Int J Infect. 2019 July; 6(3):e92356. doi: 10.5812/iji.92356.

Published online 2019 July 31. **Research Article**

Diagnostic Differentiation of Crimean Congo Hemorrhagic Fever, Influenza and Bacterial Meningitis by Classic and Fuzzy Mathematics

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Received 2019 April 16; **Revised** 2019 July 19; **Accepted** 2019 July 24.

Abstract

Background: A correct diagnosis of a disease among several diseases with the same clinical symptoms is very important and is a difficult task in medical science. Misdiagnosis of these diseases in the short term causes very high and serious damage to the health of patients and usually results in loss of golden time.
Objectives: In this paper, our purpose is to achieve the best conclusion, which contributes to the diagnosis of the critical illness without losing the golden opportunity based on clinical data and using mathematical models, especially fuzzy mathematics.
Methods: The data regarding patient's signs and symptoms were collected in the hospitals. We attained the best choice of diseases among the considered options of diseases by using basic fuzzy rules, fuzzy control techniques, fuzzy mathematics and fuzzy systems. To write the basic fuzzy rules, the information that we used was adopted by experts in infectious diseases or data records of patients who reached a definite diagnosis of disease by various tests. Then, by using these rules, the system of mathematical equations was formed. By solving this system, coefficients of a linear equation were estimated witch its values according to the clinical signs of a patient indicates the probability that the patient will be infected with that disease. In this process, the number of patients studied is n not effective. But the more patients are studied, the more accurately the coefficients of the diagnosis equation are obtained.
Results: The symptoms of some patients whose disease have been definitely diagnosed were used as inputs of the system of our equations and it was observed that the system's outputs approximately coincide the exact diagnosis of the disease, which indicates that the equations obtained for the diagnosis of diseases are acceptable.
Conclusions: The findings of this study can help to correctly diagnose the disease without losing golden opportunities. We hope that using the results of this research, the error in the initial diagnosis of diseases is significantly reduced.

Keywords: Fuzzy Logic, Mathematics, Fuzzy Control, Diagnosis, Differential Diagnosis, Crimean-Congo Hemorrhagic Fever (CCHF), Bacterial Meningitis, Severe Influenza

1. Background

The problems of proper disease diagnosis among patients with almost identical symptoms are complex in applied medicine (1). Medical mistakes are common and may be accompanied by irreversible and ominous consequences (2). This is challenging, especially when there is a great number of disease diagnosis and numerous types of clinical symptoms in terms of quality, quantity, and number and these symptoms are almost identical in propounded diseases. Most general practitioners and some specialists and experienced physicians have trouble drawing the correct conclusions from assumptions that are often ambiguous (3-5). In many cases, doctors do not have much time to diagnose some diseases and the consequences of an incorrect diagnosis may be irreversible. Moreover, given that a physician needs the patient's symptoms and experience to diagnose diseases, even a qualified physician may have a wrong initial diagnosis at the time of examination and does not consider some diseases. Even if all propounded diseases have been considered, a physician may be wrong because of almost identical symptoms in some diseases. The fuzzy method is one of the most useful ways to reduce ambiguity in diagnostic practices (6).

In this article, we intend to design a fuzzy system for optimal diagnosis of a disease among several diagnoses based on the basic rules, which are obtained by professionals and patient's records that was collected from the medical records related to the department of Mashhad's Imam Reza Hospital and Birjand's Valiasr and Imam Reza hospitals (7-9). In this study, we diagnosed the best option of an infectious disease among some types of infectious ones with almost identical clinical symptoms such as fever, headache, nausea, heart rate, blood pressure, and other similar symptoms. In order to achieve the related basic fuzzy rules, the information and symptoms of diseases were obtained by various methods. Some parts of existent basic fuzzy rules for diseases was developed by infectious disease specialist or found in scientific books and medical journals. Another part of fuzzy rules, some of them are currently unavailable, is obtained by reviewing the patient's records. To this purpose, indications and existent data in records of hospitalized patients were studied and basic fuzzy rules for the propounded diseases were obtained by mathematical and control methods.

