Biostatistical Analysis and Possible Forecasting of Relationship Between Uric Acid and Specific Laboratory Tests in Cases of Gouty Arthritis

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Acute gouty arthritis represents an inflammatory response to microcrystals of monosodium urate that precipitate in joint tissues from supersaturated body fluids or are shed from preexisting articular deposits [1]. Gout is a metabolic disease characterized by recurrent episodes of arthritis associated with the presence of monosodium urate crystals in the tissue or synovial fluid during the attack.These forms of crystal-induced arthritis usually affect peripheral joints, including knee, ankle, wrist, and metacarpophalangeal and metatarsophalangeal joints. All of them may be associated with other inflammatory, endocrine diseases [2]. The present study was done to highlight the relationship between increased levels of uric acid and specific laboratory tests in order to possible forecast development of further disease in patients with gouty arthrithis.The present study was done on 34 patients hospitalized in Felix Hospital of Rehabilitation in 2015-2016, with age between 44 and 74, having the main diagnosis of gouty arthritis.We studied the following laboratory tests:urea and other related analysis, like uric acid, creatinine, cholesterol, glutamate pyruvate transaminase and glutamate oxalate transaminase.

Keywords: gouty arthritis, laboratory tests, biostatisical analysis, medication

Acute gouty arthritis represents an inflammatory response to microcrystals of monosodium urate that precipitate in joint tissues from supersaturated body fluids or are shed from preexisting articular deposits [1]. Gout is a metabolic disease characterised by recurrent episodes of arthritis associated with the presence of monosodium urate crystals in the tissue or synovial fluid during the attack. These forms of crystal-induced arthritis usually affect peripheral joints, including knee, ankle, wrist, and metacarpophalangeal and metatarsophalangeal joints. All of them may be associated with other inflammatory, endocrine diseases [2].

Gout - is a chronic disorder caused by the uric acid metabolism disorder that is clinically manifested by recurrent arthritis and the formation of subcutaneous buttocks (tofu) formed from accumulations of monosodic ureic microcrystals [4].

Global data on epidemiological information show that hyperuricemia occurs in 5% of males and 2-3% of women worldwide but only 10% of subjects with hyperuricemia will develop gout. Family predisposition is detectable in 30% of cases [4,5].

In Europe, 0.3% of the population is affected with gout, but in North America only about 0.27% [6.7]. In United Kingdom, gout disease research shows that the prevalence rate of this disease is 1.39%, of which women suffer 3.6: 1 compared to men, this rate decreasing to women during premenopause. The index of the spread for the disease is higher among older people aged 75 years -> 7% for men and > 4% for females [5,7].

Experimental part

Materials and methods

All patients who participated in the study were volunteers and gave their written consent by signing free informed consent, and the study population was selected according to the inclusion and exclusion criteria.

Variables used in present study are uric acid, creatinine, urea, glucose, cholesterol, triglycerides and ESR and are presented in table 1. Corresponding variables are presented also as follows:

Uric acid results from the degradation of nucleic acids, representing the final product of purine metabolism. Urinary acid overproduction occurs in the following situations: excessive catabolism of nucleic acids (gout), mass production and destruction of cells (leukemia) or inability to excrete the final product (renal failure) [8].

Creatinine is creatine anhydride (methylguanidyl acetic acid) and is its release form; Is formed in muscle tissue. A disruption of renal function reduces creatinine excretion, causing elevated serum creatinine. Thus, creatinine concentrations provide an approximation of the glomerular filtration rate [9].

Urea is the main final nitrate product of amino acid metabolism, derived from stomach and intestinal cleavage of proteins under the action of proteolytic ferments and their absorption through the intestinal wall [10-12].

Glucose - is the most important monosaccharide in the blood. It results from the digestion of carbohydrates and the hepatic conversion of glycogen into glucose. Glucagon accelerates the conversion of glycogen into glucose and thus increases blood glucose [10-12]

ALT, alanine aminotransferase or glutamyltransaminase (TGP) is an enzyme that is part of the transferase class and catalyses the reversible transfer of the amino (NH2) group from an α-ketoglutarate amino acid (alanine) resulting in pyruvic acid and glutamate formation [13,14].

