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Ontology-Based Decision Supporting System for Diagnosis and Treatment of Leukemia

Kabada Sori Ayana*

Ambo University Institute of Technology, School of Informatics and Electrical Engineering, Department of Information Technology, Ethiopia

***Corresponding Author:** Kabada Sori Ayana, Ambo University Institute of Technology, School of Informatics and Electrical Engineering, Department of Information Technology, Ethiopia.*

ABSTRACT

The decision for diagnosis and recommendation of a Leukemia patient is made based on expert knowledge. How an expert interpret the patient's condition may be different due to the knowledge handling problem which is tedious and very time consuming and mainly leads to a wrong decision. As well, the number of doctors and hospitals are not matched with the number of patient in the community. Nevertheless, this paper uses semantic technology concept for building ontology, knowledge repository, which helps leukemia patient to diagnosis and get medical recommendations by inferring types of disease and its specific recommendation that help a patient to counteract the disease. The proposed system accepts the symptoms, blood test value from the user and as well as ask the user different question about the risk factor of the diseases to detect whether it's leukemia or not. If it is leukemia the system, classify the type of leukemia, and recommend the treatment decisions. The proposed system use protégé tools to develop ontology. Moreover, a well-known evaluation method such as accuracy, precision, recall, and F-measure are used to evaluate the effectiveness and efficiency of the model. Based on the performed evaluation the proposed ontology-based model achieved 95% precision, 94.8% recall, 94.7% F1-score, and 94.1% accuracy.

Keywords: *Leukemia, ontology, semantic web Technology, expert system, Ethiopia.*

INTRODUCTION

Leukemia is a cancer of blood or bone marrow, which control production of different types of cells such as red blood cells that carry oxygen, white blood cells (WBCs) that fight infection, and platelets that help blood to clot. Every day, billions of new blood cells are made in the bone marrow; most of them are red cells. But, when you have leukemia bone marrow produce high number of WBCs than other blood cells and they will stop dying normally and will not carry out their function in the body, such as fighting infections and healing wounds. WBCs can be formed from two different cells, lymphoid or myeloid. When either lymphoid or myeloid is affected by cancer determines the kind of leukemia and the affect can be sudden or "acute" or can be developing slowly or "chronic". This results in 4 subtypes of leukemia: acute lymphocytic leukemia (ALL), acute myelogenous leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML)[1][1]. Leukemia occurs in every part of the world and its incident has increased in most countries worldwide, due to a growing and aging population and to an expansion of key risk factors[2]. Nevertheless, it need right decision for diagnosis and treatment by medical personnel.

In Ethiopia there is an issue of leukemia diagnosis and treatment due to lack of expert, facilities, sufficient hospitals, adequate equipment, medicine and supplies and networking of institution in capacity building [3]. Hence, the number of death is rapidly growing. In 2016, 8.9% people are estimated to have died from the various forms of cancer among this 310,165 are died due to leukemia[2]. According to the latest WHO data published in 2017, Leukemia Deaths in Ethiopia reached 3,442 or 0.54% of total deaths[3].

The identification of disease symptoms plays a critical role in the successful diagnosis and treatment of diseases. A symptom and blood test

[1] https://www.medicinenet.com/leukemia/article.htm

[2] https://ourworldindata.org/cancer

[3] https://www.worldlifeexpectancy.com/ethiopia-leukemia

value used as evidence for the existence of disease, in this case, a leukemia disease. Nevertheless, there are diseases that share similar symptoms and blood test value which challenge a diagnosis of diseases. This challenge is due to a knowledge-handling problem.

In this work, an Ontology based decision-supporting system for leukemia diagnosis and treatment is proposed. The proposed model takes an advantage of semantic technology, more specifically ontology, to represent the domain leukemia knowledge through the description of concepts related to patient symptoms, blood test value and different risk factor of disease. It also uses the knowledge contained in the semantic repository and a rule based engine to infer type of disease and its specific recommendation that help patient to counteract the disease.

Related Work

There are large numbers of research findings related to ontology technology involved in medical

applications. The Ontologies in health sector are very emerging today see in[4][5][6][7][8][9]. In this section we present the existing ontology prototypes that have been implemented as solution for healthcare services.

