Versatility of fuzzy logic in chronic diseases: A review

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- Back-propagation
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- Fuzzy logic
- Neural networks

**Abstract**

The review aims at providing current state of evidence in the field of medicine with fuzzy logic for diagnosing diseases. Literature reveals that fuzzy logic has been used effectively in medicine. Different types of methodologies have been applied to diagnose the diseases based on symptoms, historical and clinical data of an individual. Increase in the number of recent applications of medicine with fuzzy logic is an indication of growing popularity of fuzzy systems. Fuzzy intelligent systems developed during 2007–2018 have been studied to explore various techniques applied for disease prediction. In the traditional approach, a physician is required to diagnose disease based on historical and clinical data but the intelligent system will help physicians as well as individuals to detect disease at any location of the world. The studies of various fuzzy logic systems and classified fuzzy logic applications in the field of diabetes, iris, heart, breast cancer, dental, cholera, brain tumor, liver, asthma, viral, Parkinson, lung, kidney, huntington and chest diseases have been included in the review. This study indicates all the benefits of the fuzzy logic to the society and direction to tackle the diseases that still need software for their accurate detection. Further, different case studies for celiac disease have been reported earlier. The current review aims at exploring the future direction for fuzzy methodologies and domain on celiac disease.

**Introduction**

Due to limited knowledge among all diseases and its subparts, it is very difficult for each and every physician to diagnose the disease with accuracy. Fuzzy logic is a growing area through which we can generate such type of hybrid systems for mankind for disease detection with prediction [1,2]. Due to similar symptoms, among multiple diseases, it’s very complex to diagnose the disease without laboratory tests. But from the fuzzy software’s, similar types of expert systems have been developed in almost every field of medicine [3]. The term fuzzy logic relates better approach to probability which produces an outcome based on true or false with an appropriate degree of fuzzification. To perform fuzzification of the data, we need membership function to convert out dataset from crisp to fuzzy set for evaluation. Earlier crisp sets were used for findings a particular disease but with the advancement of fuzzy logic, we can expand our findings with the fuzzy set by applying different types of membership functions like triangular and trapezoidal commonly in each and every application [4–7]. The evaluation process is based on fuzzy if-then rules for the final outcome depends upon input and output parameters refereed as an inference engine. The process of defuzzification is to convert the outcome in the same way as given in the form of input by implementing different methods of defuzzification [7]. Center of average or centroid method is commonly applicable in every application. Fuzzy logic has been implemented in almost all the medical problems but still, there are few diseases that still need better implementation through fuzzy logic [8,9]. Fuzzy logic supposed to be one of the beneficial tools to mimic the human thinking with approximate reasoning which is entirely gratified for fuzzy probability. Due to incomplete erudition was given by patients, incorrect laboratory tests, unlabeled sampling; the accuracy of tools commences to design fuzzy systems in healthcare examinations. Due to similar symptoms, among multiple diseases, it’s very perplexing to diagnose the disease without laboratory tests. There is an emergent need to be focused on those dilemmas that yet needs appropriate software to diagnose diseases without laboratory outcome. A lot of research has been accomplished on multiple chronic disorders with fuzzy logic but no research work has been proclaimed yet on celiac disease with fuzzy logic. There are some barriers like the cost of clinical testing, ambiguity among multiple testing techniques and time-consuming approach but with the help of the celiac fuzzy system, individuals can diagnose celiac disease with probability level based on symptoms. One of the rapidly growing problems throughout the world is Celiac disease which affects almost all the countries at any age. It is a type of chronic disorder which generate mucosa problem in the small intestine when any individual will take gluten in the diet in the form of wheat, rye and barley [10]. Lot of researchers have done their work on the basis of symptoms, diet, age,
breastfeeding, introduction of gluten at which age but the only recommendation is gluten-free diet to tackle this serious disease. It is a type of auto-immune disorder that present in those individuals carrying HLA DQ2/DQ8 with or without symptoms [11]. The major symptoms present in celiac patients as abdominal pain, height, weight, abdominal bloating and other auto-associated problems. This disease can be diagnosed with various markers like tTG, IgA, biopsy as well as with genetic testing [12,13]. Because of the similarity among symptoms with other diseases it’s very complex for any physician to diagnose celiac disease. So, the emergent needs to develop such type of system to detect celiac disease to the society with accuracy. Fuzzy logic has been implemented in nearly all the medical problems but still, there are rare diseases like the celiac disease that still require better implementation through fuzzy logic.

