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Prevalence of risk factors for cervical cancer induced by papillomavirus infection: A fuzzy inference system modeling

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ABSTRACT

We investigated the additional risk factors, histological analysis, papillomavirus (HPV) load, number of pregnancies to screening accuracy in cervical cancer incidence in women screened at different ages using individual patient data from 58 women at high risk compared to reference cases. The goal of this study was to investigate the occurrence of invasive cervix cancer based on the prevalence of HPV infection among women between 18 and 80 years of age in Setif and Algiers Prefecture in Algeria. For this purpose, the sensitivity and specificity of HPV detection and the combination of the former tests were treated using artificial intelligence technique especially fuzzy logic inference. The results of this study may contribute to our understanding of cervical cancer and may provide useful data for the disease prognosis and therfore the prevention and treatment of this condition. After the system is established, we can based on the input values (HPV, Age and number of pregnancy) set randomly glance the cancer incidence at output in both numeric and linguistic term.

Key words: risk factors; HPV; cervical cancer, fuzzy logic

INTRODUCTION

The main cause of cervical cancer is infection with HPV. Human papillomavirus (HPV) infection appears to be involved in the development of cervical cancer in more than 90% of cases [1]. Studies suggest that giving birth to many children may slightly increase the risk of cervical cancer among women with HPV infection. The etiology of this cancer has been linked to several types of HPV, with a high preponderance. Most cases of cervical cancer are caused by just two high-risk types of HPV-type 16 and type 18 [2]. The presence of these high-risk viruses in almost all cervical cancers implies the highest worldwide attributable fraction so far reported for a specific cause of any major human cancer. The extreme rarity of HPV-negative cancers reinforces the rationale for HPV testing in addition to, or even instead of, cervical cytology in routine cervical screening [3].

Although much attention has focused on the HPV types associated with cervical intraepithelial neoplasia (CIN) and cancer, fewer others have detected specific HPV types in mild genital warts. In these cases, the most often detected viruses are HPV6 or HPV11 [4]. Strong epidemiologic and molecular data link HPV infection to cervical and other anogenital cancers [5].

Screening is one of the best defenses against cervical cancer. Most of women who develop the tumor have never been screened. Changes observed in dysplasia and carcinoma in situ, were qualitatively similar and remained rather constant throughout the histological spectrum of putative precursor lesions [6]. In our study, the results of the surveys were recorded in terms of age, viral load and cervical cytology in routine cervical screening. Our attention was focused on the HPV types associated with cervical interstitial neoplasia (CIN) and cancer. Detection of genital wart-associated viruses has most often been reported as groupings of HPV types. To analyze the factors involved in the occurrence of cervical cancer, it is very complex and uncertain. The effect of HPV does not necessarily give the same result from one woman to another. Other factors can influence the cervical cancer incidence like number of pregnancy and age of women. As human physiology and immune system differs from one person to another, it seems impossible that they will have the same consequences. The transition from one category to another is in a fuzzy environment. The analysis of these parameters by fuzzy logic is then perfectly adequate. For this, we give an overview on the basic principles of fuzzy logic inference. Statistical and health information systems are weak and the underlying empirical data may not be available or may be of poor quality. Because of the weakness of the underlying empirical data a number of the indicators presented here are associated with significant uncertainty [7].

MATERIALS AND METHODS

Visual inspections and biopsies were performed using the Preventive Oncology International microbiopsy protocol for pathological diagnosis. Cervical epithelial tissue specimens were collected and tested. According to the results, women were infected with HPV were classified in a group, and the remaining individuals were classified as the control group. Participants included 54 women. Human papillomavirus (HPV) detection contributes to most cases of cervical cancer, and HPV genotypes exhibit different distributions according to ages, viral load and histological results.

Fuzzy logic approach

The fuzzy logic approach, a sub-field of intelligent systems, is being widely used to solve a wide variety of problems in medical, biological and environmental applications. Fuzzy logic deals with the analysis on a higher level, using linguistic information acquired from domain experts. The fuzzy logic concept provides a natural way of dealing with problems, and the source of imprecision is an absence of sharply defined criteria rather than the presence of random variables. The fuzzy approach considers cases where linguistic uncertainties play some role in the control mechanism of the phenomena concerned [8]. Fuzzy logic deals with reasoning on a higher level, using linguistic information acquired from domain experts. The above-mentioned capabilities make fuzzy logic a very powerful tool to solve many ecological problems, where data may be complex or in an insufficient amount [9]. The Fuzzy inference systems (FIS) are powerful tools for the simulation of nonlinear behaviors with the help of fuzzy logic and linguistic fuzzy rules [10]. Especially for medical expert systems, theoretical framework of fuzzy logic in a rich environment is very adequate. The adequacy of each approach is borne out by the success of the model in practice [11].

