Original Article

Determination of Minimum Data Set for Designing a Diagnosis Decision Support System and Medication Follow-Up for Multiple Sclerosis

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(Received: 17 Oct. 2019; Revised: 6 Dec. 2019; Accepted: 13 Jan. 2020)

Abstract

Background and Purpose: Diagnosis of multiple sclerosis (MS) is complicated because of the lack of definite factor. Decision support systems are expert systems which help physicians in decision-making process. First step in designing the system is identification of a minimum dataset (MDS). This study aimed to determine minimum dataset required to design diagnosis decision support system.

***Materials and Methods*:** This research was a descriptive cross-sectional study. Data were gathered from medical guideline approved by Ministry of Health, Treatment and Medical Training, Multiple Sclerosis diagnosis, international guideline of Royal college of England, and McDonald Diagnostic criteria. Data collection tool was a designed checklist consisting of 100 items provided to 25 neurologists and MS fellowships of medical universities and private clinics in Iran.

***Results*:** Out of 100 designed information's items, 10 items were omitted due to CVR less than 0.49. Employment status items, history of MS in 3rd grade relatives, history of viral diseases, orbital MRI, optical coherence tomography, brain CT-scan, ESR, CRP, visually evoked potentials, delay duration of P100 for each eyes are all examples of information elements that have been omitted.

***Conclusion*:** Determining the minimum dataset related to MS is an important step in designing diagnosis decision support system and medication follow-up. Therefore, MDSs can help those responsible for gathering standard information of patients with Multiple Sclerosis (MS), and causes improvement in management of information for this disease.

***Keywords*:** Multiple Sclerosis; Diagnosis; Decision Making; Physicians

***Citation**:* Khenarinezhad S, Mohammadzadeh N, **GhaziSaeedi M*, NaserMoghadasi** A*. Determination of Minimum Data Set for Designing a Diagnosis Decision Support System and Medication Follow-Up for Multiple Sclerosis. Iran J Health Sci. 2020; 8(1): 29-39.

1. Introduction

One of the biggest challenges that health systems and organizations are faced in 21st century is increased burden resulting from chronic diseases which lead to body's physical changes and limits in functions of the patient (1, 2). Multiple sclerosis (MS) is a chronic autoimmune and neural disease that affects functionality system. MS is the most common disability neural disease known in young adults (3). According to the reports of World Health Organization, more than 2 million individuals around the world suffered from MS(4). In addition, the prevalence of MS in women compared to men is about 3:1 in most parts of the world (5). This disease causes motor disorders, such as muscle weakness and movements incoordination(3). The cause of MS is still unknown, but genetic factors, infection with Epstein-Barr virus, smoking and vitamin D deficiency play important roles in the incidence of this disease. At the same time, no definite factor has been found as a reason of the occurrence of this disease yet(6). Diagnosis of chronic diseases, such as MS, which is a variable and unpredictable disease, is complicated for physicians and healthcare system; in addition, misdiagnosis and inappropriate treatment in patients with MS is a common issue. Therefore, by making progress in technology and artificial intelligence, it is expected that tools and systems would be provided for physicians to help them in better and well-timed diagnosis and treatment. Clinical decision support systems are expert systems that assist physicians in decision-making process by diagnostic reasoning process (7, 8). This system also saves patients' information in a database, and then presents advices and recommendations related to each patient to physicians and specialists(9). The first step in designing such systems is determining information requirements or necessary minimum dataset. Minimum datasets (MDS) are standard evaluation tools which are used as a leader during the process of gathering data, and lead to availability of correct and accurate data(10, 11). MDS can be helpful in programming, development, management, and evaluation of performances, and improves the quality of care process and management of the disease(12). Therefore, establishing and developing standard and integrated MDSs for gathering data at national level might be of high importance (11). This study aimed at establishing a minimum dataset in clinical decision support system for the diagnosis and medication follow-up of MS in Iran.