Further Section “Literature review on chronic diseases with fuzzy logic” of the paper presents different surveys taken in the medical field with diseases, author/years, methodologies, tool used and findings with fuzzy logic. Section “Background study on celiac disease” covers case studies conducted in different countries on celiac disease. Finally, Section “Concluding remarks” presents concluding remarks with fuzzy logic in medical applications.

Literature review on chronic diseases with fuzzy logic

There are enormous numbers of software’s available in the market to diagnose diseases according to symptoms. Fuzzy logic has tried to solve so many diseases due to fuzzy sets with fuzzy if-then rules. Lot of applications can be found in several medical problems. Some of the important and useful contributions by different researchers have been discussed. Polat K in 2007, worked on diagnosis diabetes disease by using adaptive neuro-fuzzy approach. Diabetes is a type of disease based on high sugar in the blood affecting blood cells. Neuro-Fuzzy approach was implemented in MATLAB with eight distinct features and further reduced to four input parameters. The system showed 85% sensitivity and 92% specificity with system accuracy of 89.47%. The selected individuals that have been used in diagnosing diabetes based on Pima-India women retrieved from UCI repository. The study was processed on 768 individuals among them 268 diabetes patients were recognized. The final testing was done through PCA with ANFIS having RMSE of just 0.262 [14]. After a couple of years, Moein S et al. proposed a model on Iris disease by using the back-propagation algorithm in 2009. Iris is a type of disease as immune reconstitution caused by bacteria. The implementation was done with four input and three output variables in NETLAB and fuzzy-logic toolbox. 150 patients were diagnosed in this iris study with classification. K-folding approach was applied to get better accuracy and performance as the system outcome was 100% accurate and performance turned to be 80% [15]. In 2011, Soni J et al. developed heart disease predicting system by using Decision Tree, Naïve Bayes and Nearest Neighborhood algorithm. It is a type of cardiovascular disease related to damaged vessels and blood cells. This system was based on fifteen attributes as inputs for prediction. Tangara tool has been used for the implementation of heart disease prediction. Decision tree proved to be the best algorithm among all to show 89% accuracy with IHDDS software and Naïve Bayes considered to best for speedy detection taking 609 ms for prediction of heart disease. The system was compared with the results of WHO organisation for better accuracy [16]. In the same year, Adeli and Zarabadipour proposed a model on breast cancer and hepatitis using genetic and other algorithms. It is the deadliest type of cancer generated in females affecting lungs which will cause difficult to breathe and symptoms in the form of a cough. His study based on Back-Propagation and Feed-Forward algorithm to meet the optimum results. The study was conducted in Chennai on 271 individuals based on a questionnaire approach. The selection of symptoms and their classification was better judged after adding 50 healthy individuals among 271 patients. It is a type of hybrid system which can predict asthma and lung cancer along with tuberculosis. The analysis of the system was done through SPSS.
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<td>MATLAB</td>
<td>89.47% Accuracy, Sensitivity 85%, Specificity 92% and RMSE 0.262</td>
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<td>Iris Disease</td>
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<td>Breast Cancer</td>
<td>Adeli M and Zarabadipour H (2013) [17]</td>
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<td>Parkinson Disease</td>
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<tr>
<td>Huntington Disease</td>
<td>Lauritisc A (2018) [28]</td>
<td>Feed Forward Back Propagation NN, RNN, GRNN with 3 linguistic and 1 output variables, 27 rules</td>
<td>MATLAB Neural Network and Fuzzy Logic Toolbox</td>
<td>FFBPN best among all with 95% Confidence Interval and 0.0809 MSE</td>
</tr>
<tr>
<td>Chest Disease</td>
<td>Kayali I (2018) [29]</td>
<td>Back-Propagation, Forward and Backward Chaining</td>
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</tr>
</tbody>
</table>
software which showed 95% accurate in nature. The sensitivity of the system is 100% with 75% specificity [26]. Recently in 2018, Zarandi focused on chronic kidney disease based on fuzzy-logic and adaptive neuro-fuzzy technique. It is a type of long-lasting disease in which the kidney did not perform own work in the body as the need for filtration from eatable products. Sometimes it does not have any symptoms and can be diagnosed only with the blood test and can be resolved by removing the kidney from the body. The methodology was opted using Mamdani approach with nine input and one output parameter. Fuzzy rules were developed according to the historical record of existing patients. The whole study conducted in Iran with 400 samples of individuals to be tested with kidney disease or not. The up-gradation of the system was done by the Gaussian function. The accuracy of the system was 80% evaluated through fuzzy rules and rule viewer in MATLAB [27]. The brief summary of existing studies represented as shown in Table 1:

Lauraitis in 2018 performed analysis on Huntington disease using neural network and fuzzy logic toolbox in MATLAB. This disease related to age in which affected individual having clear symptoms of mis-movements, emotional, loss of thinking etc. due to damage nerve cells in the brain. Various types of algorithms have been applied to get the best results for the system like feed-forward, back-propagation, RNN and GRNN algorithms. Only 27 rules have been developed to design the system with three input and one output variable. The study consists of 20 individuals for testing the system among random selection from 3032 health records. The system concluded with the best outcome using a feed-forward approach having RMSE less than 1% with optimum prediction [28]. From the viewpoint of Kayali in 2018 designed chest disease software using data miner tool with neural-network and fuzzy-logic. This disease totally related to lung disease and affect chest of an individual in the way of the airway. The approach used for the prediction based on forward and backward chaining. With the help of this expert system, final testing can be done in a more accurate way than existing laboratory approach [29]. This paper depicts by just putting one contribution to one disease but actually, so many studies have been done by multiple authors to mankind. Because of accuracy and flexibility through fuzzy if-then rules, we can easily manage by predicting certain diseases by getting necessary information through existing algorithms and clinical background. Fuzzy logic software will help physicians to do judgment in a better way along with existing knowledge of their own domain. Idowu and his team members have implemented a fuzzy model to prognosticate health diseases based on environmental problems. The study was conveyed in Nigeria with a thorough discussion to examine diseases that constantly transpired due to environmental factors [30]. Chowdhury proposed a model to distinguish colorectal cancer using fuzzy logic. The detection was based on fuzzy if-then rules for evaluation to produce an issue with multiple attributes [31]. Manogaran developed a model to diagnose the heart disease neuro-fuzzy system in 2018 with learning modules of the neural network. Learning has been produced in the form of a supervised approach in which the output of an application with an outcome has previously been perceived. The integration of neural and fuzzy logic leads to the concept of neuro-fuzzy to tackle the heart diagnosis system in a better way [32]. The similar representation was performed by Nilashi et al. in 2018 to diagnose hepatitis disease with neuro-fuzzy technique. The combination of neuro-fuzzy illustrates the system with adaptive learning during the allocation of input parameters using the neural network and computing the evaluation of the system with fuzzy logic [33]. Melin in 2018 classified the risk of hypertension and blood pressure problem with the hybrid model approach using the neural network and fuzzy logic. Such type of hybrid system is essential to solve the quandaries with the latest techniques of learning intermixed with fuzzy logic [34]. Paul et al. in 2018 defined a model to classify the risk level of heart disease with a fuzzy rule based system. Adaptive weights have been implemented by researchers to formulate the rules of the inference engine. The result of this system is to recognize the risk level of heart disease [35]. Soltani et al molded on glaucoma diagnosis using a fuzzy logic approach. The implementation has been done with image processing algorithms to diagnose the disease at the earliest. This type of expert system was based on image processing and fuzzy logic with Mamdani technique in 2018 [36]. Gupta embodied natural language with fuzzy logic to deal with real-life problems in 2018. The natural language with the crisp to fuzzy inputs on the basis of synonyms has been produced in the review. This kind of system will be profitable for society [37].