In[4] the authors provide the computerization and execution of a breast cancer follow-up clinical practice guideline. The computerization of the clinical practice guideline led to the development of a breast cancer ontology. They present their breast cancer ontology which models the knowledge inherent within the breast cancer follow-up clinical practice guideline - the breast cancer ontology serves as the knowledge source to determine patient-specific recommendations. They discuss the ontology engineering process that highlights the specification of their breast cancer ontology in terms of clinical concepts and the relationships between the concepts expressed as OWL classes and properties, using the protégé ontology development tool.

In [5] the authors present a benign/malignant breast cancer classification model based on a combination of ontology and case-based reasoning to effectively classify breast cancer tumors as either malignant or benign. This classification system makes use of clinical data. Two CBR object-oriented frameworks based on ontology are used jCOLIBRI and myCBR.

In [6] breast cancer ontology has been built and gathers the terms used by lay people to talk about breast cancer. The resulting ontology has been the core of a health consumer query reformulation application. This work proposes the use of spreading activation technique through the ontology to infer new concepts from the ones initially identified in a health consumer question.

In [10] They proposed ontology development for type II diabetes mellitus clinical support system. Their system helps no-expert health provider in diabetes as they suggest essential activities for improving life quality and achieving goals of diabetes mellitus treatment.

In [7] the authors illustrated Ontology-Based System for Cancer Diseases Knowledge Management. The developed system used to identify different type of cancer and its stage based on sign and symptom of patients and it also provide different recommendation based on the identified type and stage of cancer. Were the process of identifying type, stage and providing recommendation of different cancer type can interact with a database of cancer ontologies through the query module, which maps from the query of the asking module to the structure of the vocabulary of the ontologies stored in the database of cancer ontologies. The author evaluates the developed system using 40 test cases of different type of cancer collected from different source which include 14 cases for breast cancer, 12 cases for lung and liver cancer, and 2 cases for other types of cancer. Finally, the author gets 92% correct classification, 3% misclassification and 5% unknown cancer type, since the system does not cover all types of cancer.

In [8] the authors developed the diagnosis of Liver cancer ontology using SPARQL using protégé tools. The system may have five subclass under liver cancer class namely; risk factors, the symtoms, the diagnosis, the treatment and the type of liver cancer where each of them has their own subclass. Then different query relations have been used using SPARQL to extract and identify the liver cancer type based the symtoms; and then to provide treatment based on the identified type of liver cancer. This work contributed in formulation of new taxonomical hierarchies and medical data.

In [9]the author illustrated An Ontology-Based Decision Support System for the Diagnosis of Plant Diseases. The developed system used to help the farmer by identifying type of diseases based on its symptoms and it also provide recommendation based on the identified type of diseases. On the first phase the author developed Phytopathology Ontology to provide a standard vocabulary for Phytopathology domain, helping integrate data sources and to represent the main source of computable domain knowledge that is exploited by the system for decision support purposes. After the knowledge's about plant diseases has been represented in standard way they set SWRL rule which used to allow representation of expert knowledge and to drive reasoning process about plant diseases in order to diagnosis and obtain recommendation for treatment of diagnosed diseases. Once a disease has been diagnosed, the system, through its semantic indexing module, performs a search for documents that can be interested to the farmer. Finally, they evaluate the proposed system by measuring its precision, recall, F-measures for diagnosis of short-cycle crops and perennial crops and they get F-measure of 0.7394 and 0.7199 respectively.

Furthermore, many researches have been conducted on diagnosis and treatment of leukemia by different algorithm as shown in[10][11][12][13][14].

In[11] Sonali Mishra et.al developed algorithm for classification of microscopic images by using discrete cosine transformation for detection of acute lymphoblastic leukemia, a kind of blood cancer. Discrete cosine transformation coefficientis taken as the feature for the classification process. Extracted features will be approximately90.Finally, SVM classifier is used to classify the images as normal and abnormal within accuracy of 89 %.But the developed system does not provide formal explicit specification of a shared recommendation.

