. Assessment (in points) of the functional limitations of patients with ADEM according to the "Functional Limitation Profile" test data depending on the type of course of ADEM

Behavior categories	A first episode of the demyelinating disease	Multiphasic course of disseminated encephalomyelitis
Social interaction	186.7±15.6	384.5±146.8
Clarity of mind	280.5±46.2	299.3±141
Body care and motion	170.8±12.7	333±119.9
Household activity	223.1±25.8	223.3±95
Leisure and entertainments	183.8±11.2	207.5±33.7
Walk	293.1±33.7	311.8±122.3
Movement	135.6±7.6	243*
Work	269.3±21.5	302.5±82.6
Communication	122.3±6.1	181.5±40.4^
Emotions	34	-
Sleep and rest	104±4.6	48.5±0.7*
Food	181±13.7	227.5±77.6

*Note. * - The reliability of differences in results of the groups of patients with a first episode of demyelinating disease and with mulitiphasic course of disseminated encephalomyelitis is P <0.001, ^ - P <0.01.*

4. DISCUSSION

Quality of life measures pursue the important goal of assessing the disease impact in patients' terms. In quality of life questionnaires the patient is invited to self-asses his/her life satisfaction (general or overall well-being), emotional or psychiatric symptoms such as anxiety or depression (cognitive component, evaluation of emotional feelings), symptoms of the disease (such as pain, fatigue etc.), and the functional impact of the disease (such as ability to ambulate, self-care, occupational performance, social and family participation, etc.) [47]. "Functional Limitation Profile" and "Sickness Impact Profile - 68" tests measures allow an understanding of the impact of ADEM on the patient's life, providing additional information to those obtained by the traditional objective clinical

instruments of measurement of disease severity , such as, for example, the EDSS.

Despite the obvious importance of patients' self-assessment of their quality of life and assessment of impact of ADEM on their quality of life, this question has not been widely studied so far.

In our study the analysis of interrogation of patients with acute disseminated encephalomyelitis according to the tests "Functional Limitation Profile" and "Sickness Impact Profile - 68" showed significant changes of their functional condition connected with the occurrence of the disease.

The patients with a diagnosis of acute disseminated encephalomyelitis according to the test "Functional Limitation Profile" showed the impairment of functional condition most often in 3 categories: "work", "leisure and entertainment", "social interaction". Categories "communication", "emotion", "food" were the least impaired.

The patients with a diagnosis of acute disseminated encephalomyelitis according to the test "Sickness Impact Profile - 68" showed functional condition impairment most often in the categories "social behavior", the categories "mobility control", "emotional stability", "degree of mobility" were the least impaired. The highest percent in relation to the maximum possible point was observed in the category "social behavior" and the lowest - in the category "somatic autonomy".

For the more accurate assessment of the disease impact on the functional status of patients with ADEM it is advisable to compare this patients to a socio-demographically-matched healthy control group regarding their quality of life and assess the value of psychosocial functioning and quality of life measures as discrimination markers between patients with ADEM and healthy individuals.

Also for the most accurate assessment of the disease impact on the functional status of patients diagnosed with acute disseminated encephalomyelitis it is advisable to carry out their secondary interrogation depending on the transformation of ADEM into multiple sclerosis). Such interrogation of patients in the disease dynamics enables detecting possible changes in the categories of life that are the most affected by the disease occurrence. The perspective direction of the future studies is assessment of quality of life of patients with different variants of acute disseminated encephalomyelitis course aimed at discovering a possible retrospective link between the variant of the disease course and categories of life of patients that are impaired the most by the disease occurrence.

5. CONCLUSION

Therefore, according to the results of two tests ("Functional Limitation Profile" and "Sickness Impact Profile - 68"), the presence of acute disseminated encephalomyelitis significantly affects the quality of life of patients. It results in appearance of functional limitations in all spheres of life, most frequently – in the social sphere, least frequently – in the emotional sphere. Severity of neurologic deficit and increase in the number of demyelination foci on MRI have a negative impact on patients' self-assessment of their quality of life. However, gender of patients and the presence of disseminated encephalomyelitis relapses influence on the degree of functional limitation. The disease has a significant impact on the emotional state of women and patients with multiphasic course of disseminated encephalomyelitis. It is also reflected in the disorders of their sleep and rest. Social sphere of life is suffering more in men and patients with a first episode of disseminated encephalomyelitis.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Bergner M, Bobbit R, Carter W, Gilson B. The Sickness Impact Profile: Development and Final Revision of a Health Condition Measure. Med Care. 1981;8:787-805.
2. Harris CC, Harris K, Lee J. Acute disseminated encephalomyelitis. Neurosci. Nurs. 2007;39(4):208-212.
3. Gard RK. Acute disseminated encephalomyelitis. Postgraduate Medical Journal. 2003;79:11–17.
4. Murthy JM. Acute disseminated encephalomyelitis. Neurol. 2002;50:238-243.
5. Ann Yeh E. Detection of coronavirus in the central nervous system of a child with acute disseminated encephalomyelitis. Pediatrics. 2004;113:73-76.