In this paper, three particular types of infectious diseases have been studied that have almost identical clinical symptoms: Crimean Congo hemorrhagic fever (CCHF), bacterial meningitis and severe flu. After collecting the basic rules (10), we designed valid outputs of the system by the new entries, which were proposed as IF-THEN in the fuzzy rules (7-9, 11). Using the designed system, we determined the priority of system outputs, which were the diseases and the probability of the patient's infection by the defined diseases, according to the priority of each disease. Thus, using fuzzy control, we determined which disease possess the first priority and which are the subsequent ones. In the designed system, there is an equation corresponding to every disease that the solution of which is the probability of having that disease for a patient. Then we tested the designed system with the aid of patients' data. If the non-fuzzy operations cause relatively good results, we conclude that the system is relatively reliable; otherwise, the accuracy of the objective functions is increased until the system becomes relatively optimal (8, 11).

2. Objectives

The findings of this study that are based on medical data and mathematical models, especially fuzzy mathematics, can help to correctly diagnose the disease without losing golden opportunities (3, 12-15). Therefore, we hope that using the results of this research, the error in the initial diagnosis of diseases is significantly reduced. It should be noted that propounded initial diagnosis in this article is done even before any type of time-consuming tests and helps the physician to choose the correct diagnosis and treatment for the diseases without losing the golden times. So with this initial diagnosis and the priority of the diagnosis that is achieved using fuzzy mathematics, the physician begins the treatment and medical procedures and in the later stages he determines the diagnosis of disease by specialized tests and examinations, thus time is not wasted for the trial and error of checking different diseases (11, 16). Finally, we will try to design applied software that provides quick and easy use of the obtained results in this research. This software provides the doctor with a list of probable diseases and determines each priority. In this way, the risk of neglecting some diseases by doctors is reduced to almost zero so that even a general physician would be able to diagnose specific diseases.

3. Methods

3.1. Making Algebraic Equations for Diseases Diagnosis

In this research, we proceeded to study three infectious diseases: CCHF, bacterial meningitis, severe influenza, which have almost the same symptoms. This section aims to obtain equations for diagnosing these three diseases and prioritize their diagnosis. To this purpose, the health records of the patients who were certainly afflicted with one of these three diseases were collected. In this regard, 66 health records for CCHF, 54 health records for bacterial meningitis, and 61 health records for severe Influenza were studied and the related symptoms were extracted. Some symptoms were measured quantitatively such as fever and the others were descriptive, such as sweating, body pain, bleeding, etc. The values of 0, 0.25, 0.5, 0.75, and 1 were calculated for slight, mild, severe, and very severe based on the considered symptom severity, respectively. Then regarding the general form of these diseases equations, the related equation for each health record was written and the best correspondent equation to each set of equations was fitted.

The discussed system in this article proceeds to diagnose the best disease feature among several disease features with almost the same symptoms. This system includes 16 inputs and 3 outputs. The system inputs are x_1, x_2, ..., x_{16} that each value of each shows one of the symptoms resulted from clinical examinations. For example, x_1 is the variable associated with the patient's fever, x_2 is the variable for the headache and other variables are related to one of the 16 symptoms discussed. The three outputs y_1, y_2, y_3 are related to the diagnosis of CCHF, bacterial meningitis, and severe influenza, respectively and their corresponding equations are as follows:

$$\begin{aligned} y_1 &= a_1x_1 + a_2x_2 + a_3x_3 + \cdots + a_{16}x_{16} \\ y_2 &= b_1x_1 + b_2x_2 + b_3x_3 + \cdots + b_{16}x_{16} \\ y_3 &= c_1x_1 + c_2x_2 + c_3x_3 + \cdots + c_{16}x_{16} \end{aligned} \quad (1)$$

The function y_1 is written for 66 patients with certain diagnosis of CCHF, each one is supposed to have a value of 10 for the function y_1:

$$\begin{aligned} y_1^1 &= 0.5a_1 + 0.5a_2 + 0.75a_4 + 0.25a_5 + 0.25a_6 \\ &\quad + 0.75a_7 + 0.5a_9 + 0.5a_{10} + a_{12} + 0.5a_{14} + a_{16} \\ &= 10 \\ y_1^2 &= 0.25a_3 + 0.5a_4 + 0.5a_5 + 0.75a_7 + 0.25a_8 \\ &\quad + 0.75a_9 + 0.75a_{10} + 0.5a_{12} + 0.25a_{14} + 0.5a_{16} \\ &= 10 \\ &\dots \\ y_1^{66} &= 0.5a_1 + 0.25a_2 + 0.25a_3 + a_4 + 0.75a_5 + 0.25a_6 \\ &\quad + 0.75a_7 + 0.25a_8 + a_9 + a_{10} + 0.75a_{12} + 0.5a_{13} \\ &\quad + 0.5a_{14} + 0.5a_{15} + a_{16} \\ &= 10 \end{aligned} \quad (2)$$