In [12]the author conducted study on Automated Leukemia Detection Using Microscopic Images. The conducted study shows that the developed system will automatically detect the leukemia by collecting infected blood cell image from different source. Finally, they achieved 93.57% of accuracy. The system may not provide recommendation for the diagnosed cell and still recommendation is provided by the expert.

In [13] Develop Novel approach to find the various stages of Chronic Myeloid Leukemia using Dynamic Short Distance Pattern Matching Algorithm for finding the optimal sequence alignment to reduce the time, space complexity and increase the efficiency of sequence alignment in the large data set and find the stages of CML. In the developed system they have used a combined divide and conquer algorithm and distance approach to compare the different sequences by collecting DNA Sequences of 10 to 20 normal and abnormal persons. By doing this they have been identified the best method which possesses less time complexity and space complexity to get the final optimal alignment. But the developed system does not provide formal explicit specification of a shared recommendation.

In[14] the author presented a Two-Stage Expert System for Diagnosis of Leukemia Based on Type-2 Fuzzy Logic. The system contains two stages. In the first stage, the inference of the blood test state i.e. sickness or healthy blood test is determined by considering Platelet (PLT), Hematocrit (HCT), White Blood Cell (WBC), Red Blood Cell (RBC) and hemoglobin as system inputs. For construction and evaluation of the system in the first stage a dataset containing 345 blood tests (113 women, 193 men and 39 children) of a governmental hospital where used. In the second stage, signs of leukemia, duration of disease until its progress and the output of the first phase are combined and the final diagnosis of the system are obtained. Finally, the developed expert system has the ability to diagnose leukemia with the average accuracy of about 97%. But the developed system does not provide real time response, It's lower speed and longer run time of system, for diagnosis and recommendation. Restricted number of usage input variable and does not simply capable to receiving feedback for implementation of learning strategy.

METHODOLOGY

This section introduces the steps followed for ontology based leukemia diagnosis and treatment system. The proposed ontology based leukemia diagnosis and treatment system architecture is presented in the following Figure 1.

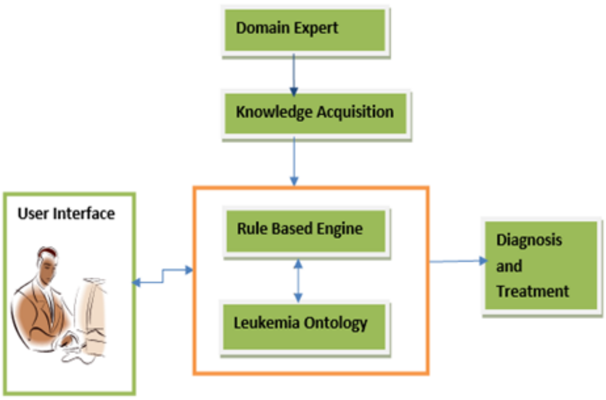

Figure1. *The Proposed Ontology based Leukemia diagnosis and Treatment architecture*

Domain Expert

Domain expert is a person with special knowledge or skills in a particular area of Endeavour, in this case hematologist-oncologist, is a domain expert who are specialized to diagnosis leukemia.

Knowledge Acquisition

Knowledge acquisition is the process of planning, analyzing, of domain expert knowledge in order to represent in knowledge base. In this case knowledge of domain expert can be acquired by interviewing with specialist physician and by analyzing different document which is available on different website. Then this acquired knowledge can be represented in ontology based knowledge base.

Leukemia Ontology

Ontology is a richer semantic web language that used to provide more vocabularies for semantic representation of the information. It has ability to support the indispensable integration of knowledge and data to achieve a common and shared knowledge that can be transmitted between people and between application systems. Also, it is a set of classes, properties, individual and data value.

In this study protégé tools are used to develop leukemia ontology. Protégé is a free open source editing tool and developed by Stanford University. It support semantic web language and developed in java language[15]. The brief description of classes, properties, and individual of leukemia ontology are presented in the following subsection.

Class

The leukemia ontology define patient and disease main class. The disease class contain leukemia class, which further contains Diagnosis, Risk factor, symptoms, treatment and Type class. Beside the diagnosis class include blood test, bone marrow test and physical exam sub classes; and risk factor class contains exposure to certain chemicals, family history of leukemia, genetic disorder, life style and previous cancer treatment subclasses. The class of leukemia ontology are mentioned in the Figure 2 and a brief description for some of them are given as follows.