6. Sonneville R. Post-infectious encephalitis in adults: Diagnosis and management. J. Infection. 2009;58:321-328.
7. Tenembaum S. Acute disseminated encephalomyelitis: A long-term follow-up study of 84pediatric patients. Neurology. 2002;22(59(8)):1224-1231.
8. Yamamoto Y. Acute disseminated encephalomyelitis following dengue fever. J. Infect. Chemother. 2002;8(2):175-177.
9. Chowdhary J. Measles with Acute Disseminated Encephalomyelitis (ADEM). Indian Pediatrics. 2009;46.
10. Ogava Y. A case of acute disseminated encephalomyelitis presenting with vertigo. Auris Nasus Larynx. 2008;35:127-130.
11. Sawanyawisuth K. MRI findings in acute disseminated encephalomyelitis following varicella infection in an adult Case Reports. J. Clinical Neuroscience. 2007;14:1230-1233.
12. Voudris KA. Acute disseminated encephalomyelitis associated with parainfluenza virus infection of childhood. Brain Dev. 2002;24(2):112-124.
13. Dale RC. Early relapse risk after a first CNS inflammatory demyelination episode: examining international consensus definitions. Dev. Med. Child Neurol. 2007, 49(12):887-893.
14. Kinomoto K. Acute Encephalomyelitis Associated with Acute Viral Hepatitis Type B. Inter. Med. 2009;48:241-243.
15. Cahnzos-Romero T. Demyelinating disorders: Not only multiple sclerosis. Abstracts from 8th congress of the European Federation of Intern. Medicine. 2009, 20: 282-283.
16. Fujimoto T. Epstein-Barr virus infections of the central nervous system. Intern. Med. 2003;42:33-40.
17. John W. Young. Acute inflammatory encephalomyelitis following Campylobacter enteritis associated with high titre antiganglioside GM1 IgG antibodies Case Reports. J. Clinical Neuroscience. 2009;16:597-598.
18. Njeukui TJ. Acute disseminated encephalomyelitis associated with *Mycoplasma* pneumonia infection. Rev. Med. Brux. 2008;29(2):103-106.
19. Stam B. Neuroinvasion by *Mycoplasma Pneumoniae* in ADEM. International Journal of STG and AIDS. 2006;17(7): 493-495.
20. Stam B. Neuroinvasion by *Mycoplasma pneumoniae* in acute disseminated encephalomyelitis. Emerg Infect Dis. 2008;14(4):641-643.
21. Termote B. Encephalitis following *Mycoplasma* pneumonia (2007: 6b). Acute disseminated encephalomyelitis. Eur. Radiol. 2007;17(9):2436-2438.
22. Gaing C. Acute disseminated encephalomyelitis associated with Campylobacter jejuni infection and antiganglioside GM1 Ig G antibodies. J. Neurol. 2005;252:613-614.
23. Omata T. Child with acute disseminated encephalomyelitis (ADEM) initially presenting with psychiatric symptoms. No to Hattatsu. 2008;40 (6):465-468.
24. Orr D. Acute disseminated encephalomyelitis temporally associated with Campylobacter gastroenteritis. J. Neurol. Neurosurg. Psychiatry. 2004; 75(5):792-793.
25. Dale RC. Acute disseminated encephalomyelitis, multiphasic disseminated encephalomyelitis and multiple sclerosis in children. Brain. 2000; 123:2407-2224.
26. Gard RK. Acute disseminated encephalomyelitis. Postgraduate Medical Journal. 2003;79:11-17.
27. Ito S. Acute disseminated encephalomyelitis and post-streptococcal acute glomerulonephritis. Brain Dev. 2002;24(2):88-90.
28. Noel S. Adult acute disseminated encephalomyelitis associated with post-streptococcal infection. J. Clin. Neurosci. 2005;12(3):298-300.
29. Fujikiet F. Aseptic meningitis as initial presentation of ADEM. J. Neurol. Sci. 2008;272:129-131.
30. Samile N. Acute disseminated encephalomyelitis in children. A descriptive study in Tehran, Iran. Saudi Med J. 2007;28(3):396-399.
31. Hamidon BB. Acute disseminated encephalomyelitis (ADEM) presenting with seizures secondary to anti-tetanus toxin vaccination. Med. J. Malaysia. 2003;58(5): n780-782.
32. Sejvar JJ. Neurologic adverse events associated with smallpox vaccination in the United States 2002-2004. JAMA. 2005; 294:2744 – 2750.
33. Tenembaum S. Disseminated encephalomyelitis in children. Clinical Neurology and Neurosurgery. 2008;110: 928–938.

