Viral Hepatitis Diagnosis: A Survey of Artificial Intelligent Techniques

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Abstract: Background; The using of clinical decision support systems (CDSSs) may improve chronic disease management, which requires recurrent visits to multiple health professionals, ongoing disease control, treatment monitoring, and patient behavior modification. The objective of this survey is to determine if these CDSSs improve the processes of chronic care including diagnosis, treatment, and monitoring of diseases.
Methods**:** The survey covers articles extracted from relevant databases. It uses search terms related to information technology and viral hepatitis which are published between 2000 and 2016.
Results: Overall, 80% of studies asserted the benefits provided by information technology (IT); 75% of studies asserted the benefits concerned with medical domain;25% of studies do not clearly define the added benefits due IT. The CDSS current state requires many improvements to support the management of liver diseases such as HCV, liver fibrosis, and cirrhosis.

Key-words: Artificial Intelligence, CDSS, Viral Hepatitis Disease, HCV, HBV, fuzzy ontology.

1 Introduction

Liver is the largest organ inside the body. It helps body to digest food, store energy and remove poisons. Hepatitis is a general term referring to inflammation of the liver. It can caused by both infections viral, bacterial, fungal and parasitic organisms and noninfectious (e.g., alcohol, drugs, autoimmune and metabolic diseases). Viral hepatitis can result in acute disease with many symptoms including nausea, abdominal pain, fatigue, malaise and jaundice. Hepatitis C is a liver disease caused by HCV can lead to chronic infection. The disease will go on to develop into cirrhosis and hepatic cellular. Hepatitis C only is transmitted via infected blood. Chronic hepatitis C affects more than 180 million people around the world (3% of world's)[1]. It causes around 250,000 deaths per year. The percentage of 75% of HCV patients can develop chronic hepatitis C with ongoing viral replication in the liver, and detectable HCV RNA in serum or plasma eventually results in cirrhosis. The remaining 25% of the infected patients recovers from the infection without evidence of viral replication. Countries with high rates of chronic infection include Egypt (22%), Pakistan (4.8%) and China (3.2%). These countries promote unsafe injections using contaminated equipment [1]. Researchers and practitioners face challenges in two main points. The first point is from the medical view, .Early diagnosis and aggressive therapy may improve the outcomes in Hepatocellular Carcinoma (HCC). Systematic and algorithmic approaches would ensure optimal therapy for each patient [2]. It is still difficult to early prognosis the need to liver transplantation automatically. However, it is possible to predict acute liver failure due to drugs or viral hepatitis [3]. It is difficult to predict the response of the therapy on patients infected with HCV. This prediction affects in treatment because of high cost and significant unfavorable reactions [4]. The second point is from the information technology (IT) view. Technology can't replace human experts in the diagnosis process, but it only tries to help them to generate or select data which are relevant. The challenges that face IT systems in the diagnosis and/or treatment have to be solved by the available observations and knowledge. Medical errors occur due to human negligence, inaccurate information and improper flow of communication in the clinic [5]. There is a lack of efficient analysis tools according to rich information of patient profile to discover hidden relationships and trends. There are tools serve to diagnosis the patients infected with HCV or not [6]. The objective of this study is to explain and review how ITcan help to enhance the diagnosis of viral hepatitis related to fibrosis degree for chronic patients and HCC.

2 Methods

2.1 Data sources and search

The articles are identified by conducting search in many databases including PubMed, IEEEXplore, ScienceDirect, Springer, and IJCSI. We use the keywords related to our studied disease such as viral hepatitis, HCV, HBV, chronic HCV, liver cirrhosis, liver cancer, and liver fibrosis. In addition, the survey relates medical concepts to IT concepts such as information technology, information system, artificial intelligent, fuzzy OWL, disease ontology, information retrieval, semantic web, and fuzzy expert systems. The survey covers the period from 2000 to 2016.In order to extract relevant articles, keywords are searched within each document's title and keywords list.

