Intelligent analysis of some factors accompanying hepatitis B

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Abstract. **Background**. It is evident that the B hepatitis disease is favored by several risk factors. Among the factors analyzed in this study, gender, diabetes, arterial hypertension, and body mass index. The age of the first infection is related to these variables. As the system is very complex, because other factors can have an effect and which are ignored, this study processes data using artificial intelligence techniques. **Method**. The study concerns 30 patients diagnosed at our service of the university hospital of Setif in Algeria. The study period runs from 2011 to 2020. The risk factors are considered imprecise and therefore fuzzy. A fuzzy inference system is applied in this study. The data is fuzzyfied and a rule base is established. **Results**. As the principles of fuzzy logic deal with the uncertain, this allowed us to take care of this imprecision and complexity. The established rule base maps the inputs, which are the risk factors, to hepatitis as the output variable. **Conclusion**. Several factors promote hepatitis B. The physiological system differs from one individual to another. Also, the weight of each factor is ignored. Given this complexity, the principles of fuzzy logic proposed are adequate. Once the system has been completed, it allows the random introduction of values at the input to automatically read the result at the output. This tool can be considered as a prevention system in the appearance and and establish a typical profile of people likely to be affected by hepatitis

*Keywords***:** Hepatitis B, Risk factors, İntelligne techniques, *Fuz*zy logic

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1. Introduction

Hepatitis B is a viral inflammatory disease affecting the liver. Its mode of transmission is essentially contact with contaminated blood. While this infection is often mild, in about 10% of cases it progresses to a chronic infection. This hepatocyte infection can cause acute hepatitis and sometimes cirrhosis or liver cancer [1]. Hepatocellular carcinomas rank second in the world among fatal cancers, despite the availability of a vaccine [2]. Hepatitis B is characterized by a negative HBeAg status and a positive HBe phase associated with viral replication. Adding to that, this profile is very complex regarding the viral base. This can be the cause of hepatocellular carcinomas [3]. The WHO reports that approximately 257 million are classified as chronic carriers [4]. Over a period of nine years, patients diagnosed at the level of our hospital department for hepatitis, different parameters are taken. A database is built summarizing these entire characteristics specific to each patient. This study attempts to establish a typical profile of these patients. Hepatitis B and C are mapped to accompanying factors. As these factors are multiple and complex, this study is limited to five main ones which are sex, diabetes, blood pressure, age at first infection and body mass index. Despite this limitation, the effect and interaction of these factors remains complex. The individual physiological response is far from being homogeneous and mathematically analyzable. The study proposes an artificial intelligence technique in data analysis. The application of the principles of fuzzy inference is perfectly suited. The principles of this logic ensure that the uncertainty and imprecision inherent in the nature of the data are compensated for. The proposed system makes it possible to establish a typical profile of people likely to have hepatitis with maximum precision.

2. Material and method

During a period from 2011 to 2020, patients were diagnosed with hepatitis B in our department at the University Hospital of Setif in Algeria. For each patient, physiological parameters are sampled in the database. The factors considered in this study are: gender, diabetes, blood pressure, and body mass index related to the age at first infection.

2.1.Risk factors

The direct relationship of these factors with hepatitis is reviewed below.

Gender and hepatitis

Studies report that the hepatocarcinogenesis factor resulting from HBV is much more pronounced in men than in women [5]. Even in the case of subjects vaccinated at birth with a booster at 18 years of age, the prevalence of chronic carriers is higher in males than in females [6]. In general, hepatocellular carcinomas resulting from hepatitis B virus infection occur much more in men than in women [7]. This only reveals liver disease between the two sexes appeared long ago. This, can be explained in a certain way by the hormonal androgenic and estrogenic effects [8]. Moreover, this does not only concern hepatitis but also other diseases [9–13], either in terms of risk factors or in terms of disease progression [14].