2. Materials and Methods

This research was a descriptive cross-sectional study. In order to extract information items required for diagnosis decision support system and medication follow-up, a literature review based on PubMed, Scopus, Google Scholar, and Web of Science was performed. Terms used in the databases were as follows: "Multiple sclerosis", "Minimum data set", "Dataset", "Diagnosis", "Clinical decision support system", "Guidelines". The data related to the diagnosis of MS were gathered from medical guidelines approved by the Ministry of Health, Treatment and Medical Training, Multiple Sclerosis diagnosis international guideline of Royal College of England(13), McDonald Diagnostic Criteria, Version 2017(14). Then, in order to extract information items, a designed checklist was used. The checklist consisted of 7 sections and 100 items including

demographic and historical data of patients (13 items), clinical data of symptoms and signs (20 items), and data related to the type of MS disease (5 items), data related to paraclinical procedures (10 items of imaging, and 18 items laboratory tests), data related to used medications (16 items), data related to therapeutic line (3 items), data related to medication follow-up (9 items related to how to take medication, and 6 items related to assessment before prescription of the medication), and is designed based on two-score scale of "I agree" and "I disagree". A blank row was considered at the end of each section for specialists to write their comments and recommendations on information items. In order to validate the extracted information items, reliability and validity of the checklist were assessed. Validation of the checklist was performed in terms of two aspects: Face validity of the checklist was confirmed by interdisciplinary specialists, including health information management expert and neurologist, and in order to confirm the content validity of the checklist based on Lawshe Table (1975), content validity ratio (CVR) was used(15). The sample population included the neurologists and MS fellowships who were selected through easy sampling method based on Lawshe Table.

$$CVR = \frac{n_E - \frac{N}{2}}{\frac{N}{2}}$$

In order to determine the content validity, the related checklist based on Lawshe Table was provided for neurologists and MS fellowships at medical universities and private clinics through Email, and finally 15 checklists were returned online. The inclusion criteria for the participants in this study was scientific grade of the individuals; thus, MS fellowships and neurologists expert in the diagnosis and treatment of MS were considered for this study. Due to 15 individuals available, the necessary score for each item to enter the study was considered to be 0.49 based on Lawshe Table, and the items obtaining scores lower than 0.49 were omitted from the study, and were not considered in the goal system. Reliability of the checklist was also approved based on statistician opinion due to using valid guideline for gathering information items.

The present study was extracted from the dissertation with the registry number of 111/F/3/280 and ethical code of IR.TUMS.SPH.REC.1398.065 at the grade of Master of Science in Health Information Technology at Tehran University of Medical Sciences.

3. *Results*

In general 7 sections of information items essential in clinical decision support system and medication follow-up of MS were identified. They included demographic and historical information of the patient, clinical information of symptoms, and signs of the disease, information related to type of the MS disease, information on paraclinical procedures, medication information, and information related to therapeutic line and medication follow-up. Totally, 100 items were determined as data items, as follow:

3.1.Demographic and historical information of patients

The patients' information about gender, age, employment status, marital status, educational level, history of previous neurologic disease, history of previous neurologic symptoms, history of MS in 1st grade relatives, history of MS in 2nd grade relatives, history of MS in 3rd grade relatives, history of viral diseases, number

of clinical attacks, and the duration of attack were all collected in the current study.

3.2. Clinical data of symptoms and signs of the disease

Numbness and burning in the limbs, dysphagia, weakness and fatigue, muscles spasm, blurred vision, diplopia, reduced vision and blindness, incoordination, nystagmus, Vertigo, urinary urgency or retention, sexual disorders, Lhermitte's phenomenon, nausea, constipation, seizure, and lack of fever and infection were the clinical data of symptoms and signs of the disease.

3.3. Data related to type of MS

Clinically isolated syndrome, active progressive, inactive progressive, active relapsing, and inactive relapsing were among the data related to the type of MS.

3.4. Data on paraclinical procedures

They were divided into two parts:

A. Imaging data: Brain MRI, spinal MRI, orbital MRI, optical coherence tomography, brain CT-scan, dissemination in space (DIS), dissemination in time (DIT), type of lesion, location of lesion, and number of lesions.

B. Laboratory test data: cell blood count (CBC), liver function test (AST, ALT), blood urea nitrogen test (BUN), creatine (CR), thyroid test (TSH), Erythrocyte sedimentation rate (ESR), C-reactive protein test (CRP), antinuclear antibody test (ANA), serum vitamin D3 level (Oh VIT D3 25), vitamin B12 level (serum level B12), cerebrospinal fluids, number of oligoclonal bands, immunoglobulin G index (IgG index),visual-evoked potentials test, delay duration of P100 for each eyes, and anti-aquaporin (Anti-Aqpa, Anti-MOG).

3.5. Data related to pharmacotherapy

Interferon beta, Avonex, Rebif, Plegridy, Glatiramer Acetate, Aubagio, Tecfidera, Fingolimod, Ocrelizumab, Tysabri, Lemtrada, Rituximab, Mitoxantrone, Azathioprin, CellCept, and Vitamin D.

