



Modern doctors' view on the problem of diagnostics and treatment of asthenic syndrome in different regions of the Russian Federation

Yana D. Belousova¹, Anastasiya M. Tynterova¹, Vladimir V. Rafalskiy¹

1 Immanuel Kant Baltic Federal University, 14 A. Nevskogo St., Kaliningrad 236016 Russia

Corresponding author: Yana D. Belousova (yana-belousova@inbox.ru)

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Abstract

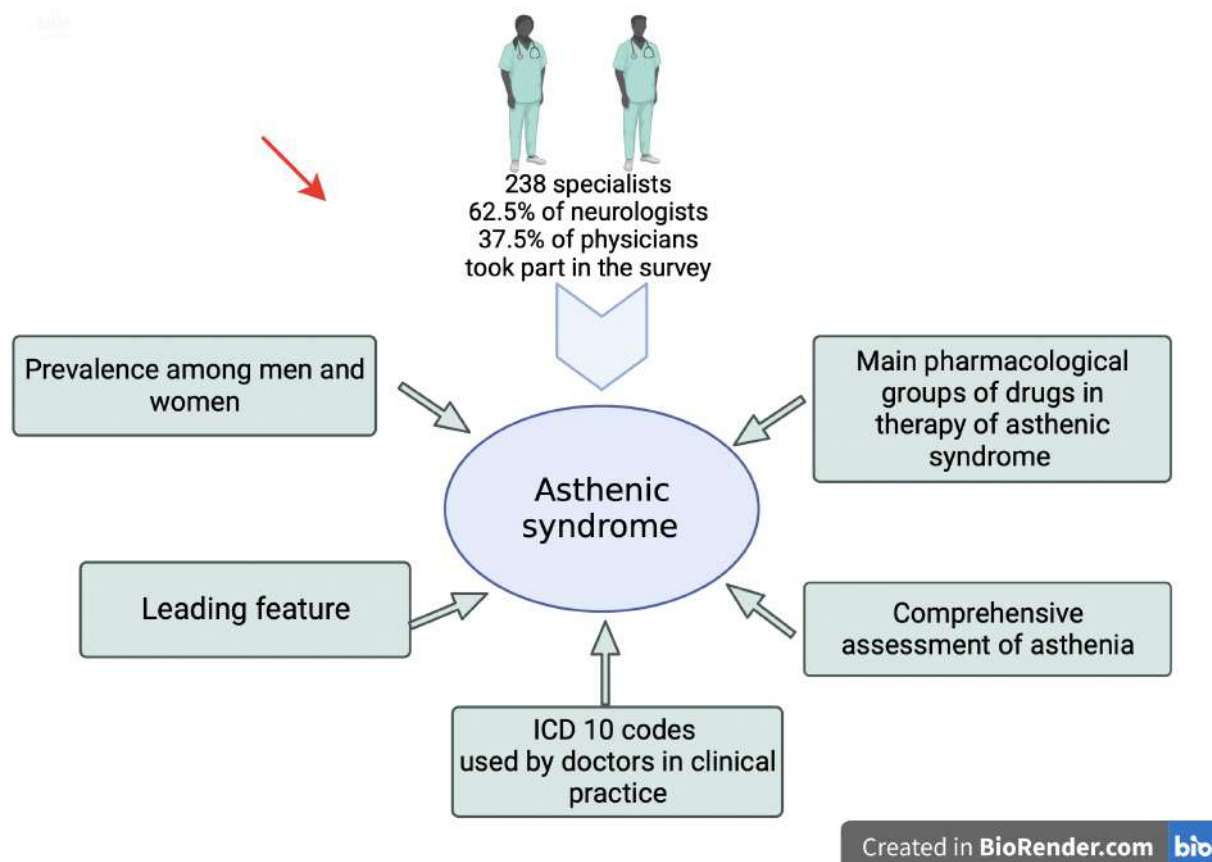
Introduction: The problem of asthenic disorders is determined by their high prevalence, the lack of diagnostic criteria and recommendations for therapy, and the absence of unified principles of coding in ICD-10. **The aim of the study** was to evaluate the current practice of neurologists and physicians of the Russian Federation (RF) in the diagnosis and pharmacotherapy of asthenic syndrome (AS).