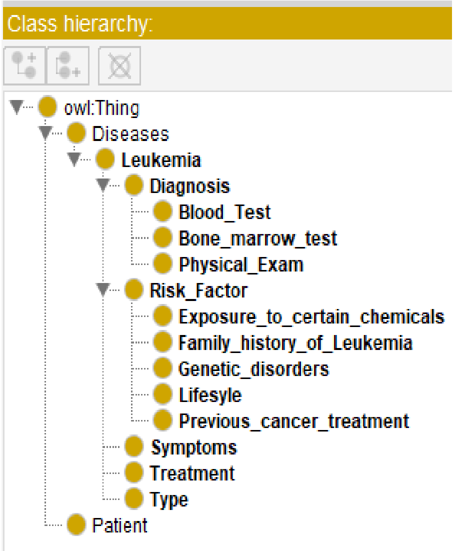

Figure2. *Class hierarchy of Leukemia ontology*

Patient class contains information about patient; and it is linked with disease class and its subclass via different relationship. This class contain all type of individuals and essential information that used to describe each patient such as patient place of work, age, and gender.

Disease class provide information about what type of disease we are describing. Regarding to this study it focus on leukemia disease, the individual of this class have relationship with patient class.

Object Property

In this section Object property, that describes the relationships between two individual classes in the same domain were presented. Each object property has a domain and range that can be used by reson are to make conclusions and identify inconsistencies.

The object property used in this study are stated in the Figure 3 and a brief description for some of them are given as follows.

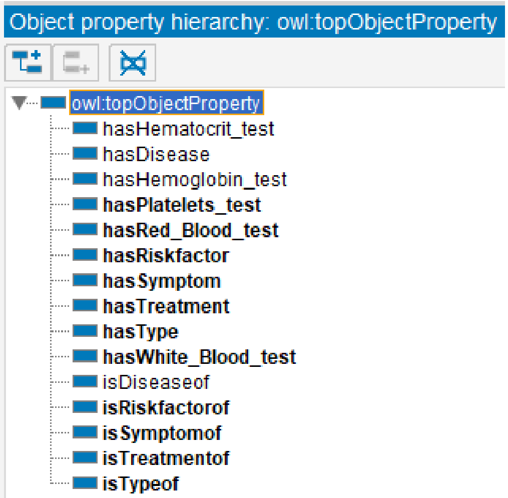

Figure3. *Object property hierarchy of leukemia ontology*

Has Disease: This object property isused to provide the link among individual of class patient and disease. Its domain is patient and the range is a disease. For example, a patient"Kindalem" has "acute Lymphocytic leukemia" disease

hasHemoglobin_test: This property is used to provide the relationship between the patient and the blood test class. For instance, a patient "Melaku" has a "hemoglobin" blood test in the laboratory

hasHematocrit_test: This property is used to provide the relationship between the patient and the blood test class. For instance, a patient "Melaku" has a "Hematocrit" blood test in the laboratory. The domain of this property is patient class and the range is blood test

hasPlatelets_test: This property is used to provide the relationship between the patient and the blood test class. For instance, a patient "Melaku" has a "Platelet" blood test in the laboratory. The domain of this property is patient class and the range is blood test

hasRed_Blood_test: This property is used to provide the relationship between the patient and the blood test class. For instance, a patient "Melaku" has a "red blood" test in the laboratory. The domain of this property is patient class and the range is blood test

isRiskfactorof: This property is used to indicate the Risk factor of Leukemia disease. The domain of this property is Risk_factor class, the range is Leukemia, and his inverse property is hasRiskfactor.

isSymptomof: This object property is used to provide the relationship between an individual symptom and leukemia class. The domain of this property is symptom and leukemia class is its range. It has an inverse property of hasSymptom.

isTreatmentof: This property is used to provide relationship among Treatment and Leukemia class. The domain of this property is Treatment class, the range is Leukemia, and his inverse property is hasTreatment.

isTypeof: This property is used to provide relationship among Type and Leukemia class. For instance, "acute Lymphocytic leukemia" is a type of "Leukemia". The domain of this property is Typeclass and the range is Leukemia. It also has an inverse property of hasType.

hasWhite_Blood_test: This property is used to provide the relationship between the patient and the blood test class. For instance, a patient "Melaku" has a "white blood" test in the laboratory. The domain of this property is patient class and the range is blood test.