In this study, we propose a fuzzy algorithm in decision-making. For all the algorithms presented below, there is a common rule form for rules that associate an observation vector.

Fuzzy Logic Modeling:

Assemble Input-Output Data rules basis

As the effect of each parameter remains in the field of imprecise and fuzzy, each variable is represented by a membership function. The degree of influence on the risk factor is reflected by a degree in the fuzzy membership function. The first step is to collect all inputs expression of problem. The rules determined by the choice of the fuzzy membership function are defined for each input variable.

In general form, If X_1 is $X_1(1)$, and X_2 is $X_2(2)$, and ….X_n is $X_n(n)$, then Y_1 is $Y_1(1)$.

After system is done, we can choose randomly values for inputs and read instantly the result at output [12].

Fuzzy inference systems (FIS) are powerful tools for the simulation of nonlinear behaviors with the help of fuzzy logic and linguistic fuzzy rules [13]. For example, there is not a straight-line relationship between the types of human papillomaviruses, age, number of pregnancy and cervical cancer incidence.

In our case, each input variable represents a degree of occurrence of each cervical cancer level concerned. As the degree of risk cannot be measured with precision, saw its uncertain nature, this level is represented by a fuzzy contour. All the risk factors are the inputs of the system. “If-then” rules lie in the basis of Fuzzy Expert System. Here, linguistic values such as small, medium, or big are used and these linguistic values have appropriate membership values. After deciding on designing a Fuzzy system the first step to follow is to collect the rules of “if-then” determined by the human expert or the medical observations collected from experimental data.

The output of the fuzzy reasoning system is the degree of risk of occurrence of a hazardous effect. A three-input and two output systems are constructed. The relationship between the inputs (HPV, Age & Number of pregnancy) (Table1,2,3) with the two output variables (viral load and histology) is analyzed fuzzy term. This is explained by the uncertainty and imprecision related to the physiological nature of the patients (Table 4,5

Table 1. Viral load at different stages of cervical cancer relative luminescence units in different tissues

	Normal cervix	LSIL	HSIL	ASC		Normal cervix	LSIL	HSIL	ASC
1	12	16	10234	95632	30				98612
2	125	42	32015	58210	31				74536
3	24	23	32546	35412	32				25413
4	310	320	62124	85612	33				52153
5	30	52	32507	20234	34				42365
6	125	12	12540	32015	35				15230
7	42	14000	23564	32546	36				23541
8	500	18	21546	12520	37				25403
9	51	95	52021	31507	38				52453
10	12	600	19548	45236	39				42365
11	19	654	58210	54103	40				74236
12	25	325	25412	51453	41				25403
13	65	25	85612	42365	42				52453
14	89	24	45236	45236	43				42365
15	102	15	54103	54103	44				95210
16	97	67	21453	51453	45				78520
17	56	54	42365	42365	46				78920
18	84	84	15230	85210	47				56200
19	75	97	23541	85620	48				93120
20	35	104	65140	79520	49				2546
21	54	102	21543	15210	50				15000
22	41	15	21540	63120	51				32600
23	59	14626	32560	32546	52				45230
24	103	19	23651	62124	53				36201
25	58	98	12543	31507	54				53610

N°	Age	Histo CIN	Nb. of Pr.	N°	Age	Histo CIN	Nb. of Pr.
1	63	CIN1	6	28	63	CIN3	5
2	18	CIN1	0	29	50	CIN3	8
3	75	CIN3	8	30	62	CIN3	5
4	52	CIN2	4	31	48	CIN2	0
5	38	CIN3	2	32	38	CIN3	4
6	51	CIN1	0	33	39	CIN2	4
7	65	CIN1	5	34	68	CIN3	6
8	45	CIN2	3	35	52	CIN2	2
9	78	CIN3	5	36	52	CIN2	4
10	49	CIN3	3	37	64	CIN1	0
11	45	CIN3	--	38	52	CIN1	4
12	39	CIN3	3	39	60	CIN3	8
13	59	CIN2	6	40	53	CIN3	--
14	80	CIN3	5	41	52	CIN2	--
15	51	CIN1	--	42	38	CIN2	0
16	41	CIN1	2	43	48	CIN3	5
17	68	CIN2	3	44	58	CIN2	4
18	63	CIN1	4	45	40	CIN3	3
19	68	CIN2	3	46	68	CIN3	4
20	54	CIN2	--	47	63	CIN3	6
21	60	CIN3	--	48	44	CIN3	2
22	73	CIN3	6	49	72	CIN2	--
23	60	CIN3	4	50	74	CIN3	4
24	48	CIN2	8	51	41	CIN3	3
25	65	--	3	52	56	CIN3	1
26	48	CIN2	5	53	62	CIN2	0
27	76	CIN3	--	54	50	CIN2	2