Materials and methods: An anonymous author-developed questionnaire survey of physicians on the issues of diagnostics and treatment of asthenia was conducted on the Google forms platform.

Results: Total 238 specialists from 23 regions of the RF, 62.5% of neurologists and 37.5% of physicians, took part in the survey. Women suffer from AS more often than men. AS is most frequently verified at the age of 40-60 (65.5%) and under 40 (39.6%). Doctors use the codes G90.8 – other disorders of the autonomic nervous system – and I67.8 – other specified cerebral vascular lesions. The main causes of AS are affective disorders in 67.2% of patients and infectious diseases in 70% of patients. Almost 67% of doctors use anxiety and depression assessment scale, and only 13% of respondents use MFI-20 scale. The choice of therapy depended on the psychopathologic syndrome in 73.9% of cases. Most doctors favored nootropic drugs, metabolic action drugs, and B vitamins.

Conclusion: The current medical practice of diagnosing and treating AS was studied and informative data were obtained with regard to understanding the clinical-typological structure and nosological affiliation of AS. The results demonstrate the expediency of developing a unified algorithm for the management of patients with various manifestations of AS.

Graphical Abstract



Keywords

asthenia, asthenic syndrome, pharmacotherapy, nootropic drugs

Introduction

The term “asthenia” is widely used in the clinical practice of physicians of different specialties regarding symptoms of pathological fatigue, rapid exhaustion, decreased energy potential and motivation for action (Putilina 2013; Chutko and Surushkina 2020). Being a multifactorial disease, asthenia can occur in a healthy population after physical or emotional stress, as a comorbid condition against the background of other nosologies and as an independent syndrome (Finsterer et al. 2013; Hulme et al. 2018). Recently, interest in the problem of diagnostics and therapy of asthenic syndrome has significantly increased, which is associated with the wide prevalence and polymorphism of its manifestations, especially in the conditions of life after coronavirus infection (Joli et al. 2022; Kedor et al. 2022).

The leading complaints most often described by patients are lethargy, drowsiness, irritability, headache, rapid fatigue under normal physical and emotional load, memory impairment, decreased attention and workability (Shuteeva 2018; Shishkova 2020). To assess the asthenic

syndrome, the scales for assessing asthenia severity – Fatigue Severity Scale (FSS), the Fatigue Impact Scale (FIS), and the Multidimensional Fatigue Inventory (MFI-20) – are traditionally used (Valko et al. 2008; Jelsness-Jørgensen et al. 2022). However, the use of these scales provides only a screening assessment without revealing the polymorphism of symptoms of the neuropsychiatric spectrum, which necessitates the use of a comprehensive diagnostic approach with the use of psychometric scales and questionnaires to assess cognitive function, affective, vegetative and insomniac disorders (Maisel et al. 2021). To date, the issue of pharmacotherapy of asthenic states remains controversial. On the one hand, this is due to the large list of drugs used in the treatment of asthenia, on the other hand, due to the lack of clear clinical recommendations for the therapy of asthenic syndrome, and, finally, due to the fact that in clinical practice asthenia is often not considered as an independent syndrome requiring treatment (Watanabe et al. 2008).

The unformed model of diagnostic search, insufficient clarity of etiopathogenesis, lack of unified approach to

formulating the ICD-10 diagnosis, and multidirectional approaches to therapy determine the relevance of the problem of asthenia worldwide and create predictors for further research to create a scientifically sound methodology and clinical recommendations for this disorder. The present study was conducted to assess the current practice of neurologists and therapists in the Russian Federation in the diagnosis and therapy of asthenic syndrome.

Materials and methods

Study design, setting

This is a prospective, non-interventional study that was approved by the the Independent Ethical Committee of I. Kant Baltic Federal University (BFU) Clinical Trials Center (Minutes № 31 of 30.05.2022) and was conducted from September to November 2022. The sample size was not calculated beforehand. The study was conducted as a questionnaire survey of physicians from different regions of the Russian Federation on the issues of diagnosis and treatment of asthenic syndrome.

Participants

Neurologists and general practitioners from different regions of the country participated in the study. A total of 238 completed forms were received. Specialists from 23 regions of Russia took part in the survey. 148 neurologists (62.5 %) and 90 general practitioners (including general practitioners, cardiologists and geriatricians) (37.5 %) participated in the study. The average length of service of the doctors was more than 10 years. In 88% of cases, the respondents represented outpatient care, in 12% – multidisciplinary hospitals.