Diabetes and hepatitis

Type 2 diabetic patients are often tested during their blood sugar monitoring. This will expose them to a high risk of contamination by the hepatitis B or C virus [15]. These procedures, especially when it comes to poor blood sampling, put this population at the highest risk of hepatitis [16][17]. When blood sampling for diabetes monitoring is combined with hemodialysis, this risk is much greater [18–20]. Other studies report that the risk is much higher when there is an association between diabetes and HBV infection [21–26].

Blood pressure and hepatitis

The effect of blood pressure and cirrhosis has been the subject of several studies. It has been found that treatment with enzymes inhibitors, used in the treatment of high blood pressure, has contributed to the reduction of chronic viral liver fibrosis [27].The relationship between HCV infection and cardiovascular disease demonstrates an increased cardiovascular risk due to HCV infection.

Effect of age at the first infection on hepatitis

he age of HBsAg serodeclaration is associated with the viral infection of hepatitis as well as its evolution into cirrhosis. This can be considered as a non-negligible risk factor [28-30]. The clinical threshold for this is when the age is greater than 50 years at the time of HbsAg serodeclaration [31,32]. The age of menopause is a determining factor in chronic hepatitis. This is of lower risk before this age and higher after. This median age in women is around 48 years, varying between 40 and 60 years [33]. This may explain the effect of age in women aged between 50 and 60 years after menopause on chronic hepatitis te without HBsAg [34].

BMI and hepatitis

Studies report that there is a possible relationship between BMI and chronic liver carcinoma and even liver cancer and that BMI may be a risk factor [35-37]. From a simple hepatic stenosis, a high BMI in HBsAg carriers can cause it to switch to a benign stage and even to cirrhosis [38]. Also, it should be noted that the metabolic risk associated with hepatic steatosis, which is considered to be cofactors in the development of fibrosis, is directly linked to obesity. This is all the more significant when the cases are prone to chronic hepatitis B or C [39-41].

2.2. Fuzzy inference analysis

In an attempt to solve imprecise situations in the real world, a theory of fuzzy sets was developed by Lotfi Zadeh in 1965 [42]. Nowadays, fuzzy logic has found its applications in various fields, including the medical field [43]. The advantage of fuzzy inference is that it is able to translate a human expert's uncertainty and knowledge to extract a sharp decision. Add to this, the rules used can be adapted to all situations [44]. Fuzzy inference consists of matching a set of input variables to an output variable based on fuzzy rules [45]. This study uses a 'Mamdani Fuzzy' fuzzy inference system. The result after defuzzification is obtained from the rules requiring prior fuzzification [46].

The principle of operation operates on the mini-max of the functions. The basis of the rules is of the form:

If X_1 is A_1 and ….and X_n is A_n then Y is B.

The numerical variables must be converted into linguistic variables by the process of 'fuzzyfication' represented here by (A and B) defined in the universe of discourse (X and Y).

As the output of the system must be sharp, it is necessary to extract a sharp value from the fuzzy set. Defuzzification then operates inversely to fuzzification. This study uses the surface center of gravity method after aggregating all the established rules. Schematic of the structure of the fuzzy analysis model. (Figure 1a,b).