2.2 Exclusion/ Inclusion criteria

The articles selected in this review are only written in English language. Moreover, there are exclusion/inclusion criteria that are used to filter the relevant articles.

2.2.1 Inclusion criteria

- The study proposes or reports on the design and development of viral hepatitis systems.
- The study proposes or reports on a new technology for developing diagnosis of viral hepatitis patients in viral hepatitis systems.
- The study proposes or reports on a process, method, technique, reference, or architecture that supports the design of viral hepatitis systems.
- The study proposes a healthcare standard in viral hepatitis systems.

2.2.2 Exclusion criteria

- The study proposes on the design of viral hepatitis system without using service orientation.
- The study presents contribution in areas other than viral hepatitis systems.
- The study is a table of contents, copyright form, conference, or workshop agenda.
- Duplicated articles.

The study selection is performed by selecting relevant article based on titles, abstracts, and keywords by considering of the inclusion and exclusion criteria. A set of the selected studies is fully read and analyzed [6, 9, 10, 14, 25, 28,31,33]. Another set is studied by only read their abstracts and conclusions [5, 12, 15, 16, 27, 30, 35]. The last set is studied by abstract only [4, 21, 24, 34, 36].

2.3 Data extraction and quality

The extracted data was summarized and grouped into two topics including medical and information technology. Each topic has publication year, architectural approach, healthcare, and challenges and limitations. In term architectural approach focuses on how to implement artificial intelligence (AI) in the medical domain. In term healthcare extracts medical data to achieve reasoning. Predicating the response of a therapy on patients affects in viral HCV hepatitis treatment because of high cost and significant unfavorable reactions [4]. It is difficult to prognosis early with liver transplantation, but it is possible to predict acute liver failure due to drugs or viral hepatitis [3]. The technology doesn't replace human experts in the diagnosis point, but it only tries to help them to generate or select data which are relevant. However, there are many challenges and limitations that face IT systems in the diagnosis or treatment. They have to be solved by less specified observations and knowledge. Medical errors occur due to human negligence, inaccurate information, and improper flow of communication in the clinic. These limitations, in few systems, are solved by ontology. Figure 1 explains part of viral hepatitis diseases ontology. The ontology techniques are combination of AI and machine language to help to share and reuse the knowledge. It contains natural language processing techniques and knowledge representation techniques as well. The ontology techniques can be used as channels of communication between human beings and systems. They can be further used for information retrieval, knowledge management and building of proper communication links to clinics or hospitals [5, 7]. In [8], different challenges arise in the study design with the OWL ontology as a consequence; completeness of data entry cannot be checked. Available data are not satisfied for the prediction of therapies of patients to get accurate results [9].

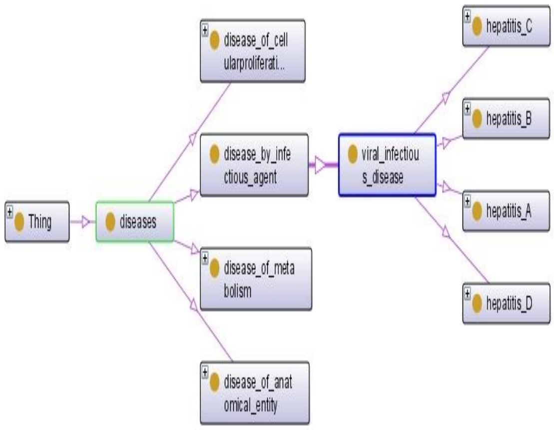

Fig.1 Disease ontology

Missing value may be a major problem in the study [10]. In this study, they work on same group of patients in same hospital, but they face some limitations like the number of patients is small to confirm the results. Chi et al.,[11] face the problem of interaction between a patient's conditions and the related knowledge sources.