Inclusion and exclusion criteria

Inclusion and non-inclusion criteria were not considered in the present study.

Outcome Measures

Online questionnaire “Pharmacoepidemiology of asthenic syndrome” was developed at I. Kant BFU by a group of authors, including doctors of clinical pharmacology and neurology at the Department of Internal Medicine. Initially, the questionnaire was tested as part of a cycle of additional professional education for neurologists and physicians. Then, the final version was posted on the Google forms platform. The questionnaire was anonymous and consisted of 15 questions, four of which were socio-demographic, and the rest were aimed at assessing the respondents' awareness of the etiology, diagnosis and treatment of asthenic syndrome (Suppl. material).

Statistical analysis

A statistical analysis was performed using the program package “SPSS 23” and Microsoft Excel spreadsheet editor. The arithmetic mean (M) and the standard deviation (SD) were used for samples consistent with the normal distribution. The quantitative indicators were analyzed by calculating the proportion (percentage) of the total number of observations. Quantitative variables were reported as proportions (expressed in percentages). Quantitative variables were compared using the χ^2 criterion or Fisher's exact test. Differences were considered statistically significant at $p \leq 0.05$.

Results

This is one of the few studies that focused on assessing the established practices of neurologists and general practitioners regarding the diagnosis and treatment of asthenic syndrome, as well as awareness of the structure, etiology, and epidemiology of this condition.

The first block of questions focused on general data about the physicians participating in the survey. The next block of questions included assessment of demographic data of patients with asthenia. When asked who suffers from asthenic syndrome more often, respondents could give several answers. Thus, the frequency of mentioning female patients amounted to 79.4%, male patients – 5.5%, and women and men at the same time – 15.1% of all the cases. Mostly, asthenia was verified in patients in the age category of 40–60 years (65.5%) and under 40 years (39.6%). Asthenia was less common in other age categories: 61–70 years (23%), 71–80 years (17.4%), and over 80 years (11.5%).

Also, physicians were asked how often they diagnosed asthenic disorder in the last 12 months. It was found that 50.8% of the respondents had made this diagnosis more than 10 times a month, 44.5% – 5–10 times a month, and only 4.7% – fewer than 5 times a month.

The next block of questions concerned the assessment of the opinion of therapeutic and neurological physicians regarding the etiology and clinical manifestations of asthenic syndrome. The main characteristics of asthenic syndrome according to the survey data are presented in Table 1.

Table 1. Main characteristics of asthenic syndrome according to the survey of physicians of therapeutic and neurological profile

Cause of asthenic syndrome	n (%)
Acute cerebrovascular accident (ACA)	108 (45.3)
Traumatic brain injury	55 (23)
Infectious diseases (including COVID-19)	167 (70)
Affective disorders (depression, anxiety, etc.)	160 (67.2)
Endocrine diseases	115 (48.3)
Cancer	96 (40.3)
Diseases of the autonomic nervous system	133 (55.8)
Leading feature	n (%)
Anxiety	148 (62.0)
Depressive syndrome (HADS, BECA etc.)	67 (28.2)
Disorders in the motivational and personal sphere	95 (40.0)
Somatization	84 (35.3)
Decreased concentration	170 (71.4)
Memory decline	142 (59.6)
Sleep disorder	159 (66.8)

As can be seen from the Table, according to the respondents, the main reason for the development of asthenic syndrome is a spectrum of affective disorders and neuroinfectious lesions. According to the doctors' opinion, the leading signs are such symptoms as decreased concentration, sleep disorder (difficulty with sleep quality; initiating or maintaining sleep; distress and impairments of daytime functioning, associated with sleep disorders), anxiety, and memory loss.

Also, physicians were asked about the formulation of the diagnosis in accordance with ICD-10. A part of respondents (5%) indicated that they did not code asthenic syndrome, leaving the wording "asthenic syndrome" in the structure of the main diagnosis. The rest of the respondents indicated ICD codes of different rubrication (the data are presented in Table 2).