Data Property

Data property is another property of ontology, which used to describe the relationship between individual class within a domain and its data value. In other word, it is a property with a data type including decimal, long, float, boolean, string, language, name, integer, date, date Time, etc. in their range. Thus, it play a great role while describing individuals features and allowing data value to be saved. The data property used in this study are presented in Figure4. hasPlace_of_work, hasTelephone, hasGender, hasAge are Data property used for providing extra information to individual of patient class in order to differentiate them.

hasHematocrit_value, hasRed_Blood_test_value, hasWhite_Blood_test_value,

hasPlatelets_test_value, hasHomoglobin_test_value are used to store data about tested blood of patient. Those data property are very important in identifying the sickness and normality of blood, since the main cause of Leukemia are associated with the sickness of blood.

Moreover, hasDuration data property is used to store data about duration of the leukemia disease until its progress. This property is important in classifying the type of leukemia.

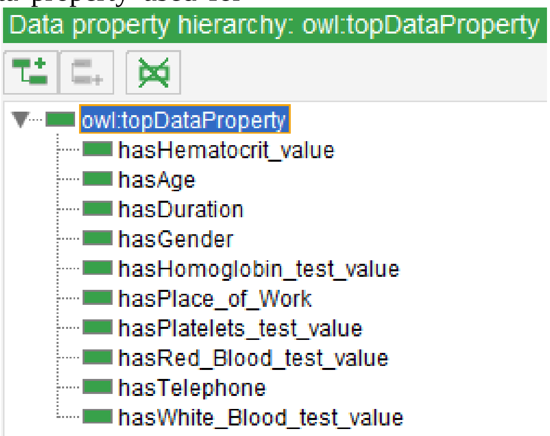

Figure4. *Data property hierarchy of leukemia ontology*

Individuals

Individual is a specific instance of the class or object, which represent the ground or atomic level of the ontology knowledge base. As has been mentioned, this work is focused on the diagnosis of leukemia into its type and sharing knowledge for the user about the Treatment of Leukemia. Regarding Type of Leukemia, some of the individual stored are acute lymphocytic leukemia, acute malignant leukemia, chronic lymphocytic leukemia, and chronic malignant leukemia. Some of the individuals stored regarding symptom class are Vomit, headache, Anorexia, enlarged lymph node , infection, enlarged liver or spleen, Anemia, asthenia, sweating, bleeding, fatigue, weight loss, fever ,confusion ,shortness of breath. Similarly, about treatment some of the individuals stored are chemotherapy, radiation therapy, biological therapy, targeted therapy, stem cell transplant, surgical removal of the spleen and Supportive treatments.

Beside, about a risk factor, some of the individuals stored are tobacco, cigarette, benzene, atomic bomb, atomic weapons plant, nuclear reactor accident, Agent Orange, Down syndrome, Fanconi anemia, ataxia-telangiectasia, Bloom syndrome, parent with CLL.

For blood test class the testing value individuals a restored for each blood cell type including red blood cell, white blood cell, platelets, hemoglobin and hematocrit.

Rule Based Engine

The developed ontology provide a standardized vocabulary, and represent the main source of computable leukemia domain knowledge that used by the system for diagnosis and treatment of disease.

As mentioned in section 3.2 data were collected from different source regarding to leukemia and based on such information the author developed a set of rule. The rule were developed by using a Semantic Web Rule Language (SWRL) that allow representing the acquired expert knowledge [1]. In the below some of the general inferential rule that lead to the diagnosis and treatment of a disease are mentioned.