AST (TGO) - aspartate aminotransferase is an enzyme that is part of the transaminase class and catalyses the

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transfer of the amino group from aspartate to the ketone ketoglutarate group with oxalacetic acid formation.

ESR is the rate at which the red blood cells in an anticoagulated blood sample sediment in one hour.

Sedimentation of the red blood cells occurs when erythrocytes aggregate as a column. Normally, the blood samples in the blood sample settle down slowly due to their negative surface load, which causes the adjacent cells to reject when the intercellular distance drops below a minimum. In certain diseases that cause the growth of acute phase proteins (α-globulins, fibrinogen) or immunoglobulins, the plasma proteins attach to the surface of the red blood cells and reduce the surface potential causing the aggregation of the red blood cells and increasing their sedimentation [17,18].

As Research Metodology : the data's were taken from the Felix Hospital of Rehabilitation

Variables are as follows:

Y dependent variable are, CREATININE , UREA , CREATININE, GLUCOSE, CHOLESTEROL, TRIGLYCERIDES AND ESR

X independent variable: URIC ACID

Table 1

VALUES FOR THE VARIABLES USED IN PRESENT STUDY : URIC ACID, CREATININE, UREA, GLUCOSE, CHOLESTEROL, TRIGLYCERIDES AND ESR

Nr. crt	URIC ACID	ESR	CREATININE	UREA	GGT	TGO	TGP	GLUCOSE	CHOLESTEROL	TRIGLYCERIDES
1	6.40	15		40				87	189	136
2	6.40	22		36				92	215	209
3	6.40	20		32				89	234	137
4	10.30	45		58.41		130	267	98	210	247
5	8.30	20		35				132	223	209
6	9.70	85	2.7	76.47				72	213	132
7	5.60	34		37		40.79	37.97	78	249.18	215.08
8	6.60	10		23		53.22	56.44	112.58	187	223.92
9	2.30	27		29				82	190	141
10	8.50	43	1.8	68.76	71.42	31.83		117.39	210	154
11	6.10	10		31				89	212	134
12	7.00	7		39			40.27	86	274.77	294.77
13	6.80	12		36				78	210	157
14	13.00	32		21		49.10	55.74	72	180	136
15	6.70	32		36				89	220	142
16	5.00	3		34				88	176	154
17	8.00	32		37		86.56	76.86	138	192	135
18	4.90	20		53.36				85	189	168.5
19	7.30	23		32				129	246	331.14
20	5.60	15		31				79	143	213
21	8.10	28		35			48.66	82	285.73	153
22	6.70	6		36				87	232	150
23	5.90	2		35		46.15	51.6	77	210	240.02
24	5.70	20		29				88	280.77	361.03
25	8.10	22		28		44.6	42.29	85	307.56	164.13
26	3.60	18		34				89	251.98	143
27	5.90	60		35				91	279.64	290.36
28	7.40	23		32				90	232	156
29	7.90	18	1.5	36				80	210	146
30	8.20	22		38				87	210	139
31	6.90	45		32				167.22	176	154
32	14.10	15		48.11				110.8	140	506.45
33	3.50	5		39				98	222	190.85
34	8.30	5		45.96		48.23	53.21	81	276.14	187.76

Statistical analysis

In the present paper an statistical analysis of the relationship between the uric acid, urea, URIC ACID , UREA , CREATININE, GLUCOSE, CHOLESTEROL, TRIGLYCERIDES AND ESR is done . Calculations of statistical values for the variables chosed in simulations are Mean, Median, Standard Deviation, Simply variation Coefficient, Skewness Coeffficient of assymetry, Kurtosis Coefficient, Analysis of clouds of points

- MEAN

The average value - arithmetic mean is determined by reporting the sum of the individual values of the variable to the total number of units in the population and is calculated with the following relation [3]:

$$\bar{X} = \frac{\sum_{i=1}^{k} X_i \cdot N_i}{\sum_{i=1}^{k} N_i},$$

The mean value calculated for the variable x is represented on the second line in table 2

The number of noticedobservations is 34 (k = 34). (values were obtained with the EVIEWS.8 SOFTWARE)

- MEDIAN

Median - The median value is that variable's level for which the number of units between the minimum value of the variable and the median is equal to the number of units between the median value and the maximum value.