Table 2. ICD 10 codes used by doctors in clinical practice when verifying the diagnosis of asthenic syndrome

ICD-10 code	%	n
G90 Disorders of the autonomic nervous system		
G90.8 Other disorders of the autonomic (autonomic) nervous system	35.3	84
G90.9 Autonomic nervous system disorder unspecified	8.8	21
I67 Other cerebrovascular diseases		
I67.2 Cerebral atherosclerosis	0.8	2
I67.4 Hypertensive encephalopathy	0.4	1
I67.8 Other specified cerebral vascular lesions	15.1	36
I67.9 Unspecified cerebrovascular disease	9.2	22
G93 Other cerebral lesions		
G93.0 Cerebral cysts	0.4	1
G93.3 Fatigue syndrome after viral disease	4.2	10
G93.4 Unspecified encephalopathy	8	19
G93.8 Other specified brain lesions	3.4	8
U09.9 Condition after COVID-19	4.6	11
F48 Other neurotic disorders		
F48.0 Neurasthenia	4.6	11
F48.9 Unspecified neurotic disorder	0.4	1
F06.6 Organic emotional labile (asthenic) disorder	2.1	5
G96 Other central nervous system disorders		
G96.8 Other specified lesions of the central nervous system	1.2	3
G96.9 Unspecified central nervous system lesions	0.8	2
R54 Aging		
Other ICD codes (F41.1; G44.8; G80; G94.9; G95; I11.9; I93.4; J06.9; J67.9; R24; R53; T90.8; U07.1)	3.9	13

As shown in Table 2, the most frequent diagnoses are G90.8 – other disorders of the autonomic nervous system – and I67.8 – other specified cerebral vascular lesions.

To clarify the diagnostic tactics of physicians in relation to patients with asthenic syndrome, the respondents were asked to indicate what additional diagnostic methods and neuropsychological tests and scales they use to verify the diagnosis. The results showed that 68.7% of the respondents additionally prescribe laboratory tests, 43.8% – electrocardiogram (ECG), and 34.3% of the respondents use evaluation of triplex scanning of brachiocephalic arteries. In some cases, doctors prescribe electroencephalogram (EEG) – 18% and echocardiography (ECHO) – 13.3%.

Most physicians use neuropsychological testing with validated questionnaires and scales in the comprehensive assessment of asthenia (Fig. 1). The level of asthenia is directly investigated using the subjective asthenia rating scale MFI-20 and the Fatigue Severity Scale FSS (van't Leven et al. 2009). The Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE) scales are used to assess cognitive function in patients with asthenia (Lieb et al. 2007; Matura et al. 2018). The psycho-emotional status examination includes the Beck Depression Inventory (BDI), The Hamilton Anxiety Rating Scale (HAM-A/HARS) and The Hospital Anxiety and Depression Scale (HADS).

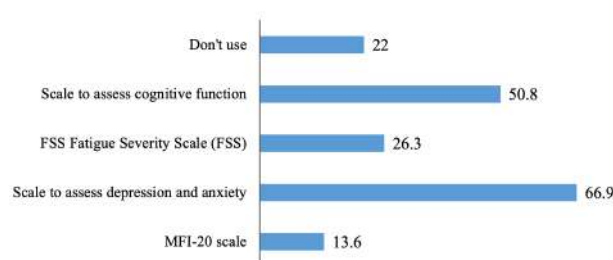


Figure 1. Neuropsychological tests and scales used to diagnose a patient with asthenic syndrome (%).

Block of questions about pharmacotherapy of asthenic syndrome included several components, such as selection criteria, main groups of drugs, duration of therapy of asthenia, as well as additional methods of treatment, including non-medication.

The main criteria for the choice of drug therapy are the leading clinical and psychopathologic syndromes in the practice of 73.9% of neurologists and therapists and their own experience of drug use in the practice of 60.3% of respondents. The cost of the drug and its availability in the pharmacy network were mentioned by 31.6 % and 25.6 % of respondents, respectively. Advertisements by pharmaceutical companies is important for 13.7% of respondents.

The next block of questions was proposed in order to find out the existing therapeutic approaches to the treatment of asthenic syndrome. The results of the survey of physicians regarding drug treatment are presented in Table 3.

A comparative analysis among the most prescribed groups of drugs in the therapy of asthenic syndrome revealed statistically significant differences ($p=0.01$) with regard to the use of the group of adaptogens by neurologists. There were no significant differences in other characteristics between the groups ($p>0.05$).