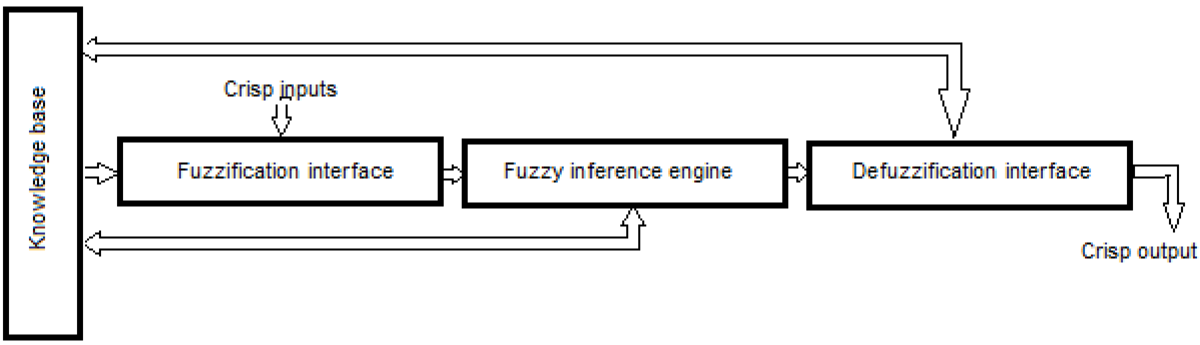

Figure 1a. Fuzzy Inference System

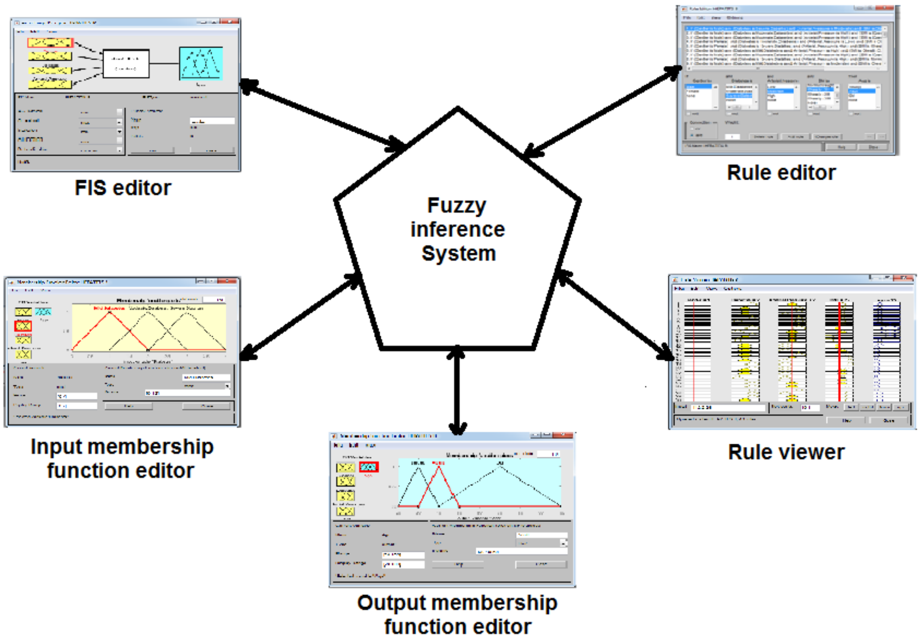

Figure 1b. Fuzzy system and its integral components in MATLAB 2016a software

Fuzzy Modeling Details

The application of fuzzy logic is developed in this study to establish a typical profile of a patient likely to be affected by hepatitis B. Based on the significant cases diagnosed (Table 1). The system built has four input variables and one output. (Figure 2a,b).

Table 1. Parameters of diagnosed cases

N°	Gender	Diabetes	H. blood Pressure	BMI	Age at first infection
1	M	No	No	29,74	48
2	M	Yes	No	28,73	72
3	M	Y/ From 22 Years	Y/ From 1 Years	24,69	66
4	M	Yes	No	29,32	36
5	M	Y/ From 9 Years	Y/ From 15 Years	22,22	41
6	F	No	Y/ From 3 Years	19,36	64
7	F	No	Y/ From 1 Years	37,18	72
8	M	Y/ From 4 Years	No	32,65	36
9	M	Y/ From 4 Months	No	30,42	78
10	F	No	No	23,44	31
11	F	No	Y/ From 30 Years	25,78	69
12	F	Y/4 Years	No	36,73	37
13	F	No	Yes	22,68	48
14	M	No	No	20,83	32
15	M	No	No	25,95	13
16	M	Y/ From 1 Years	No	21,61	29
17	M	No	No	20,76	32
18	M	Y/ From 16 Years	No	27,55	61
19	M	No	No	26,83	26
20	F	No	No	29,38	49
21	F	Y/ From 20 Years	Y/ From 21 Years	34,63	69
22	F	No	No	27,16	31
23	M	No	No	26,03	51
24	M	No	No	22,04	65
25	F	Y/ From 5 Years	No	31,16	62
26	M	Y/ From 3 Years	Yes	31,79	63
27	F	No	No	14,48	83
28	F	No	No	31,11	30
29	M	No	No	27,17	24
30	M	Y/ From 3 Years	No	29,07	60