3.6. Data related to therapeutic line

First line, Second line, and Third-line

3.7. Data on medication follow-up

Divided into two groups:

A. Data related to how to take medication: Oral, subcutaneous, intravenous, daily, weekly, three times a week, every 28 days, every three months, every six months, and twice a week.

B. Data related to assessment before prescription of medication: blood test, liver function test, cardiology consultation and cardiogram, ophthalmology consultation, skin examination, chickenpox vaccine, pregnancy test, tuberculosis test, and echocardiography.

In this stage, after the survey, information items score less than 0.49 based on specialists' comments and according to Lawshe Table were omitted. Therefore, ten information items were not used in designing system due to scores below 0.49. Finally, 90 items were selected as necessary minimum dataset. In the first section, which was related to demographic and historic information of patients, employment status items, history of MS in 3rd grade relatives, the history of viral diseases, and achieved score below 0.49 were omitted (Table 1).

Table 1. Identification and selection of demographic and history data of patient

Section	Subsection	Content Validity Ratio (CVR)
Patient demographic and historical data	Gender	1
	Age	1
	Employment status	0.2
	Marital status	0.73
	Educational level	0.6
	Neurologic disease history	1
	Neurologic symptom history	1
	MS history in 1st grade relatives	1
	MS history in 2nd grade relatives	0.73
	MS history in 3rd grade relatives	-0.2
	History of viral diseases	0.2
	Number of clinical attacks	0.86
	Attack duration	0.73

The second section was on clinical information of symptoms and signs of the disease. In this section, all items achieved scores more than 0.49, and based on specialists' opinion, all items were required for designing the decision support system (Table 2).

Table 2. Identification and selection of data on symptoms and signs of the disease

Section	Subsection	Content Validity Ratio (CVR)
Clinical data (Signs and Symptoms)	Numbness and burning in the limbs	0.86
	Dysphagia	1
	Weakness and fatigue	0.86
	Muscles spasm	0.73
	Blurred vision	1
	Diplopia	1
	Reduced vision and blindness	1
	Incoordination	1
	Nystagmus	0.6
	Vertigo	1
	Urinary urgency or retention	1
	Sexual disorders	1
	Lhermitte's phenomenon.	1
	Nausea	0.6
	Constipation	0.6
	Seizure	0.86
	Lack of fever and infection	0.73

In the third section, information on types of Multiple Sclerosis was involved. All items in this section were accepted based on the opinions of specialists and according to Lawshe Table due to obtaining score as required datasets. The fourth section consisted of data on paraclinical procedures which was divided into two sub-sections: 1-radiography procedures and its results 2- laboratory tests. In the sub-section of radiography procedures and its results, the items of orbital MRI, optical coherence tomography, brain CT-scan were omitted, whereas in the subsection of laboratory tests, the tests of ESR, CRP, visually evoked potentials, delay duration of P100 for each eye due to obtaining score less than 0.49 were all omitted (Table 3).

Table 3. Identification and selection of data on paraclinical procedures

Section	Subsection	Content Validity Ratio (CVR)
Radiographic and results data	Brain MRI	1
	Spinal MRI	1
	MRI orbital	0.46
	Optical coherence tomography	0.33
	Brain CT-scan	-0.73
	Dissemination in space	1
	Dissemination in time	1
	Lesion type	0.86
	Lesion location	1
	Number of lesion	0.6
Laboratory test data	CBC	1
	ALT	1
	AST	1
	BUN	0.6
	CR	0.6
	TSH	0.86
	ESR	0.46
	CRP	0.33
	ANA	0.86
	OH VIT D3 25	0.86
	SERUM LEVEL B12	0.86
	Cerebrospinal fluid	1
	Number of oligoclonal bands	1
	IgG index value of	0.6
	Visually evoked potential test	0.33
	Delay duration of P100 for each eyes	0.33
	Anti-AQPA	1
	Anti-MOG	0.6

The fifth section was on information related to medications used by patients with MS, which due to CVR more than 0.49, all of the items in this section were accepted as minimum dataset of treatment. The sixth section was on information related to therapeutic line of patients with MS which consisted of three types of therapeutic lines. All the items in this section were accepted as minimum dataset of treatment due to CVR more than 0.49.

The final section was on medication follow-up of patients with MS, which was divided into two below sub-sections: 1- Information on how to take the medication. 2- Information on assessment of before prescription of the medication.