Table 3. Main pharmacological groups of drugs in therapy of asthenic syndrome n (%)

Main pharmacological groups of drugs	Neurologists, n=148	Physicians, n=90	P
B vitamins	48 (32.4)	33 (36.6)	0.07
Metabolic drugs	71 (47.9)	49 (54.4)	0.330
GABA derivatives	17 (11.4)	14 (15.5)	0.361
Adaptogens	37 (25.0)*	5 (5.5)	0.001
Drugs containing choline alposcerate	40 (27.0)	32 (35.5)	0.166
Antioxidants	59 (39.9)	43 (47.7)	0.238
Nootropic drugs	128 (86.5)	76 (84.4)	0.635
Complex antioxidant/vitamin drugs	45 (30.4)	29 (32.2)	0.771
Anxiolytics	7 (4.7)	3 (3.3)	0.600

Note: * - statistically significant differences between groups ($p < 0.05$).

Regarding the duration of the therapy, 58.1% of respondents indicated the maximum duration of treatment – 4-8 weeks, 28.8% – 8-16 weeks, and 8.5% prescribed medications for fewer than 4 weeks. Psychotherapy and cognitive-behavioral therapy occupy leading positions among non-medication methods of treatment – 72.8% and 71.1%, respectively. Alternative types of psychotherapy such as music therapy and art therapy were chosen by 47.2% of respondents. Physical therapy is considered effective by 31.1% and the use of homeopathic medicines – by 14% of respondents. Such methods as physical therapy, physical activity and acupuncture were chosen by 0.4% of respondents.

Discussion

The analysis of the results of the questionnaire proves the relevance of this study. Considering that in routine practice asthenia is diagnosed by the majority of doctors more than 10 times a month, we can judge about the high prevalence of this condition, which is consistent with the data of domestic and foreign studies in recent years.

A study by Swiss researchers (Valko et al. 2008) found that increased fatigue during physical and mental exertion is one of the most common complaints of patients visiting a polyclinic, with a frequency ranging from 6% to 45%. A study conducted in the UK (Watanabe et al. 2008) showed that the prevalence of chronic fatigue in the general population was 27.3%. In a study conducted in a city in the Netherlands (van't Leven et al. 2009), the results were obtained demonstrating that the prevalence of chronic asthenia was 30.5%, and most cases of chronic fatigue were in women aged between 40 and 60 years. In the United States, according to a study by Matura et al. (2018), the population of people suffering from asthenia reaches 45%.

The main etiologic factors of asthenic syndrome development, according to the majority of respondents, are affective disorders and infectious diseases. The close relationship between asthenia and depression and anxiety is explained, on the one hand, by the common anatomofunctional links with cerebral structures associated with

the manifestation of these disorders, on the other hand, by the disorder of neurotransmitter metabolism of serotonin, norepinephrine and dopamine, which is also a common pathogenetic factor for asthenic and affective disorders (Lieb et al. 2007). Infectious diseases are now considered as one of the main factors in the development of asthenic syndrome. In most cases, this is due to a wide range of asthenic disorders in patients who have undergone COVID 19, which is expressed in the term "post-COVID asthenic syndrome" (Perrin et al. 2020). According to Russian and foreign literature, the prevalence of this syndrome ranges from 46% to 86% (Petrova et al. 2021; Sandler et al. 2021). The main manifestations of asthenia after COVID 19 are decreased concentration of attention and memory, emotional lability, motivational disorders, sleep disorders, and appetite deterioration (Petrova et al. 2021).

Despite the identification of infectious and psychopathologic factors as fundamental in the development of asthenic syndrome, most physicians most often make the diagnoses G90.8 and I67.8, reflecting diseases of the autonomous nervous system and cerebrovascular pathology, while the ICD-10 classification has codes for post-coital syndrome (U09.9) and psychiatric disorders (F00 – F99).