N°	HPV				N°	HPV			
	PCR		HCII			PCR		HCII	
	A	B	A	B		A	B	A	B
1	-	-	-	-	28	-	-	-	-
2	-	-	-	-	29	-	-	-	-
3	-	-	-	-	30	+	+	+	+
4	-	-	-	-	31	-	+	-	+
5	-	-	-	-	32	-	+	-	-
6	-	-	-	-	33	-	+	-	+
7	-	-	-	-	34	+	+	+	+
8	-	-	-	-	35	-	+	-	-
9	+	+	+	+	36	-	+	-	+
10	-	+	-	+	37	-	+	-	+
11	+	+	+	+	38	-	+	-	+
12	+	+	+	+	39	+	+	-	+
13	+	+	+	+	40	+	+	+	+
14	+	+	-	+	41	+	+	+	+
15	-	+	-	+	42	+	+	-	+
16	-	+	-	+	43	-	+	-	+
17	-	+	-	+	44	+	+	+	-
18	-	+	-	+	45	-	+	-	+
19	-	+	-	+	46	-	+	-	+
20	-	+	-	+	47	-	+	-	+
21	-	+	-	+	48	-	+	+	+
22	-	+	-	+	49	-	+	-	+
23	-	+	-	+	50	+	+	-	-
24	-	+	-	+	51	+	+	-	+
25	-	-	-	-	52	-	+	-	+
26	-	-	-	-	53	-	+	-	+
27	-	-	-	-	54	-	+	-	+

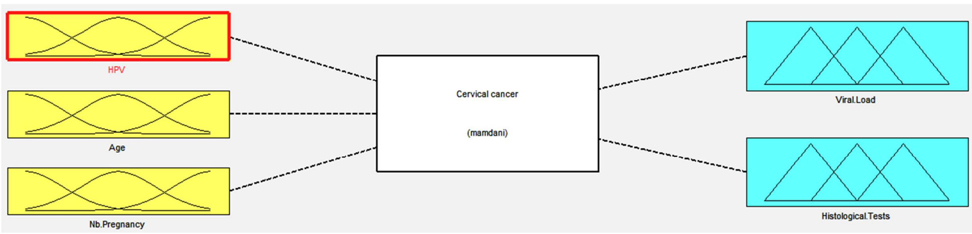

Figure 1. block diagram of the system with three inputs and two outputs

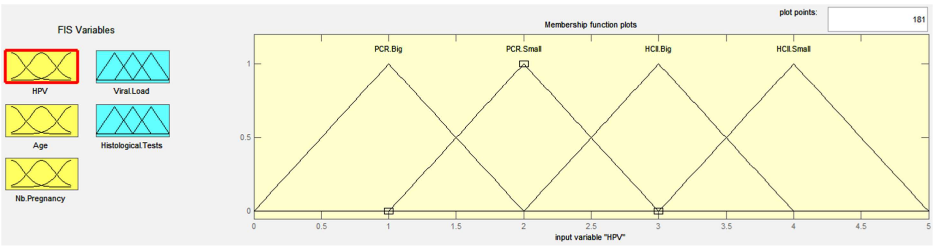

Figure 2 shows the fuzzyfication of input 1 representing the "HPV" variable
Figure 2. Fuzzyfication of "HPV" in four membership functions

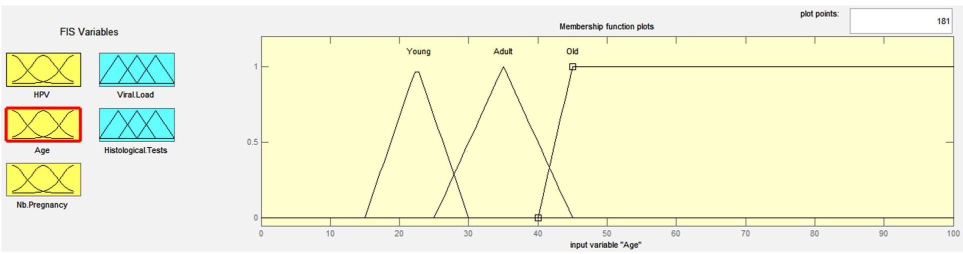

Figure 3 shows the fuzzyfication of input 2 representing the "Age" variable.
Figure 3. Fuzzyfication of "Age" in three membership functions