3 Results

Relevant articles are identified by keywords, abstracts and titles. The study collected 16,611 articles which are divided in five international databases as: PubMed (1468),Springer (5,907), IEEEXplore (1,610), Science Direct (7,557), and IJCSI (69).These research articles match the inclusion/exclusion criteria. The study is done in two main phases. Firstly, there are80 research articles that result from the study of abstracts and titles of articles. These articles are entered to the second phase. Secondly, the full text reviews of these articles result in 40 research articles. Figure 2 shows the flowchart of results with steps. All the systems and databases returned a total of 150 results, of which 40 were repeated or with an irrelevant title for this study. Out of these papers, 30 were dismissed after reading their abstracts. Finally, a total of 70 papers were selected as relevant .Figure 3 shows the relation between the numbers of the relevant articles resulted from the searching in the international databases with their databases.

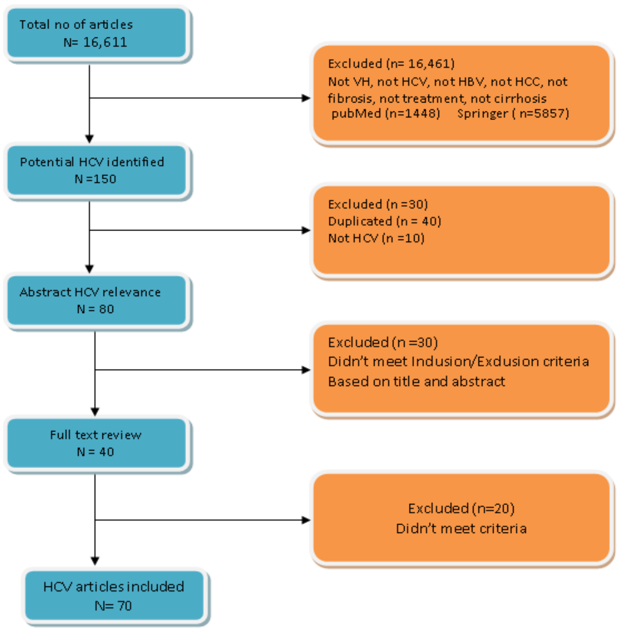

Fig.2 Results flowchart

These relevant articles have been published in different year ranged from 2000 to 2016.

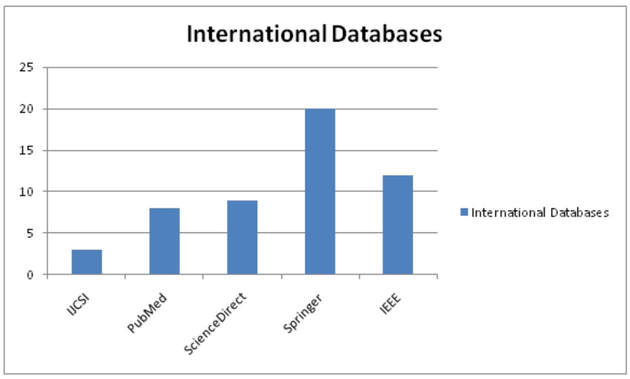

Fig.3 No of relevant articles in their DBs

Figure 4 shows the number of publication per published year. This review shows that the majority of studies (80%) reported the design and development of tools to specify data quality for implementation in medical domains.

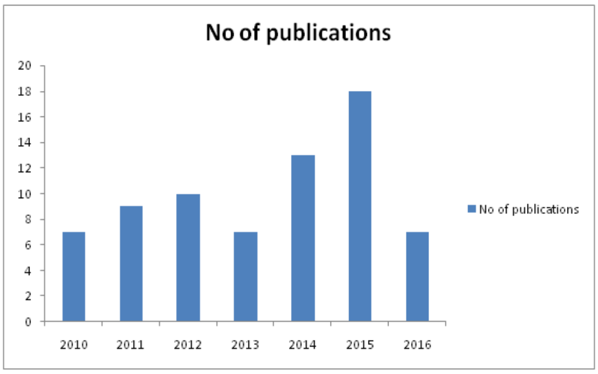

Fig.4 No of articles per year

3.1 Application of technology

Table 1 states the various applications of technology for chronic diseases management from diagnosis to treatment and predicate of another disease of development of disease. There are many applications for these applications as described.