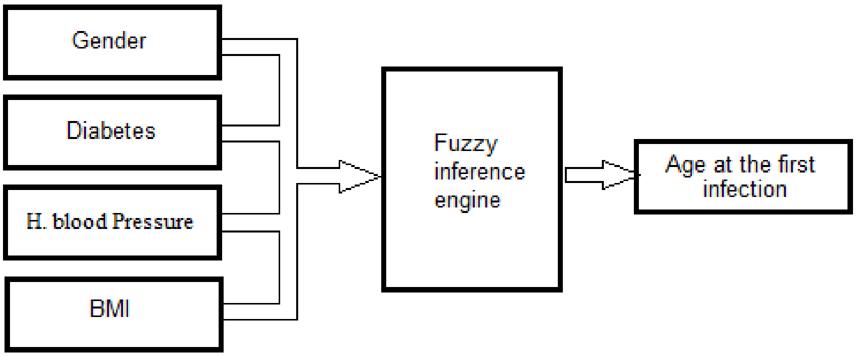

Figure 2a. Schematic of the structure of the fuzzy analysis model

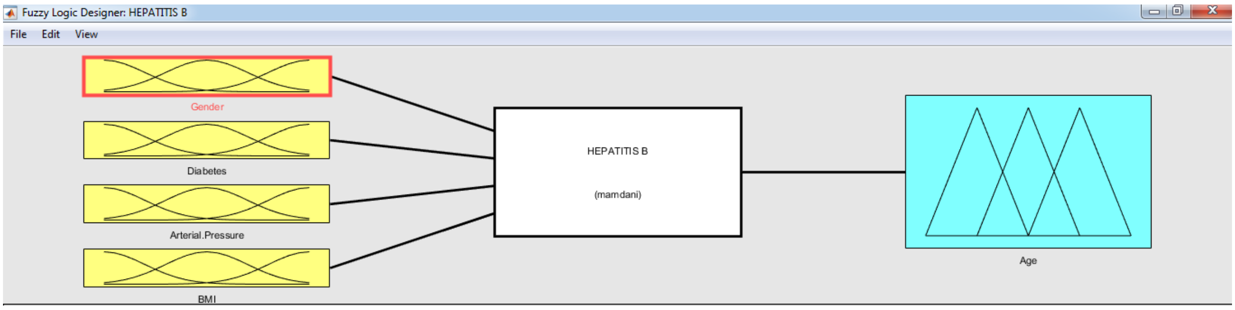

Figure 2b. General structure and membership functions of the model

Inputs fuzzification

a. Gender variable: Variable *'Gender'* is not fuzzified. The 'male' sex is expressed by [1] and [2] for the 'female' sex (Figure 3).