There is usually no solution for a system of 66 equations with 16 unknowns. In order to show this, we solve the system, including the first 16 equations from the system (Equation 2). Considering that this answer does not apply to the 17th, 18th, 19th, and 20th equations of the system (Equation 2), we conclude that this system of equations has no solution. Therefore, we find the best approximation for the unknowns a_1 through a_{16} that are the best coefficients in the function y_1. To do this, we define the function f of 66 variables y_1^1 through y_1^{66} as:

$$f\left(y_1^1, y_1^2, \ldots, y_1^{66}\right) = \sum_{i=1}^{66} |y_1^i - 10| \quad (3)$$

To obtain the best values of the variables a_1 through a_{16}, we minimize the function f. In other words, we are to solve the following nonlinear programming problem.

$$Minf\left(y_1^1, y_1^2, \ldots, y_1^{66}\right) \quad (4)$$

As such, we can convert the nonlinear problem (Equation 4) into a linear programming problem (11, 16, 17):

For $i = 1, 2, \ldots, 66$, there exists the numbers w_1^i and z_1^i such that:

$$\begin{aligned} y_1^i - 10 &= w_1^i - z_1^i \\ |y_1^i - 10| &= w_1^i + z_1^i \\ w_1^i &\geq 0 \\ z_1^i &\geq 0 \end{aligned} \quad (5)$$

Then, by changing these variables in (Equation 4) and rearranging the variables and constant values, this problem converts to the following linear minimization problem:

$$\begin{aligned} & Minf\left(y_1^1, y_1^2, \ldots, y_1^{66}\right) = \textstyle\sum_{i=1}^{66} \left(w_1^i + z_1^i\right) \\ & y_1^i - w_1^i + z_1^i = 10, \quad i = 1, 2, \ldots, 66 \\ & w_1^i \geq 0, \quad i = 1, 2, \ldots, 66 \\ & z_1^i \geq 0, \quad i = 1, 2, \ldots, 66 \end{aligned} \quad (6)$$

We solved the problem (Equation 6) by using the Linprog in MATLAB software and the values a_i are obtained. Therefore, the diagnosis function of CCHF is obtained as the below:

$$\begin{aligned} y_1 &= 0.3554x_1 + 1.0851x_2 + 0.3823x_3 + 1.2791x_4 \\ &\quad + 0.5999x_5 + 0.5401x_6 + 3.3721x_7 - 0.5644x_8 \\ &\quad + 0.1452x_9 + 1.2276x_{10} + 2.8836x_{11} + 3.6718x_{12} \\ &\quad - 0.1634x_{13} - 0.9057x_{14} - 0.0939x_{15} + 1.6010x_{16} \end{aligned}$$

By inserting the values of x_i ; $i = 1, 2, \ldots, 16$ resulting from the clinical examinations of a patient, we calculate y_1. The closer the value of y_1 to 10, the higher is the possibility of being infected by CCHF. To obtain the equations y_2 and y_3 in (Equation 1) as the outputs of the diagnostic system for the diagnosis of bacterial meningitis and severe influenza, respectively, we proceed by the same process. The equation y_2 is written for 54 patients with certain diagnosis of bacterial meningitis, each one is supposed to have a value of 20 for the function y_2 and the equation y_3 is also written for 61 patients with certain diagnosis of Severe Influenza, each one is supposed to have value of 30 for the function y_3. Considering these systems and using the method discussed for CCHF, the functions y_2 and y_3 are obtained as follows:

$$\begin{aligned} y_2 &= 1.9188x_1 + 3.8439x_2 + 4.4720x_3 + 0.5818x_4 \\ &\quad - 1.4306x_5 + 2.6360x_6 + 1.5317x_7 - 1.3420x_8 \\ &\quad - 1.6140x_9 + 3.4834x_{10} + 2.3919x_{11} + 0.7121x_{12} \\ &\quad + 2.1401x_{13} + 3.5555x_{14} + 2.5968x_{15} + 1.4559x_{16} \end{aligned}$$

$$\begin{aligned} y_3 &= 0.4120x_1 + 8.2213x_2 + 4.3339x_3 + 1.9333x_4 \\ &\quad + 3.8232x_5 + 5.699x_6 - 4.6181x_7 + 2.5750x_8 \\ &\quad + 3.1971x_9 + 3.0353x_{10} + 7.1654x_{11} + 3.3935x_{12} \\ &\quad + 2.3661x_{13} + 3.4279x_{14} - 0.5184x_{15} + 0.7744x_{16} \end{aligned}$$

By inserting the values of x_i ; i = 1, 2, . . ., 16 resulting from the clinical examinations of a patient, we calculate y_2 and y_3. The closer the value of y_2 to 20, the higher is the possibility of being infected by bacterial meningitis. Also, the closer the value of y_3 to 30, the higher is the possibility of being infected by Severe Influenza.

4. Results

There are real 5-point-symptoms of three patients whose data had not been used in designing the mathematical model that was obtained in the previous section. These data are shown in Table 1. Now, we are going to use them as test data in order to obtain the best choice among the three diseases. According to the given values in Table 1, the obtained values of the functions y_1, y_2, and y_3 are shown in Table 2. To normalize the values, we divided the numbers in the 1st, 2nd, and 3rd rows of Table 2 by 10, 20, and 30, respectively. In other words, all values of Table 2 have been fallen in the interval (0,1). Table 3 shows the normalized values of the values presented in Table 2. In Table 3, the corresponding numbers of the three diseases for each patient are between 0 and 1. The closer the corresponding number of a certain disease for a certain patient to 1, the higher is the possibility of that disease for that patient. In contrast, the closer number to 0, the less is the possibility of the corresponding disease. In each column, the closest number to 1 is marked with *, which indicates the best selection of disease among the three diseases for the patient. Accordingly, the best selection for 1st, 2nd, and 3rd patient is CCHF, bacterial meningitis, and severe influenza, respectively. These results coincide with the physician decisive diagnosis.

5. Discussion

In this research, we used the medical symptoms and data of patients suspected of three specific diseases whose illness was identified after medical examinations. Findings resulted in the development of a series of equation systems with no solution, where the right side of each equation indicated a number, which was assigned to that disease. Through approximation solving of this system of equations, we determined the percentage for relatively optimal diagnosis of each disease. In addition, the diagnostic priorities of each disease were expressed (18). Despite all medical diagnosis standardization methods, a correct diagnosis, specifically for diseases with relatively similar signs, depends on mathematical precision. This is mainly because of two underlying reasons. First, diagnosis of a disease generally involves logical propositions, such as those mentioned in the Basic Rules. Second, medical diagnosis requires expertise and experience in dealing with uncertainties and making an experimental conclusion from a series of symptoms, which do not exactly match diagnostic symptoms and methods presented in the medical literature (19). In other words, a specialist should use complex inferential methods in mathematical or fuzzy logic to make a relatively certain conclusion and diagnosis (20). It is worth noting that the science of logic is a branch of mathematics. The application of classical mathematical methods or fuzzy mathematics, along with disease symptoms, which can be used as disease variables in mathematics, may contribute to the development of a function capable of reducing and minimizing the diagnosis error (19, 20). Therefore, a powerful framework for modeling current systems may turn the theory of fuzzy mathematics into a valuable factor for medical diagnosis progress (10). Regarding that uncertainty is an integral part of medical sciences, the fuzzy logic replaces diverse inference methods in the brain with more simple machine models. This theory is able to mathematically formulate many uncertain concepts, variables, and systems, and allow for reasoning, inference, control, and decision-making under the conditions of uncertainty (19, 21). Medical uncertainty is due to various factors and sources (3, 4). Medical uncertainties may arise from patients' signs, data, and medical history, which are often obtained from the patients or their relatives and are generally subjective and imprecise, physical examinations, which are usually associated with ambiguity, specific condition of patients before or during the tests, and a variety of other reasons (3, 4). For example, a patient's blood pressure of 16 may change during the day and vary between 15 and 18. Thus it is better to consider the fuzzy number of 16 (triangular number of 16) instead of the definitive number of 16 (22). The fuzzy theory allows for modeling verbal and imprecise concepts and terms and converting them into mathematical numbers as the system inputs. Using the fuzzy logic for this system not only improves its performance but also considers and introduces uncertain conditions and symptoms of the patients to mathematical fuzzy equations, producing more precise outputs, which will be addressed in details in the next article.