Table 1: Application of technology

Technology	Functionality
• Internet	• Sending required laboratory tests. • Accessing EMR of patients. • Enquiring general health related issues. • Providing feedback to patients by clinicians.
• Telemedicine	• Video conference with clinicians. • Receiving feedback from the clinicians.
• Phone	• Send SMS to clinicians.
• Decision support	• Integrated with patient's medical record for pattern recognition. • Suggesting the medication treatment according to patient's data.

3.2 Internet

Web 2.0 becomes a place where users can connect and share large amount of data [12]. This made information more accessible all the time. But users cannot manage all amounts of data, so there are new technologies related with internet to help users treating with their information. Big Data is used for extracting conclusions from data. Semantic Web is used for sorting data, and intelligent systems are used to deal with the information for different reasons. This openness is main driving force for the explosive growth of Internet. At the same time, web faces the major drawback of unstructured and unformatted web contents. Due to this drawback, relevant information retrieval from web is becoming a challenging job of the information technology. In [13], Fouad et al. used semantic web to implement the methodology of information retrieval.

3.3 Telemedicine and phones

Articles in this category refer to studies using technologies other than the internet. Telemedicine is a primary information technology for chronic diseases treatment like hypertension [14], and recommendation system for anti-Diabetic drugs.

3.4 Decision support

Articles in this category process large amounts of data and provide recommendations for treatment protocol, or they choose appropriate therapy to patient class. In [15,16], Panchal et al., proposed a technology in diagnosis of HBV positive or not for medical treatment. In [17] El-Sappagh et al., presented a fuzzy case-base ontology construction process to store fuzzy cases about diabetic patient by using IKARUS-Onto methodology [18] and, OWL 2 fuzzy extension in order to develop an accuracy CDSS.

4 Analysis of a sample of systems and applications

4.1 Methodologies to specify data quality for implementation

Generally, data mining is the base line in AI systems which categorized into descriptive and predictive data mining. Predictive data mining techniques supported clinical decision making. These techniques are categorized into three: association rule; classification and clustering. Association refers to relationships between sets or objects. For medical data, it may discovers that a set of findings or symptoms frequently occur together with another set of symptoms. Classification maps data items into one of several pre-defined classes. For example, classification rules about a disease can be extracted from previously known cases and then used to diagnose new patients of this disease based on their symptoms. Decision Trees (DT) [3, 6], Artificial

Neural network (ANN) [9,19,20], Bayesian Networks (BN) [21], Naïve Bayes (NB) and Support Vector Machine (SVM) [22,24] are examples of classification approaches. Clustering recognizes the class or cluster for a set of unclassified objects according to their attributes. For example, a set of diseases can be grouped into several clusters based on the similarities in their symptoms, and the common symptoms of the diseases in a cluster can be used to describe or predict that group of diseases [25]. The K-nearest neighbor (K-NN) is the most popular method of clustering [26]. Table 2 show detailed approaches with their accuracy.

Table 2: accuracy of a sample studies

Author	Approach	Published year	Accuracy
Ahmed M. Hashem	ANN , DT	2010	93.7%
Mahmoud ElHefnawi	ANN	2012	97%
Nobuaki Nakayama	ANN	2011	99.1%
Ping Qiu	AVM	2009	99%
H. Swapna Rekha	FUZZY LOGIC	2014	70%
Naoual EL Aboudi	SVM , CE	2016	97.2%
Alexandra Lukáčová	DT	2015	90%
Malay Mitra	ANN , RS	2015	94%
Alice M Richardson	DT	2013	99%
Reza Ali Mohammadpour	FUZZY LOGIC	2015	92.8%
James Lara	BN , LP	2013	95%
Enas M. F. El Houby	ANN , DT	2014	92%
Mohammed M.Eissa	GA , RS	2014	96.3%
Shaker El-Sappagh	FUZZY ONTOLOGY	2015	97.6%

This review presents the research methodologies for developing decision support services in medical domain. Review proposed methodologies in diagnosis, treatment and prediction of another diseases or prediction of the levels in patient case. E.g., telemedicine methodology is very useful in diagnosis and treatment of the chronic diseases like diabetes. Review proposed abstract and conclusion of papers [4,5,12,15,16,21,24,27,30,34,35,36]. And explains the methodology for the rest [6,9,10,14,25,28,31,33].