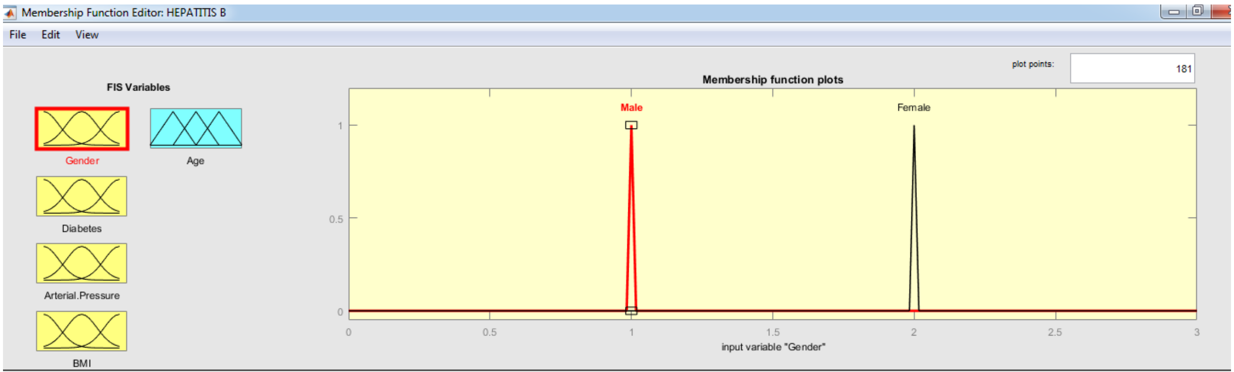

Figure 3. Gender variable representation

b. Diabetes variable: Variable *'Diabetes'* is fuzzified into three triangular membership functions. Ranges are assigned to each degree of diabetes severity. As the limits between the intervals are imprecise, each two neighboring functions overlap in order to compensate for these inaccuracies. Mild diabetes [0-2], moderate diabetes [1-3], severe diabetes [2-4]. (Figure 4).

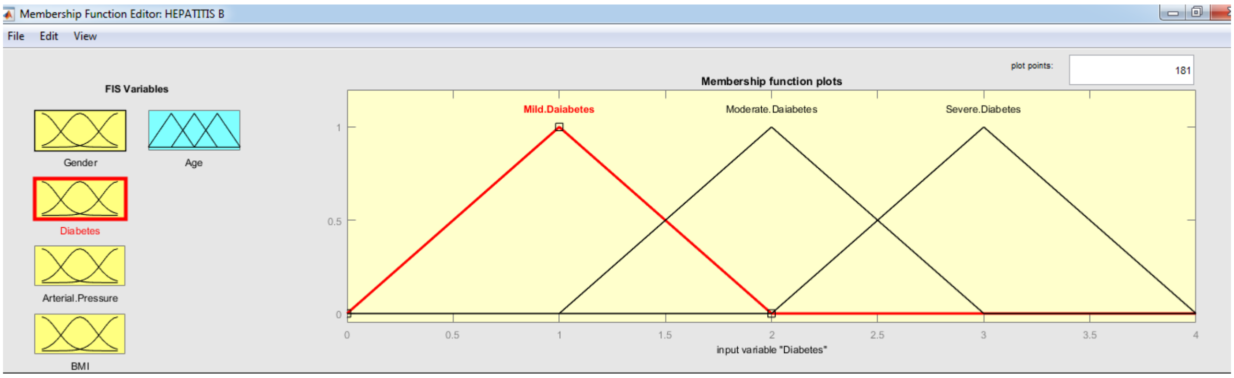

Figure 4. Diabetes variable fuzzification

c. High blood pressure variable: Variable 'High blood pressure' is fuzzified into three triangular membership functions. Ranges are assigned to each degree of blood pressure severity. In the same way, three triangular membership functions are assigned and intervals are created according to the degree of blood pressure severity. Low [0-2], moderate[1-3], High [2-4]. (Figure 5).