All the items in this section were accepted as minimum dataset due to scores more than 0.49 (Table 4). Based on the results obtained, 10 items were omitted because of CVR less than 0.49. Therefore, 90 items were identified as requiring minimum dataset for designing diagnosis decision support system and medication follow-up of MS disease.

Table 4. Identification and determination of data on medication follow-up

Section	Subsection	Content Validity Ratio (CVR)
Use medication data	Avonex (intramuscular, weekly)	1
	Rebif (subcutaneous, three times a week)	1
	Betaferon (every other day)	1
	Glatiramer Acetate 40 mg (subcutaneous, three times a week)	1
	Natalizumab300 mg (intravenous, every 28 days)	1
	Alemtuzumab 12 mg (intravenous, one year after first period in three days)	1
	Mitoxantrone 12 mg (intravenous, every six months)	1
	Rituximab (intravenous, every six months)	1
	Ocrelizumab (intravenous, every six months)	1
Assessment before prescription of medication	Blood test, liver function test (before prescription of Avonex, Rebif)	1
	Cardiology consultation, blood test, liver test, ophthalmology consultation, skin test, chickenpox vaccine (before prescription of Fingolimod)	1

4. Discussion

Based on the results, 90 required items for diagnosis decision support system and medication follow-up of MS disease were identified, and divided into seven main categories. These seven categories were as follows: demographic and historical information of the patient, clinical information of symptoms and signs, information on the type of MS disease, information on paraclinical procedures, information on pharmacotherapy, information on therapeutic line, and information on medication follow-up.

The section of information on paraclinical procedures consisted of two sub-sections of imaging procedures and laboratory tests. In addition, the section of information on medication follow-up consisted of two sub-sections of information on how to take the medication and information on assessment before medication prescription. In the study of Sharma and Gupta (2014) which was conducted to design a diagnosis system, capable to diagnose diseases for neural disorders, such as dementia, epilepsy, headache disorders, multiple sclerosis, neuro infections, malnutritional disorders, Parkinson's disease, the identified information items were divided into two major groups of demographic information and clinical information of symptoms and signs. Demographic information used in the system were age and gender, while the identified information items were approximately consistent with demographic information and information of symptoms and signs of the current study (16). Linder et al. (2008) conducted a study in order to diagnose MS disease by using computer system, and the required information items for system were identified in three major groups and nine sub-groups. Major groups consisted of demographic information, information on the type of MS disease, and information on paraclinical tests, whereas the information items of sub-groups consisted of age, gender, MS relapsing progressive, primary progressive MS, secondary progressive MS, MS relapsing remitting, cerebrospinal fluid, number of oligoclonal bands, and IgG index (17).

In the current study, all the items were considered to design diagnosis decision support system and medication follow-up of MS except information on classification of the type of MS, and our study was designed based on Lublin Criteria which is a newer classification criteria(18, 19). A project in India was performed for designing a rule-based expert system in order to diagnose neuromuscular disorders by Borgohain and Sanyal (2012). Information items required for system was only clinical information of symptoms and signs of disease. This system can diagnose Cerebral Palsy, Parkinson's disease, Multiple Sclerosis, and Muscular Dystrophy. Symptoms and signs used to diagnose MS include pricking or tingling sensation, decrease in strength of the patient, balance problems, and blurred vision, which are approximately in line with the findings of the current study (20). Ayangbekun Oluwafemi and Jimoh (2015) divided the identified information items into design expert system for the diagnosis of neurodegenerative diseases only in one group of clinical information on symptoms and signs. The symptoms and signs used for the diagnosis of MS disease are as follows: memory problem, lack of muscle control, speech difficulties, urinary problem, and tiredness. This system is capable to diagnose Alzheimer's disease, Parkinson's disease, Huntington's disease, Multiple Sclerosis and Creutzfeldt - Jakob disease (21). In 2017, Zhao et al. used two logistic regression and support vector machines (SVM) to diagnose various periods of MS disease. They classified the identified information items to diagnose MS disease into four major sections and thirteen sub-sections. Major sections consisted of information on demographic data (age, gender, ethnicity, family history for MS disease, smoking, and race), clinical data (Expanded Disability Status Scale (EDSS) score, score of performance status of central nervous system, disease step and type, and symptoms and signs), and paraclinical data (MRI and T2 lesion number). In the current study, the clinical data, such as EDSS score and score of performance status of central nervous system were not considered, but the importance of data on MRI was emphasized. Also, in demographic information section, information items, such as ethnicity, smoking, and race were not considered necessary by confirmation team (22). In the study by Zdrodowska et al. (2018), that used data mining technique to diagnose diseases, such as stroke and MS., minimum data were classified as datasets, which consisted of items, such as demographic information including age, gender, and information related to symptoms and signs(23). Daumer et al. (2017) designed a decision-making support tool for the prediction of various periods of MS disease. The identified information items for the prediction of various periods of MS were classified as three major groups and eight sub-groups. The major groups consisted of demographic information, clinical information, and information on the type of MS disease, and the subgroups consisted of age, number of attacks, age of incidence of the disease, EDSS score, clinically isolated syndrome, MS progressive remitting, MS primary progressive, and MS secondary progressive. The items of age, number of attacks, and clinically isolated syndrome are in line with the current study(24). In addition, Chase et al. (2017) used natural language processing for early diagnosis of MS disease. Existent information items were extracted from electronic health