The above Fig. 1 clearly represents several studies performed along with year information. The contribution did by various researchers to the society by using fuzzy logic from the last decade need the further extension in upcoming years. Fuzzy Logic can be implemented on celiac disease with similar methodologies implemented in MATLAB, Data Miner and other tools. 

**Background study on celiac disease**

Celiac disease is a type of auto-immune disorder disease affecting intestine after intake of gluten in the body. This disease is rapidly growing through the world due to gluten as commonly resides in barley, rye and wheat which act as a toxic agent for affecting small intestine in the body [13]. This study will focus on getting prevalence at different locations with a clinical approach in the last 15 years. In 2003, Maki et al. performed a case study on children’s in Finland. His team collected serum samples of 3654 students in 1994 and tested with tTG and biopsy in 2001. The outcomes were 50 individuals IgA and tTG positive, 10 positive HLA patients and declared 27 celiac patients with biopsy. The prevalence rate considered to be 1:99 in Finland children’s. The summary concluded diagnosing celiac disease with genetic testing as HLA DQ2/DQ8 positive aspect [38]. Another similar approach was used by Stone et al. on infants in Australia for identification of celiac disease in 2005, 119 selected individuals were tested with IgA-EMA and tTG, among them 74 celiac patients were diagnosed and proved tTG as the best method for disease detection at any age. It also focused on IgA-EMA and IgA-AGA for screening more and less than two years respectively to identify the age factor in celiac disease. The mean age for recognition considered to be 5.5 years with mostly female ratio [39]. In 2006, Gautam et al. focused on the probability of celiac disease in siblings of existing patients. It was considered to be 20–30% chances of occurrence the same event again to first or second degree relative of the same disease. 74 siblings were tested for celiac disease with tTG and biopsy procedure with an outcome of 13 celiac patients. Height and weight were observed to be major attention as compared to the healthy individual for differentiation among them [40]. In Ludhiana, Sood et al. performed celiac diagnosis procedure on 4347 school going children’s in 2006 and witness first case study on celiac disease in Punjab. The methodology opted was based on a brief questionnaire regarding the

**Fig. 1. Summary of different diseases.**

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be much higher as compared to the male ratio in celiac patients. Some disease in Delhi, India. A group of more than 10,000 populations were clinical testing was done by Makharia et al. in 2011, to diagnose celiac gluten-free products and further tested after 6 months and considered celiac patients in future. Celiac disease patients prefer to deal with Mass Index clearly differentiates from normal individuals to diagnose visualization as height, weight lower than healthy individuals. Body

1998–99. 2690 children's involved in this study and performed tTG of celiac disease on school going children in Hungary who born in 1998 and 99, with 2690 children's participated in the study

Makharia et al. (2011) Diagnosis celiac disease in Delhi, India. 10,488 populations were screened via symptoms

Digiacomo et al. (2013) The case study on 13 different countries that are the Mediterranean methodology

Aronsson et al. performed diagnosis on 6672 individuals in different Sweden, US, Germany, and Florida

Ramakrishna et al. (2015) Study on different parts of India with a total of approximate 24,000 adults. The northern region with 6207, north eastern region with 8149, and south region belongs to 8973 screened for celiac disease with tTG and Biopsy

Senapati et al. (2016) The case study on 1402 celiac patients, among them 531 as children and 871 as adults. An analysis was performed through Illumina immunochip methodology

Smarrao et al. (2017) The case study on 13 different countries that are the Mediterranean participated to identify celiac patients with 1974 patients