- **Rule 1**. If a patient has symptom of ALL; and has red blood test value 4.2-6.1; and has white blood test value 4500-11000; and has HCT value32-52 % and has PLT value 150000-400000; and has Hemoglobin value9.5-18; and has risk factor; and has sickness time sudden. It implies the patient has ALL
- **Rule 2.** If a patient has symptom of CLL; and has red blood test value 4.2-6.1; and has white blood test value 4500-11000; and has HCT value32-52 % and has PLT value 150000-400000; and has Hemoglobin value9.5-18; and has risk factor; and has sickness time long. It implies the patient has CLL
- **Rule 3.** If a patient has symptom of AML; and has red blood test value 4.2-6.1; and has white blood test value 4500-11000; and has HCT value32-52 % and has PLT value 150000-400000; and has Hemoglobin value 9.5-18; and has risk factor; and has sickness time sudden. It implies the patient has AML
- **Rule 4.** If a patient has symptom of CML; and has red blood test value 4.2-6.1; and has white blood test value 4500-11000; and has HCT value32-52 % and has PLT value 150000-400000; and has Hemoglobin value9.5-18; and has risk factor; and has sickness time sudden. It implies the patient has CML
- **Rule 5.** If a patient has type ALL. Then the patient has treatment Chemotherapy, Targeted therapy, Radiation therapy, Bone marrow transplant, Clinical trials, etc.
- **Rule 6.** If a patient has type CLL. Then the patient has treatment Chemotherapy, Monoclonal Antibodies, Targeted Therapy Drugs, Supportive Care, Stem Cell Transplant etc.
- **Rule 7.** If a patient has type AML. Then the patient has treatment Chemotherapy, Targeted Therapy Drugs, Non-Chemo Drugs, Surgery, Radiation Therapy, Stem Cell Transplant, etc.
- **Rule 8.** If a patient has type CML. Then the patient has treatment Targeted Therapies, Interferon Therapy, Chemotherapy, Radiation Therapy, Surgery, Stem Cell Transplant, etc.

Rule engine or reasoner is applied on the developed rule to infer a diagnosis and treatment of leukemia from a set of asserted fact about the disease. To infer the diagnosis and treatment of disease the engine uses the object property that refers the diagnosis and treatment of leukemia.

Diagnosis and Treatment

After rule is developed, the next step is diagnosing and recommending the possible treating option. In this step, at first module the system accepts the symptoms, blood test value from user and as well as ask the user different question about risk factor of the diseases to detect whether it's a leukemia or not. If it is a leukemia the system, classify the type of leukemia and recommends the treatment decisions.

Evaluation of the Proposed Model

In order to, fully illustrate the validity of the model accuracy, precision, recall and F-measure method are used for evaluation of the effective and efficiency of the system. Accuracy, precision, recall, and F-measure of the system can be calculated as below shown formula:

$$accuracy = \frac{TP + TN}{TP + TN + FP + FN}$$

$$precison = \frac{TP}{TP + FP}$$

$$\mathrm{recall} = \frac{\mathrm{TP}}{\mathrm{TP} + \mathrm{FN}}$$

$$\mathrm{F-measure} = \frac{2 * \mathrm{precision} * \mathrm{recall}}{\mathrm{Precision} + \mathrm{recall}}$$

The author further validated the effectiveness and efficiency of the proposed model. Based on the performed evaluation the proposed ontology-based model achieved 95% precision, 94.8% recall, 94.7% F1-score and 94.1% accuracy. It is therefore a promising result relative to previous study such as[11][12][13]. In addition to diagnosis, this study recommend the possible treatment option unlike the earlier study described in[14].

Conclusion and Future Work

In this study, the author reviewed different related work and comprehended the concept, feature and characteristics of leukemia. In addition, the author developed ontology for common knowledge representation and sharing purpose. Their also performed performance evaluation of the proposed ontology based leukemia diagnosis and treatment system. Furthermore, the proposed system, ontology based leukemia diagnosis and treatment system achieved 94.1% accuracy. There are also other approaches that are different from ontology that can be applied for similar problem. Therefore, it would be interesting if experts and researchers can develop the same title for the language in rule based, machine learning and hybrid approach to compare the result with the performance of this study. Lack of standardized patient data is one of the limitations in this study. However, preparing standardized dataset especially for Ethiopia for the further study would be interesting.

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