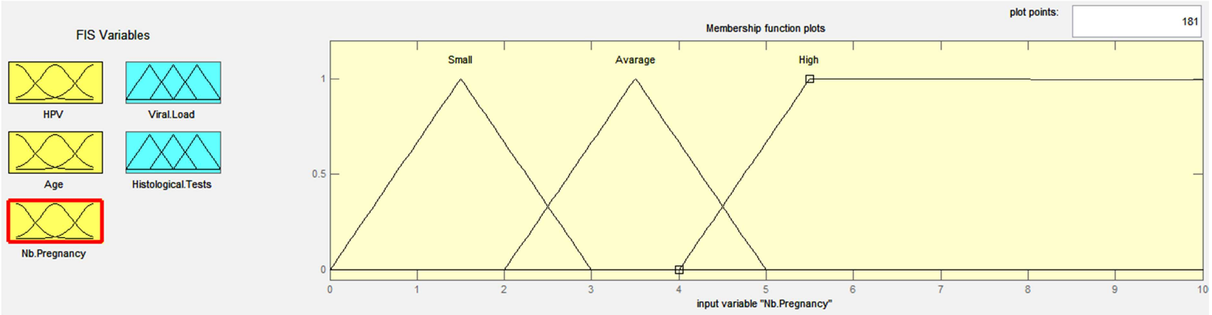

Figure 4 shows the fuzzyfication of input 3 representing the "Number of pregnancy"

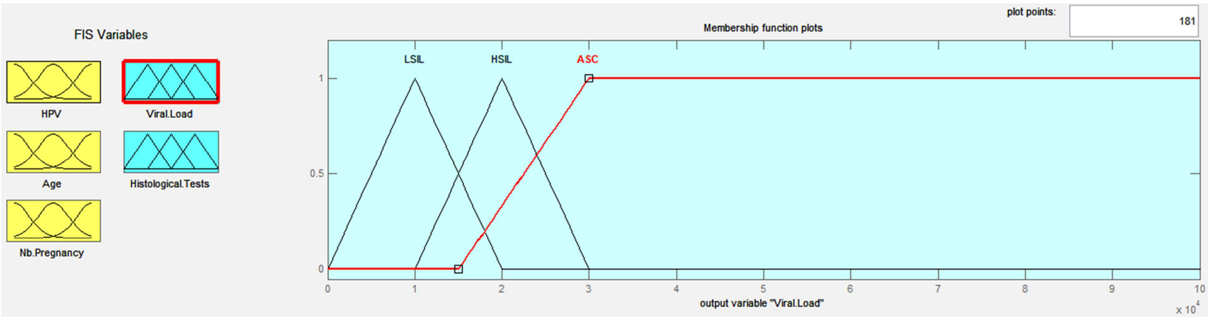

Figure 5. Fuzzyfication of "Viral-L." in three membership functions

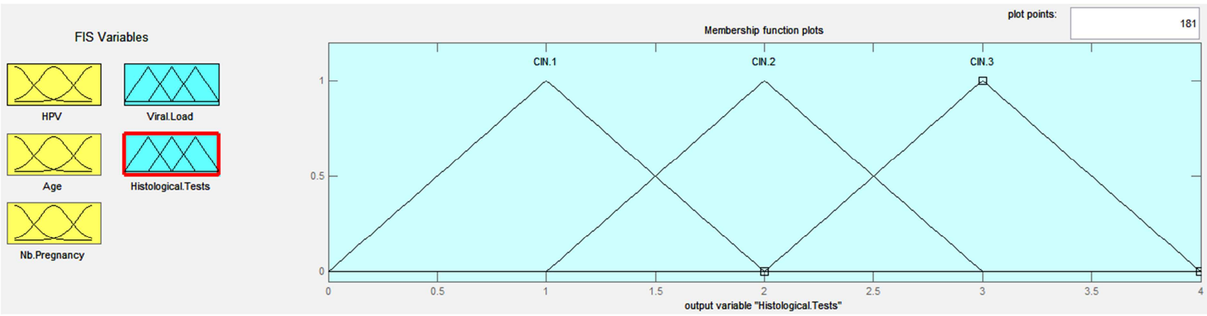

Figure 6. Fuzzyfication of "histological-T" in three membership functions

In order to make fuzzyfication the linguistic expressions below are used. The proposed fuzzy logic cervical cancer prevention system consists of three inputs variables. Fuzzy variable

4.2. Fuzzyfication of output

Once the program is established, it allows direct reading of the result to the output instantly just by randomly assigning. This constitutes a powerful tool for cervical cancer prevention.