50 positive IgA and tTG were suspected; 27 patients as the celiac disease with biopsy, prevalence of the celiac disease was 1 in 99 students

74 patients as celiac disease; IgA-EMA for over two years and IgA-AGA for less than two years for testing celiac disease, tTG considered being more specific than EMA for screening

13 celiac patients with biopsy. The major symptom observed as height and weight among them


37 children confirmed as the celiac disease with endoscopy. Mean weight, height with celiac patients were lower values as compared to healthy children’s

The final screening was done via biopsy and concluded with 31 celiac patients and reported as 1:96 as celiac

49 susceptible cases occurred as celiac disease mostly as females. 307 celiac patients and observation based on intake of the age of gluten and breastfeeding

76, 70 and 12 susceptible cases were determined and conclusion with wheat as a toxic factor in northern part of India on daily basis approximately consuming 450 gm as compared with 37 gm and 25 gm, in northeast and south region respectively

35 as an adult celiac disease with the mostly female celiac patient ratio, HLA DQ2/DQ8, as exists in all patients

568 celiac patients with marsh classifications with the largest case study throughout the world.

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<td>Sood et al. (2006) [41]</td>
<td>The case study on 4347 school going children in Ludhiana, Punjab; age 3–17 years with Questionnaire approach</td>
<td>14 children's carrying celiac disease and prevalence 1:310 in Ludhiana, Punjab</td>
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<td>Korponay-Szabo et al. (2007) [42]</td>
<td>The case study in Hungary on school children's born in between 1998 and 99, with 2690 children's participated in the study</td>
<td>37 children confirmed as the celiac disease with endoscopy. Mean weight, height with celiac patients were lower values as compared to healthy children’s</td>
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<td>Digiacomo et al. (2013) [44]</td>
<td>7762 individuals in NHANES survey, in 2009–10, Chi-square and ANOVA test was performed for screening evaluation</td>
<td>49 susceptible cases occurred as celiac disease mostly as females.</td>
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- Clinical historical approach of an individual. It was considered to be 14 celiac disease patients with a prevalence of 1:310 in Ludhiana, Punjab [41]. In view of Korponay-Szabo et al. in 2007 presented the diagnosis of celiac disease on school going children in Hungary who born in 1998–99. 2690 children’s involved in this study and performed tTG with endoscopy which confirmed 37 celiac patients. The evaluation was done by district nurses for computing height and weight among them when kids switch to studies at the age of 6. The outcome describes clear visualization as height, weight lower than healthy individuals. Body Mass Index clearly differentiates from normal individuals to diagnose celiac patients in future. Celiac disease patients prefer to deal with gluten-free products and further tested after 6 months and considered better mucosa visuals through endoscopy [42]. The symptomatic and clinical testing was done by Makharia et al. in 2011, to diagnose celiac disease in Delhi, India. A group of more than 10,000 populations were diagnosed on the basis of symptoms with questionnaire approach by door to door visit in rural and urban locations. Female ratio observed to be much higher as compared to the male ratio in celiac patients. Some of the individuals were further diagnosed based on tTG and final screening via biopsy. The final picture was 31 celiac patients and prevalence factor was 1:96 in Delhi [43]. A few years later, Digiacomo et al. in 2013 performed NHANES survey on 7762 individuals. The outcome was 49 celiac patients resulting mostly as females. This study also focused on gluten sensitivity among healthy individuals those having symptoms but did not have celiac disease. The methodology based on chi-square and ANOVA test to distinguish multi-variables [44]. In the next year; Aronsson et al. performed diagnosis on 6672 individuals in different countries. 307 celiac patients were screened as celiac patients based on their working as age and breastfeeding considered being a crucial component. The study was applied in Finland, US, Germany, Sweden, Florida etc. and predicted Sweden children's having more chance of celiac disease due to early intake of gluten. Authors analysis based on breastfeeding, age at gluten introduction and other features recommended to individuals for less risk in future for celiac disease [45]. A few years later, Digiacomo et al. in 2013 performed NHANES survey on 7762 individuals. The outcome was 49 celiac patients resulting mostly as females. This study also focused on gluten sensitivity among healthy individuals those having symptoms but did not have celiac disease. The methodology based on chi-square and ANOVA test to distinguish multi-variables [44]. In the next year; Aronsson et al. performed diagnosis on 6672 individuals in different countries. 307 celiac patients were screened as celiac patients based on their working as age and breastfeeding considered being a crucial component. The study was applied in Finland, US, Germany, Sweden, Florida etc. and predicted Sweden children's having more chance of celiac disease due to early intake of gluten. Authors analysis based on breastfeeding, age at gluten introduction and other features recommended to individuals for less risk in future for celiac disease [45]. Another comparative study was done by Ramakrishna et al. in 2015 among north, south and north-east region in India on 24,000 adults for celiac disease. 6207, 8973 and 8149 individuals were screened in north, south and north-east region respectively for celiac disease. The methodology opted as tTG test to screen the celiac patients with final conclusion via biopsy. The outcome was based on intake of wheat as a common diet in the northern region with the observation of 450 gm approximately per day as compared to less than 40 gm outside the northern region. 76 susceptible cases were found in the northern region.
as compared to 70 in the northeast with just 12 cases in south India [46]. A brief summary of various types of case-studies that have been performed on celiac disease represented in Table 2.