Chiang and Liang [12] proposed methodology to develop the telemedicine and smart home care using inference mechanism of fuzzy theory. The system stored the required contexts in knowledge ontology, including the physiological information and environmental information of the person under care, as the database of medical decision. Chen et al., [27] used fuzzy reasoning techniques and domain ontology for anti-diabetic drugs selection to develop the methodology of drugs recommendation. The methodology is based on fuzzy rules and drugs ontology to recommend the medicine. It achieved a good performance in drug selection. Jeon and Ko [28] used hybrid approach to develop the diagnosis of specific disease by collecting and analyzing domain knowledge. Their methodology was divided into three phases: selecting abstraction levels, converting ontology classes to Bayesian network nodes, and generating BN links. The first phase only identified the classes on ontology that are most useful in diagnosis diseases for e-health application. In the second phase, system automatic constructed BN nodes from ontology classes and stated probabilistic conditions to each node. The last phase is to generate links between nodes using a relational model which analyze the dependence and orders of BN nodes. The system implemented for diagnosing obesity and achieved a good performance. Zhu et al.,[14] proposed a methodology to develop the intelligent telehealth system to solve long term management of hypertension. The methodology included two phases: the first phase is the basic data communication phase. This phase built similar system structure with traditional ones supporting data transmission, central server and web service. The second phase was the artificial intelligent phase which made decisions from domain knowledge into hypertension ontology, personal data ontology and fuzzy rule inference engine. The outcome of the system was sent to patients via SMS or internet which makes the use of semantic web technology necessary. Zekri et al., [30] proposed a methodology to develop medical decision support in Alzheimer’s disease. The study is divided into stages. The first stage is the building of core ontology that represents the concepts needed for diagnosis. The second stage extended this ontology to get more efficient diagnosis. The third stage identified the vagueness points in each concept and each relation to generate fuzzy knowledge. This methodology recognized that fuzzy ontology isa useful tool for the representation of fuzzy and crisp knowledge and reasoning on it.

Gedzelman et al., [31] proposed a system to develop mobile application in IR systems with Cardio-Vascular diseases ontology. This methodology designed an environment for ontology design and enrichment based on texts. This environment comprises various tools such as a term extractor (to propose new terms extracted from the texts), a concordance (to visualize terms in their context), a Terminology Server (to help the user find existing concepts from a given term) and an ontology editor which has been designed to manage multilingual ontologies. Table 3 show characteristics of the included studies and features of decision support systems.

Kaur and Khamparia[5] stated SPARQL retrieves and manipulates query data of liver domain ontology as it supported for better medical decision. This methodology was implemented using protégé tool. Panchal et al., [15,16] proposed methodologies to improve medical decision making. Their methodologies used ANN tool to get an accurate diagnosis of viral hepatitis B (HBV).Jilani et al.,[32] proposed a diagnosis system based on ANN for hepatitis virus. The proposed system has two stages: feature extraction, and reduction and classification stages. The classification accuracy of this ANN-based diagnosis system for the diagnosis of hepatitis virus was obtained. This accuracy was around 99.1% for training data and 100% for testing data. ElHefnawi et al., [4] stated a comparison between different data mining techniques for prediction of response HCV patients to therapy Peg-IFN. From the implementation the results of ANN gave the best accuracy with five features used. Parry and MacRae [25] proposed a methodology to improve clinical systems. The methodology used development approaches like fuzzy case based reasoning to complete missing data based on a cluster of similar patients. The second approach is fuzzy ontology to predicate outcome using fuzzy DL based on available data. Moawad et al., [33] proposed building OWL Ontology for Viral Hepatitis based on Ontology of Biomedical Reality (OBR) framework. Their methodology of developing Viral Hepatitis (VH) Ontology included 3 phases; Acquisition Phase, Validation Phase, and Representing in OWL Phase. Researcher used the bottom-up approach in designing their ontology and the protégé OWL editor in implementing the ontology.