record of the patients for diagnosis. These information items consisted of demographic information and symptoms and signs. Symptoms and signs used to diagnose the MS disease were divided into fourteen major groups including autonomic dysfunction, cognition disorder, coordination, dizziness and vertigo, eye and vision, fatigue, headache, mood, pain, motor symptoms, sensory disorders, tremor and seizure, walking, and miscellaneous, and in each group, one or more symptoms related to MS disease were involved (25). Agboizebeta and Chukwuyeni (2012) designed a fuzzy rule-based expert system to diagnose different types of MS disease, and the only parameter used for designing system is the information on symptoms and signs. The symptoms and signs used for the diagnosis of MS disease are as follows: loss of balance, frequent need to urinate, double vision, facial pain, difficulty in solving problem, depression or feeling of sadness, problem with erection, trouble chewing and swallowing, hearing loss, decreased attention span, and poor judgment. At last, the mentioned system classified the patients based on symptoms into two groups of MS relapsing-remitting and primary progressive MS. Those with five or more symptoms were classified as MS relapsing remitting, and those with at least four of the symptoms, being more in men, was classified as primary progressive MS. The mentioned study was in line just with the section of symptoms and signs of the current study (26). Ghahazi et al. (2014) designed a fuzzy rule-based expert system to diagnose MS disease, which the minimum dataset used were gathered through the interviews with experts or specialists and other scientific references. Identified minimum dataset consisted of three major groups including demographic information, symptoms and signs of the disease (27). Amooji and Esmaeilipour Mianji (2015) designed a fuzzy expert system in Iran to diagnose multiple sclerosis and brain tumor disease. The set of information items involved in system for patients with MS included three major groups, as follows: demographic information, symptoms and signs, and information on paraclinical procedures. In the section of paraclinical information, the information related to MRI, existence of plaque in MRI, and cerebrospinal fluid test existed. The results of the mentioned study were almost found to be in line with the section of demographic information, symptoms and signs, and paraclinical procedures (28). With the purpose of diagnosing MS disease, Maleki et al. (2012) used MRI convolution artificial neural network which divided the required information items for diagnosis into one section including radiography procedures, number of lesions, and the type of lesion, the dataset of which was in line only with paraclinical procedure section of the current study (29) Gaspari et al. (2002) designed an expert system for the evaluation of EDSS in multiple sclerosis. This system was rule-based, and the information item in this system was the measurement of 8 functional areas in the central nervous system that was able to diagnose the degree of disability of MS patients(30). In India and Saudi Arabia, Mathew et al. (2015) designed a web based decision support system driven for the neurological disorder. Set of information items in system database included symptoms, signs, and cases of the disease (31). In Turkey, Karaca et al. (2015) used the significance of artificial neural networks algorithms classification in multiple sclerosis and its subgroups. There

were two types of data sets in this system. One data set was related to the diameter of the lesion and two included the disability status scale score (32).

Given misdiagnosis in patients with MS, and designing a pattern of necessary minimum dataset can be the first and most important stage of the establishment of diagnosis decision support system and medication follow-up for MS. minimum dataset is one of the most effective tools for the integrated availability of health information at the national level and their assessment. Therefore, programming and managing patients' performance can be helpful in accurate data gathering of cases with MS disease. Standard MDS leads to improvement of quality of healthcare services and reduction in care costs.

Acknowledgements

The authors appreciate all the specialists who participated in this study and played a role in the validation of the data elements. This study was funded by MS research center of Tehran University of Medical Sciences with the code of 42912-188-02-98.

Conflicts of Interest

The Authors declare that there is no conflict of interest.

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