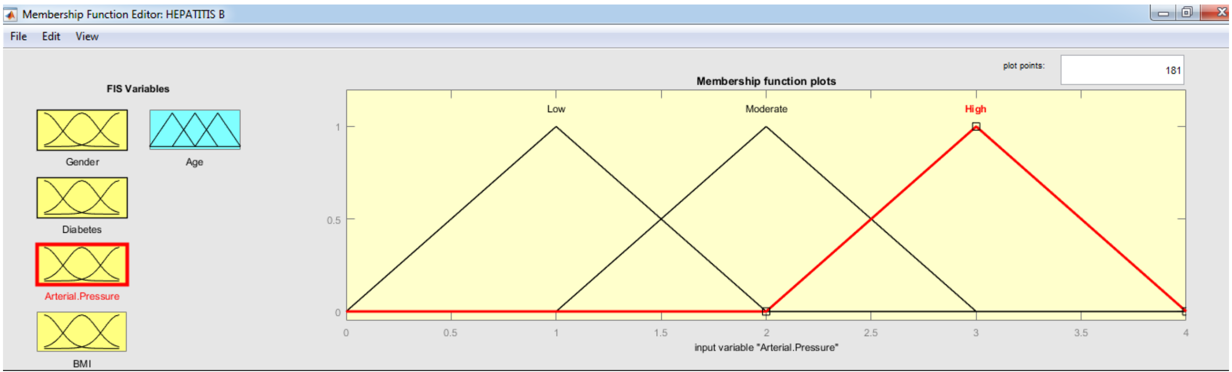

Figure 5. Arterial pressure variable fuzzification

d. BMI variable: Variable 'BMI' is fuzzified into five triangular membership functions. Ranges are assigned to each body mass index value. (Figure 6).

	Numerical representation	**Fuzzy representation**
Nutritional status	**BMI**	**BMI**
Underweight	Below 18.5	[< 20]
Normal weight	18.5–24.9	[18-27]
Obesity class I	30.0–34.9	[23-37]
Obesity class II	35.0–39.9	[33-42]
Obesity class III	Above 40	[> 38]

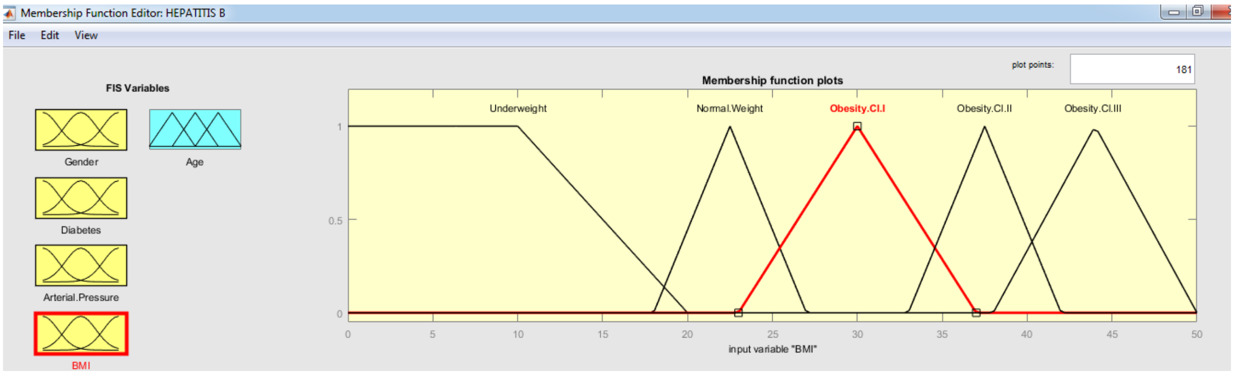

Figure 6. BMI variable fuzzification

Output fuzzification

Age at the first infection: Variable 'Age' is fuzzified into three triangular membership functions. Ranges are assigned to each age at the first infection value. In the same way, three triangular membership functions are assigned and intervals are created according to the age. Also, these values are assigned according to the ages of the diagnosed patients shown in the table above.

Young [20-40 years old], Adult [30-50 years old], Old [> 40 years old]. (Figure 7).