In [24], Elaboudi and Benhlima proposed a new approach based on PCA for feature reduction and SVM with stochastic optimization method that isCEO for classification process so as to achieve high accuracy for hepatitis diagnosis. This approach achieved accuracy 97.2 % for hepatitis diagnosis classification. Lukacova et al., [34] proposed machine learning models useful in medical practice to predict patients who should be examined as chronic hepatitis B or C. Authors developed the diagnosis of HBV with a new approach which can state the diagnosis early.

Table 3 Characteristics of the included studies and features of decision support systems

Characteristics of the included studies	Number of studies
Publication year	
• 2000-2010	10
• 2011-2013	25
• 2014-2016	44
Country of study	
• United state	16
• Spain	6
• China	8
• Egypt	17
• India	5
• Multiple countries	24
Clinical arena addressed by CDSS	
• Family medicine	2
• Internal medicine (included liver disease)	39
• Cardiology	6
• Homecare and emergency	8
• Other specialties (included cancer)	17
System features	
System integration	
• Integrated (linked system) like system integrated with function of smart phone	22
• Independent (stand-alone system)	30
System communication	
• Consulting system (give advice)	41
• Recommender system	22
System requires data entry	
• System requires user input	22
• System does not require user input	33
Users of the system one system could have different users	
• Physicians	51
• Patients	25

Mitra and Samanta [10] proposed a methodology to develop intelligent decision support systems in hepatitis diagnosis. The methodology was distributed into phases; the first phase is data preparation which analyzes hepatitis data set from UCI repository. In addition, it added data mining techniques to handle data and solved missing values problems. The second phase was the reduction of data with rough set feature selection technique. Finally, classification phase was done by incremental back propagation neural networks and levenberg-Marquardt (LM) algorithm. Hashem et al., [35] used data mining techniques in order to improve the diagnosis processes as well as for management classification of patients infected with HCV. The methodology predicted of liver fibrosis degree with accuracy 93.7%.

Mohammadpour et al., [36] proposed a study to improve the accuracy of fuzzy rule based classification which overall was 92.8%. The methodology employed fuzzy set theory for the diagnosis of CAD coronary artery disease. ElHouby [9] proposed a methodology to develop the prediction of the response of HCV patient to therapy. The methodology contained three phases started from the data preprocessing to the application of data mining techniques. The second phase is the classification process by using ANN and DT techniques. The third phase evaluated the model and compared the performance with other models. This model achieved highest accuracy 92% on data from 200 Egyptian patients with hepatitis C virus who were treated with combined therapy IFN plus RBV for 2 years were used.

Omran et al., [6] used data mining techniques to develop a prediction algorithm of HCC. The prediction algorithm implemented in 315 Egyptian patients with HCV related chronic liver disease. The technique was constructed by decision tree learning algorithm C4.5 to categorize patients into HCC and non HCC. Lara et al., [21] used hybrid model of LP and BN to identify the rate of liver fibrosis among patients. The LP linear projection was useful in HCV feature selection using physicochemical properties of nucleotide. The BN measured similarity among HCV patients with similar rate fibrosis. Maximum accuracy of the model was 95%.

Eissa et al., [37] developed approach using rough sets and genetic algorithms to classify HCV patients. The methodology of the study was divided into three phases: preprocess of HCV data sets, data reduction, and rules generation. The first phase used evaluation hybrid approach of rough set and Boolean reasoning in order to minimize the number of intervals without significant loss of class attribute mutual dependence. The second phase used dynamic reduction algorithm to get better performance. The third phases was divided into two levels as follow rule generation by rough sets and improve the classification accuracy by GA. Hybrid rough genetic model achieved with best fit accuracy 96.3% during 9 months of treatment.