Fuzzyfication of inputs

In order to make fuzzyfication the linguistic expressions below are used. The proposed fuzzy logic cervical cancer prevention system consists of three inputs variables. Fuzzy variable "HPV" has the linguistic values PCR-Small; PCR-Big; HCII-Small; HCII-Big (The presence of a type of virus can coexist with another type but with different proportions). Also, the input "Age" can be fuzzyfied in linguistic variables (The border between youth and adult for example cannot be considered sharp). The mapping values of inputs variables through the membership functions are represented in the linguistic values.

Fuzzyfication of outputs

The data for the outputs (the viral load and histological tests according cervical cancer incidence) are represented by the level of viral load which fuzzyfied in tree membership function (Low-grade squamous intraepithelial lesion; High-grade squamous intraepithelial lesion and Atypical squamous cells) (Figure 5). Figure 6 shows the fuzzyfication of histological tests output in three membership functions (CIN1 for mild dysplasia; CIN2 for moderate dysplasia; and CIN3 for both severe dysplasia and carcinoma)

Inference engine
The inference engine consists of AND operator, in fact this operator select minimum input value for the output and also this is not the logical AND. This inference engine takes three inputs from the fuzzyfier to produce the outputs results values according to the min-max composition. This method uses min-max operation between the inputs and outputs. According measured values, fuzzy rules are established. The rules must include all possible combinations from measured values.

Fuzzy Rules
The rules determined by the choice of the fuzzy membership function are defined for each input variable. In general form, each fuzzy rule is written as were A_1 and A_2 are the fuzzy sets that describe the nature of the inputs, such as Small smoker, Average smoker and Heavy smoking. The linguistic control rules of this system are given by:
If X_1 IS $X_1(1)$ and X_2 IS $X_2(2)$ and…X_n IS $X_n(n)$ Than Y_1 is $Y_1(1)$

Defuzzyfier
This system has two outputs that describe the viral load and histological tests. We can say that it shows the cervical cancer incidence according inputs variables. The numeric value output is given by the defuzzyfication process after estimating its inputs values. In this system we have center of average (C.O.A) method which has the mathematical expression that is: (Σ Si.Ri/ΣRi). In the defuzzyfication the exact expression is obtained with "centroïd" method according to validity degree. The outputs values according to the inputs values obtained from the designed fuzzy engine system [16].

RESULTS AND DISCUSSION

The constructed system is based on fuzzy logic model. It is designed for measurement of different values of cervical cancer incidence. MATLAB 10 simulation is used by applying rules. Figure 7 shows the MATLAB- rule viewer and simulation result. One plot at a time shows the relation between any inputs with output wherein the numerical values to the output values are assigned to the linguistic terms of the cancer incidence. The values of the HPV, Age and Number of pregnancy set to randomly and can be instantly read the cervical cancer incidence at the output. The designed system can be remains extensible to other variables that are not considered in this study. The design work is being carried out to design state of the art fuzzy logic cervical cancer concern prediction system in future using hybrid neuro-fuzzy system.