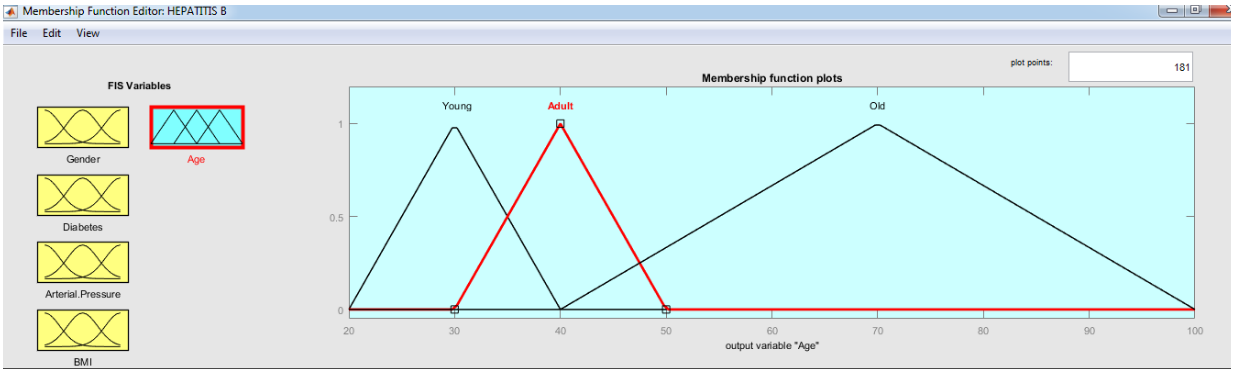

Figure 7. Age of the first infection variable fuzzification

Base rules

The general form of a rule is: If..Then. In this application, the rules are created based on the numerical values shown in Table 1.

Example:

IF gender is male AND diabetes is average AND blood pressure is high AND body mass index is low THEN age susceptible to hepatitis infection is adult

Each rule refers to the actual values recorded. The rule base must contain all possible combinations.

Defuzzification

After the fazzification process where the numeric variables are translated into linguistic variables, the fuzzy result at the numeric output has to be converted back into a numeric term. This is the process of defuzzification. The result is obtained by aggregating the set of inference rules. The method used is that of the COG (center of gravity).

In this method, the AND operator is used in each rule. The aggregation of several rules uses the OR operator. The result is a surface at which its center of gravity must be calculated according to the formula:

$$U = \frac{\int_{Min}^{Max} u.\mu(\mu)du}{\int_{Min}^{Max} \mu(\mu)du}$$

Where: U is the result of the defuzzification; u is the output variable; μ is the transfer function; Min and Max are the limits of the defuzzification

3. Result and discussion

The risk factors that promote hepatitis B are multiple. Some are known, others totally ignored, while the weight of some others is poorly understood. Also, the interaction between these factors and the physiological specificity of each individual is impossible to know. Faced with this situation, it is very difficult to model them using classical mathematical techniques.

The proposed tool makes it possible to deal with this complexity. This study is limited to only four factors. Like human reasoning, each factor is considered uncertain and therefore fuzzy.

The 'fuzzification' makes it possible to convert the numerical data recorded from each patient to the linguistic variables of human language. Input or output variables are fuzzified. The basis of the rules is established from the actual recorded data. Each rule uses the 'AND' operator. Mathematically, the result of this operator is a function that represents the minimum of each function expressing each variable. When several rules are established, it is then a question of aggregating them with the 'OR' operator. This operator takes the maximum of the results of each rule. The resulting surface represents the participation of the set of all rules.

As the final result must be expressed in net terms, defuzzification operates inversely to fuzzification. The calculation of the center of gravity of this final surface represents the final output variable. By this technique, all uncertainties are compensated (Figure 8).