El-Sappagh et al., [17] proposed building OWL ontology for diabetes based on standard medical ontologies such as SNOMED CT. The methodology improved case based reasoning(CBR) semantic effectiveness by add fuzzy theory. The proposed framework presented a case base ontology and a fuzzy semantic retrieval algorithm is integrated to build an intelligent CBR for diabetes diagnosis. The system achieved a high-level performance compared to the traditional CBR systems; the system's accuracy was 97.67%.

Santos et al., [38] proposed a methodology to develop the prediction of HCC. The methodology was divided into four stages: data collection, data imputation, clustering based oversampling, survival prediction. Elhefny et al., [7] proposed the building of obesity related cancer ontology using web ontology language OWL2 and explained the diseases hierarchy and terms according to the standard diseases ontology (DO).

Lu et al.,[26]proposed an estimation methodology to monitor fetal heart. The methodology depended on two techniques: estimation and clustering. Estimation technique uses empirical mode decomposition EMD and clustering technique used Kohonen neural network KNN.

4.2 Issues related to IT used in HCV medical domain

A total of 60 of 84 studies showed some type of added benefit of using IT for medical domain especially in liver diseases. The benefit may be in the form of improvement in clinical outcome (liver fibrosis), adoption of healthy behavior and motion sensing [12], reduced management cost and improved satisfaction of patient. The reminder studies did not add value. Overall the results indicate the benefit of IT in medical domain.

4.3 Ontology-specified implementation to develop data quality.

Alexopoulos and Wallace [18] proposed a methodology to develop fuzzy ontologies from existing crisp ontologies to enhance the effectiveness of fuzzy ontology and the output's quality and accuracy. Davarpanah et al., [39] proposed semantic bridges between upper ontology and smaller Bio-ontologies. Chiang and Liang [12] proposed a home care system, which was divided in three parts: ontology, inference mode, and interaction between motion sensing and system in different spaces. The construction of the ontology is divided into behavior ontology and environmental ontology. In [40]Grissa and Alouiproposed an algorithm to support database flexible querying by using generated fuzzy ontology. The algorithm was divided into two steps; the first step was the combination of fuzzy logic and formal concept analysis for clustering common properties. The second step was automatic generation of fuzzy ontology to answer the flexible queries. In [41] Fernando et al., presented a methodology for the improvement of fuzzy multilayer architecture to perform ontology alignment. The methodology used fuzzy logic techniques to combine different similarity measures among ontology entities with highest accuracy.

There are different approaches for using web 2.0 and especially in semantic web form by developing flexible queries using fuzzy ontology [42]. And [41]

Fernandez et al., performed ontology alignment via fuzzy layers. In [43] Bourahla proposed the reasoning over vague ontology concepts.And in [44] Kumova generated ontology from relational data base with fuzzy reasoning. Some relevant studies can be found in [48], [49] and [50].

5 Discussion

CDSS often improved the process of patient care. This review summarizes the effectiveness of clinical decision support technology for management of chronic condition. This systematic review presents some tools that support clinical decision making in liver diseases management. A number of selected relevant articles developed CDSSs with an increasing accuracy and reducing fracture rate. Other articles provided high prediction rate of the diseases development and the initiation of the therapy.

This review has a number of limitations; the full text studies included in our review were limited and conducted. The number of studies is likely to be incomplete as an evaluation studies meeting inclusion criteria in public domain. Other articles may be published outside academic literature databases or published in languages other than English language. Besides, many articles focused on the information contained on the research not on the interface which is used by the user.

6 Conclusion

The number of health applications with DSS has been increased during the last few years. Accurate diagnosis is the most important problem of medicine. Understanding the relationship between diagnosis and determine clinical protocols is effected in healthcare. This survey provided important knowledge related to clinical domain from several search studies in different medical specialties for helping in the development, implementation and evaluation of CDSS systems for long life management. According to my study on HCV there is a limitation in managing this disease. Our future work proposes a new framework in CDSS to diagnosis HCV patient to choose appropriate protocol for treatment.

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