34. Krupp LB. International Pediatric Multiple Sclerosis Study Group 2007 Consensus definitions proposed for pediatric multiple sclerosis and related disorders. Neurology. 2007;68(16 suppl 2):7-12.
35. Sonneville RT, Klein de Broucker J. Post-infectious encephalitis in adults: Diagnosis and management. Infection. 2009;58:321-28.
36. Suppiej A, Vittorini R, Fontanin M. Acute disseminated encephalomyelitis in children: Focus on relapsing patients. Pediatr Neurol. 2008;39(1):12-17.
37. Tenembaum S. Disseminated encephalomyelitis in children. Clinical neurology and neurosurgery. 2008;110: 928-938.
38. Brass SD. Multiple sclerosis and acute disseminated encephalomyelitis in childhood. Pediatr. Neurol. 2003;29(3): 227-231.
39. McGovern RA, DiMario FJ. Acute disseminated encephalomyelitis: A retrospective pediatric serie. Ann. Neurol. 2003;54(7):127-129.
40. Neuteboom RF, Catsman-Berrevoets CE, Hintzen RQ. Multiple sclerosis in children. Ned Tijdschr Geneeskd. 2007;151(26): 1464-1468.
41. Pohl D, Hennemuth I, Kries R. Paediatric multiple sclerosis and acute disseminated encephalomyelitis in Germany:results of a nationwide survey. Eur. J. Pediatr. 2007;166:405-412.
42. Toshiyuki O, Shunsaku H. Reccurence of acute disseminated encephalomyelitis after a 12-year symptom-free interval. Interval Medicine. 2004;43(8):746-749.
43. Tur C, Téllez N, Rovira A. Acute disseminated encephalomyelitis: Study of factors involved in a possible development towards multiple sclerosis. Neurologia. 2008;23(9):546-554.
44. Polman CH, Reingold SC, Banwell B, Clanet M, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the ‘‘McDonald Criteria’’. Ann Neurol. 2011;69(2):292–302.
45. Dale RC, Branson JA. Acute disseminated encephalomyelitis or multiple sclerosis: Can the initial presentation help in establishing a correct diagnosis. Arch. Dis. Child. 2005;90:636-639.
46. Dale RC, Pillai SC. Early relapse risk after a first CNS inflammatory demyelination episode: Examining international consensus definitions. Dev. Med. Child Neurol. 2007;49(12):887-893.
47. Divya SK, Mrlvin JJ, Sanjeev VK. Acute disseminated encephalomyelitis in children: Discord and neurologic and neuro imaging abnormalities and response to plasmapheresis. Pediatrics. 2005;166(2): 431-36.
48. Simon J. Williams. Measuring health condition? A review of the Sickness Impact and functional limitations profiles. Health Care Analysis. 1996;4(4):273-283.
49. Tenembaum S, Chamoles N, Fejerman N. Acute disseminated encephalomyelitis: A long-term follow-up study of 84pediatric patients. Neurology. 2002;22(59(8)):1224-1231.
50. Kanter DS, Horensky D, Sperling RA. Plasmapheresis in fulminant acute disseminated encephalomyelitis. Neurology. 1995;45:824-827.
51. Ra Jesh B. Acute disseminated encephalomyelitis. Indian J Pediatr. 2004; 71(11):1035-1038.
52. Tenembaum S. Acute disseminated encephalomyelitis. Neurology. 2007;68:23-26.

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