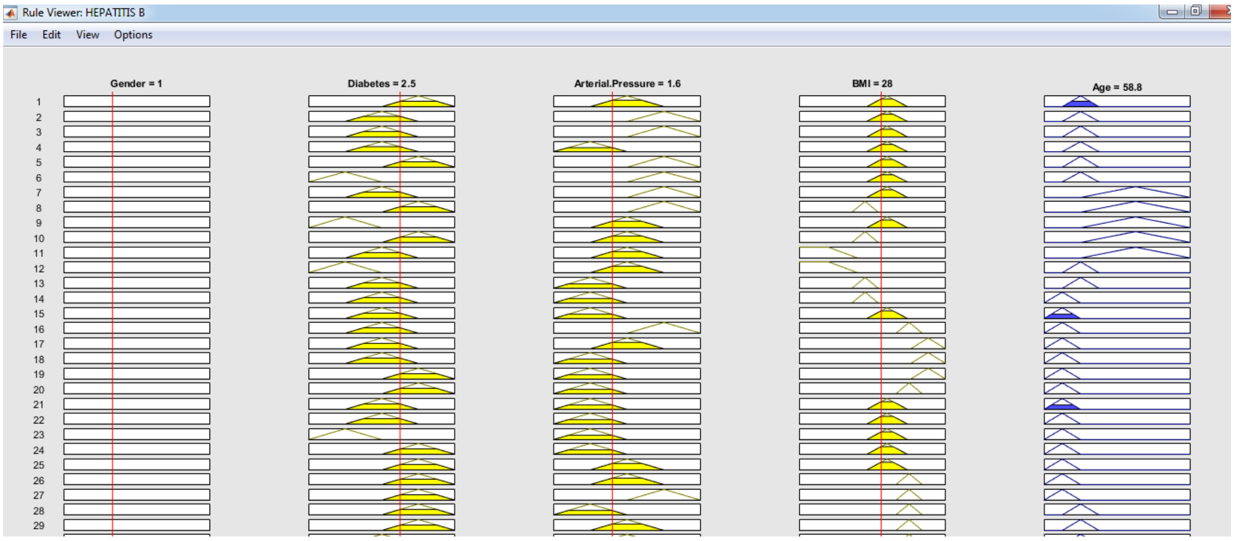

Figure 8. Application example

4. Conclusion

Given the complexity of the risk factors involved in hepatitis B, it becomes impossible to model them mathematically. Some studies attempt to analyze them statistically. However, the statistical analysis remains in the realm of the probable. The significant and the non-significant remain imprecise terms. This study offers an intelligent analysis like human reasoning where complexity is taken care of and uncertainties are compensated.

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The established application makes it possible to randomly introduce variables at the input to automatically and instantly read the result at the output. It suffices to set the patient's sex, his level of diabetes, arterial hypertension and his body mass index to predict at what age the degree likely to be affected by hepatitis B. This application remains extensible to other factors that do not are not taken here. This can be a tool to help prevent this disease.

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Nil.

Conflicts of interest:
There are no conflicts of interest.

Appendix

Membership code of Fuzzy analysis module

```
[System]
Name='HEPATITIS B'
Type='mamdani'
Version=2.0
NumInputs=4
NumOutputs=1
NumRules=40
AndMethod='min'
OrMethod='max'
ImpMethod='min'
AggMethod='max'
DefuzzMethod='centroid'

[Input1]
Name='Gender'
Range=[0 3]
NumMFs=2
MF1='Male':'trimf',[1 1 1]
MF2='Female':'trimf',[2 2 2]

[Input2]
Name='Diabetes'
Range=[0 4]
NumMFs=3
MF1='Mild.Daiabetes':'trimf',[0 1 2]
MF2='Moderate.Daiabetes':'trimf',[1 2 3]
MF3='Severe.Diabetes':'trimf',[2 3 4]

[Input3]
Name='Arterial.Pressure'
Range=[0 4]
NumMFs=3
MF1='Low':'trimf',[0 1 2]
MF2='Moderate':'trimf',[1 2 3]
MF3='High':'trimf',[2 3 4]

[Input4]
Name='BMI'
Range=[0 50]
NumMFs=5
MF1='Underweight':'trimf',[-50000 10 20]
MF2='Normal.Weight':'trimf',[18 22.5 27]
MF3='Obesity.Cl.I':'trimf',[23 30 37]
MF4='Obesity.Cl.II':'trimf',[33 37.5 42]
MF5='Obesity.Cl.III':'trimf',[38 44 50]

[Output1]
Name='Age'
Range=[20 100]
NumMFs=3
MF1='Young':'trimf',[20 30 40]
MF2='Adult':'trimf',[30 40 50]
MF3='Old':'trimf',[40 70 100]
```

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