In the next year, Senapati et al. analyzed celiac disease with Immunochip methodology on 531 children’s and 871 adults. Their findings concluded 35 celiac patients with female factor remain high as compared to male ratio. HLA DQ2/DQ8 proved to be present in all celiac patients [47]. Smarrazzo et al. in 2017; performed the study in thirteen different Mediterranean countries to diagnose celiac patients. The entire analysis based on the symptomatic study with age less than 18 years. 1974 individuals were tested and 568 proved to be celiac susceptible to marsh classification and distributed country wise ratio with consideration of largest case study on celiac disease throughout the world [48].

The above Fig. 2 represents different case-studies at every corner of the world to diagnose celiac patients with serological markers. The study based on students, infants, children’s, siblings along with selected age group to find out the prevalence of celiac disease. This study can be further expanded with or without historical and clinical data by using fuzzy logic in future in the form of a hybrid expert system.

Concluding remarks

As complex artificial intelligence systems associated with human reasoning, fuzzy logic enhances the most widespread among all in the last decade due to its accuracy in every province. It also conferred the platform opted and their findings managed by various researchers with varied methodologies to coincide the optimum results. The basic objective is to be accomplished on those diseases that yet require software to detect without clinical output. Due to the unavailability of the physician at each location; these types of expert systems will assist individuals to predict the disease. A lot of research has been succeeded in every corner on medical applications but obstacles like neurological, celiac, cervical-cancer, gluten sensitivity demand an intelligent system to develop in future with fuzzy rules because apparent to tackle uncertainty, ambiguity with incomplete information. As fuzzy logic operated on various chronic disorders but still there is a notch to tackle celiac disease with the symptomatic study. The consequences of recently published articles in fuzzy logic on chronic disorders did not show any research on celiac disease with fuzzy logic. Celiac disease can be diagnosed with accessible testing techniques like IgA, tTG, biopsy, genetic testing etc., but it can be recognized on the evidence of individual symptoms. There is a foresight that if the celiac fuzzy system will be executed in the coming years, it will serve the citizenry in the form of diminished testing cost and pain while performing the biopsy. The selection of symptoms on celiac disease will be determined with fitting input and output parameters through which the creative expert system should be stipulated. Another future criterion is to deal with several drugs that should be prescribed subsequent analysis of a disease, so that instant benefit to an individual. So, it is presumed that fuzzy logic will alter existing software’s in a better way and progress towards celiac disease in the coming future.

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Conflicts of Interest

No conflict of Interest was reported by the authors.

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Appendix A. Supplementary data

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References