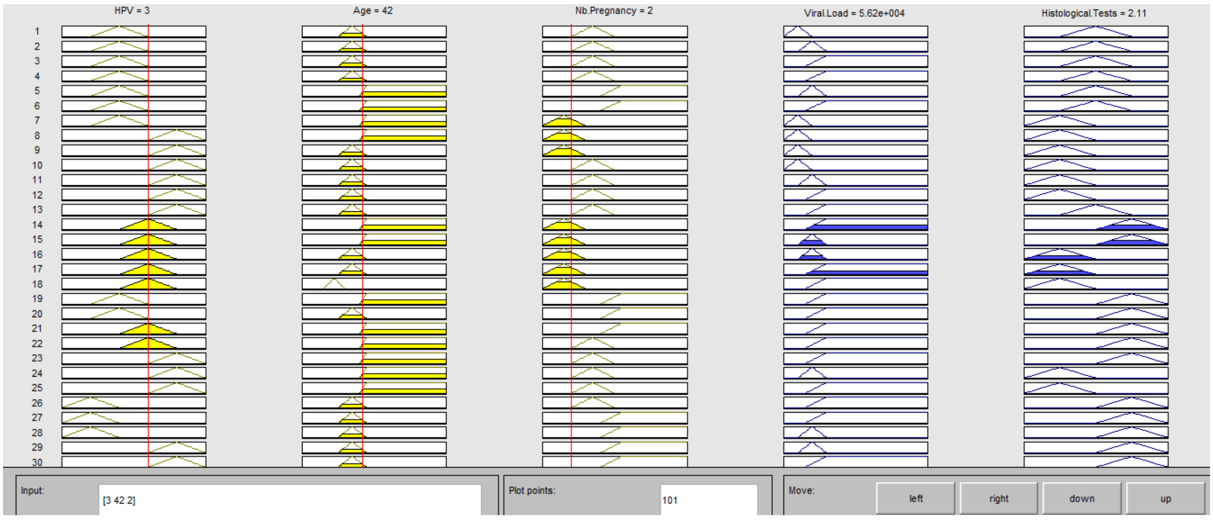

Figure 7. Application Example: attribution random variable inputs and direct reading of the output variable

CONCLUSION

The artificial intelligent system using fuzzy logic method could extend our understanding of factors affects on the nature of the cancer and its incidence rate. The intelligent software created in this study could be used for giving an idea about the cervical cancer incidence expected. Like other factors are involved in the process and that are not considered in this study, in addition to imprecision already considered in the data analysis, the system is expandable to other factors.

The goal of this study is to design and perform a pilot investigation which will provide preliminary data. Modern methods of computational intelligence such as fuzzy logic are used to achieve the medical complex analysis. The result of the fuzzy program so far, is a numeric and symbolic terms; using the fuzzy inputs data in the universe of discourse (HPV, Age and number of pregnancy). As the input parameters are characterized by uncertainty, we believe that this tool is very adequate. We emphasize that our fuzzy system is not meant to replace or substitute for an experienced physicians; on the contrary, we envisage that the fuzzy logic system should be viewed as a decision support in the most accurate. Once the established system, it allows to predict the impact of each input and its effect on the output parameter. Assessing the degree of impact allows us to define the set the factor that has the greatest impact in the cervical cancer prevention.

REFERENCES

[1] N Mayinuer, H Sulaiya, H Lili, M Huduyum, H Kundus, W Lin,. *Bosn J Basic Med Sci*, **2016**, 16(1), 46-51.
[2] H Zur hausen, *J natl cancer inst*, **2000**, 3,92(9),690-8.
[3] JM Walboomers, MV Jacobs, MM Manos, FX Bosch, JA Kummer, KV Shah, PJ Snijders, J Peto, CJ Meijer, N Muñoz, *The journal of pathology*, **1999**,189(1), 12-19.
[4] CE Greer, CM Wheeler, MB Ladner, K Beutner, MY Coyne, H Liang, A Langenberg, TS Yen, R Ralston, **1995**, *Journal of clinical microbiology*, 2058-2063.
[5] L Koutsky, Am J Med, **1997**, 5,102(5A), 3-8.
[6] C Thomas, Jr Wright, *Journal of Gynecology and Obstetrics*, **2006**, 94 (1), S22-S31.
[7] World Health Organization, **2015**, WHO Library Cataloguing-in-Publication Data, World health statistics. NLM classification: WA 900.1.
[8] Carlos Andre´s Pen˜a-Reyes, Moshe Sipper. *Artificial Intelligence in Medicine* 17 (**1999**) 131–155
[9] K Bouharati, M Hamdi-Cherif, A Mahnane, S Laaouamri, S Bouaoud, H Boukharouba, O Bouharati, N Boucenna, S Bouharati, **2016**, *Journal of Cancer and Tumor International*, 3(3): 1-8.
[10] F Demir, K Korkmaz, **2008**, Constr. Build Mater 22, 1385-1393.
[11] G Inan, AB Göktepe, K Ramyar, A Sezer, **2007**, *Build Environ*, 42, 1264-1269.
[12] S Boumaiza, S Bouharati, A Bouzidi, M Lalaoui, **2015**, *International Journal of Public Health Research*, 3(6), 352-356.
[13] EH Mamdani, **1977**, *IEEE Transactions and Computers*, C-26, 1182-1191.