Currently, there is no unified approach in the diagnosis of asthenic disorders. Traditionally, psychometric scales are used in the assessment of pathological fatigue. According to numerous literary data, the FSS fatigue severity rating scale is used in the clinical practice of foreign colleagues (Bakalidou et al. 2022). In Russia, the FSS and MFI-20 scales are widely used as the simplest and quickest to use for outpatient doctors. The MFI-20 scale deserves special attention, as it has a number of advantages, namely, the ability to assess the severity of asthenia using subscales reflecting the level of decreased activity, decreased motivation, physical, mental and general asthenia. Researchers from Austria in their review point out possible approaches to the diagnosis of asthenic disorders using data from laboratory tests, EEG and magnetic resonance imaging (Finsterer et al. 2013). In Russia, these methods are used as auxiliary methods, while the main ones are neuropsychological tests and questionnaires. The polymorphism of asthenic syndrome

manifestations makes it advisable to include in the diagnosis of this psychopathological disorder tests and scales to assess psychoemotional, cognitive disorders, autonomic nervous system dysfunction, and sleep disorders.

Treatment of asthenic disorder is complex, based on the identification of etiological factors, the main clinical syndromes of this condition and includes non-medication methods and pharmacotherapy. In the case of secondary asthenia, medical tactics should be aimed at treating the underlying disease and include specific anti-asthenic therapy.

Treatment of primary and reactive asthenia is aimed at correction of the leading symptoms using physical, psychotherapeutic and drug methods. To date, various non-medication treatment strategies have been developed and successfully applied, including lifestyle and physical activity, acupuncture, psychotherapy and physiotherapy (Geraghty et al. 2019; Larun et al. 2019; Bakalidou et al. 2022; Fang et al. 2022).

The issue of pharmacological treatment currently remains controversial and requires further clinical studies to assess the effectiveness of different groups of drugs in the therapy of asthenic syndrome of various etiologies (Castro-Marrero et al. 2017; Luo et al. 2019). The most frequently mentioned classes of drugs are adaptogens, antioxidants, B vitamins, metabolic and nootropic drugs. Given the association of asthenia with affective disorders, drugs that have an effect on neurotransmitter systems are widely used in the therapy of this disorder (Pae et al. 2009; Cleare et al. 2015). As an alternative therapy,

natural medicines and bioactive components such as ginseng, rhodiola rosea, etc., are used (Richman et al. 2019).

Conclusion

The study demonstrates the relevance of the problem of diagnosis and therapy of asthenic syndrome. Insufficient awareness of neurologists and therapists in the issues of diagnosis and coding of asthenia according to ICD-10 determines the expediency of developing a unified algorithm for the management of patients with various manifestations of asthenic syndrome. Determination of the etiological factor and the leading clinical symptom will allow to develop individual therapy trajectories for secondary and primary asthenia.

Conflict of interest

The authors have declared that no competing interests exist.

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The authors have no funding to report.

Data availability

All of the data that support the findings of this study are available in the main text or Supplementary information.

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Author contributions

- **Yana D. Belousova**, MD, PhD student ESC Institute of Medicine and Life Sciences (MEDBIO), Immanuel Kant Baltic Federal University; e-mail: yana-belousova@inbox.ru; **ORCID ID** <https://orcid.org/0000-0001-9333-1244>. Concept and design of the study, material processing, drafting the text, statistical data processing.
- **Anastasiya M. Tynterova**, MD, PhD, ESC Institute of Medicine and Life Sciences (MEDBIO), Immanuel Kant Baltic Federal University; e-mail: antynterova@mail.ru; **ORCID ID** <https://orcid.org/0000-0003-1743-4713>. Scientific management, editing the relevance of the study section, background, body of the manuscript, literature list.
- **Vladimir V. Rafalskiy**, Dr. Habil. of Medicine, Professor, Department of Therapy, ESC Institute of Medicine and Life Sciences (MEDBIO), Immanuel Kant Baltic Federal University; e-mail: v.rafalskiy@mail.ru; **ORCID ID** <https://orcid.org/0000-0002-2503-9580>. Idea development, editing, final approval of manuscript.

Supplementary material

Online questionnaire “Pharmacoepidemiology of asthenic syndrome”

Authors: Yana D. Belousova, Anastasiya M. Tynterova, Vladimir V. Rafalskiy

Data type: pdf

Explanation note: Online questionnaire “Pharmacoepidemiology of asthenic syndrome” was developed at I. Kant BFU by a group of authors, including doctors of clinical pharmacology and neurology at the Department of Internal Medicine. The questionnaire was anonymous and consisted of 15 questions, four of which were socio-demographic, and the rest were aimed at assessing the respondents’ awareness of the etiology, diagnosis and treatment of asthenic syndrome.

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