5.1. Conclusions

Symptoms of diseases are often fuzzy in medicine. In addition, many diseases have almost identical symptoms that are different in type and quality. These differences may be negligible or significant, which usually cause differential diagnoses by physicians. Thus, in order to have a correct diagnosis of a disease, different symptoms with various qualities should be taken into account. However, in many diseases, there are possibilities of misdiagnosis by

Table 1. The Real 5-Point-Symptoms of Three Patients

Row	Symptom Type	Symptom Quality			Numerical Value Corresponding to Symptom Quality		
		First Patient	Second Patient	Third Patient	First Patient	Second Patient	Third Patient
1	Fever	Mild	Severe	Severe	0.5	0.75	0.75
2	Headache	Mild	Severe	Severe	0.5	0.75	0.75
3	Nausea	Mild	Very severe	Very severe	0.5	1	1
4	Vomiting	Severe	Mild	Severe	0.75	0.5	0.75
5	Diarrhea	Very severe	-	Mild	1	0	0.5
6	Sweating	-	-	Very severe	0	0	1
7	Body pain	Severe	Slight	Severe	0.75	0.25	0.75
8	Sore throat	-	-	Very severe	0	0	1
9	Bleeding	Mild	-	-	0.5	0	0
10	Convulsion	-	-	-	0	0	0
11	Cough	Slight		Severe	0.25	0.25	0.75
12	Level of consciousness	Very severe	Slight	Mild	1	0.25	0.5
13	Vertigo	-	-	-	0	0	0
14	Complexion	Mild	Severe	Severe	0.5	0.75	0.75
15	Neck stiffness	-	Very severe	-	0	1	0
16	Retro orbital pain	Severe	Slight	-	0.75	0.25	0

Table 2. Diseases Functions' Values

Disease's Name	First Patient' Value	Second Patient' Value	Third Patient' Value
CCHF	9.9935	4.2112	8.5461
Bacterial meningitis	8.6446	15.8713	15.7745
Severe influenza	17.3714	15.5069	28.6234

Table 3. Normalized Values of the Table 2

Disease's Name	First Patient' Value	Second Patient' Value	Third Patient' Value
CCHF	0.9994*	0.4211	0.8546
Bacterial meningitis	0.4322	0.7936*	0.7887
Severe influenza	0.5790	0.5169	0.9541*

every physician, because of nearly identical symptoms. Diagnosis error is reduced by using the method proposed in the present research and may even become almost zero by having relatively accurate symptoms. The necessity of early correct diagnosis, as well as the risks of a primary incorrect diagnosis, is completely obvious and the latter may lead to the patient's death. The presented method helps to improve the society health and protects the patients' lives.

In the present paper, we have used the related data for the decisive afflicted patients with one of the discussed diseases in the mathematical model and finally, a multivariable vector function with 16 inputs (symptoms) and 3 outputs (CCHF, bacterial meningitis, and severe influenza) have been specified for each disease. Approximate determination of the above functions in the present paper has been linearly carried out, where the results have been compared with the real cases. Studying the results of the above modeling for some patients verified the modeling accuracy. Therefore, it is obvious that the presented method in this article has a contribution to the social health and protection of the patients' lives. However, the number of patients whose diseases data have been used in our modeling was not sufficient. The more patients with decisive diseases are studied, the closer the obtained model is to reality, and the results will be more real.

Footnotes

Conflict of Interests: There is not any conflict of interests regarding this study.

Ethical Approval: It is not declared by the author(s).

Funding/Support: This study was supported by Payame Noor University.

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