The median value is calculated using relationships [3]:

$Me = X_{\left[\frac{N}{2}\right]+1}$, if the population volume, N, is an odd number,

$Me = \frac{X_{\left[\frac{N}{2}\right]} + X_{\left[\frac{N}{2}\right]+1}}{2}$, if the population volume is an even number.

The median value is recorded on the third line of table 2 with results.

Where the results obtained using the Eviews software are recorded:

- the median value for the X (uric acid) variable obtained using the Eviews software is 6.75. It can be argued that for half of the patients studied, uric acid is between 2.3 and 6.7 and in the other half between 6.7 and the maximum value is 14.10;

- the mean value for Y (cholesterol) obtained using the Eviews software is 212.5. It can be said that for half of the patients studied, cholesterol ranges between 39.569 and 212.5 and in the other half between 212.5 and the maximum value being 307.56;

- the mean value for Y (creatinine) obtained using the Eviews software is 1.8. It can be argued that half of the patients studied had creatinine between the minimum value of 1.5 and the median 1.8 and in the other half between 1.8 and the maximum value being 2.7;

- the mean value for Y (glycemia) obtained using the Eviews software is 88.0. It can be argued that half of the patients studied have a blood glucose level between 20.88 and 88.0, and the other half between 88.0 and the maximum value being 167.220;

- the mean value for the Y (TGP) variable obtained using the Eviews software is 156,500. It can be said that for half of the patients studied, TG ranges from 81.263 to 156.500 and in the other half between 156.500 and the maximum value being 506.450;

- the mean value for the Y variable (TGO) obtained using the Eviews software is 48.230. It can be argued that for half of the patients studied, the TGO ranges between the minimum value of 31.83and the median value of 48.230 and in the other half between 48.230 and the maximum value being 130;

- the mean value for the Y variable (TGP) obtained using the Eviews software is 52,405. It can be argued that for half of the patients studied, the TGP ranges between the minimum value of 37,970 and the median value of 52,405 and in the other half between 52,405 and the maximum value being 267;

- the mean value for the Y variable (UREA) obtained using the Eviews software is 35,500. It can be said that for half of the patients studied UREA ranges between the minimum value 11.491 and the median value 35.500 and in the other half between 35.500 and the maximum value recorded is 76.47;

- the mean value for the Y variable (ESR) obtained using the Eviews software is 20,000. It can be said that for half of the patients studied, the ESR ranges between the minimum value of 2.0 and the median value of 20.000 and in the other half between 20.000 and the maximum value that is 85.000.

Standard variation coefficient

The average square deviation (Std.Dev.) - the mean square deviation of a variable is determined by extracting radically from the dispersion, and the dispersion of a variable is the mean value of the squares of variance variations of the variable from the mean value. For the calculation of the dispersion is used the following relation [3]:

$$\sigma_X^2 = \frac{1}{N} \cdot \sum_{i=1}^{N} (X_i - \bar{X})^2$$

And the mean square deviation is calculated with the relationship: $\sigma_X = \sqrt{\sigma_X^2}$

From simulations we obtained the deviation value of the square root for variable x and for the y variable are represented on line 6 of table 2 with statistical data.

The average pedestrian deviation is the variation of the mean to average values.

Simply variation coefficent

The simple coefficient of variation - is calculated using the ratio between the mean square deviation and the mean value [3]: $C_V = \frac{\sigma_X}{\bar{X}} \cdot 100(\%)$

The simple coefficient of variation is used to study the homogeneity of the series, as follows:

- If C_v<40% the considered series is homogeneous;
- If the C_v> 40% series is not homogeneous.

For the variable X (uric acid), the simple coefficient of variation is C_v = 34.563% <40%, so we can conclude that the X series considered is a non-homogeneous series

For the Y variable (cholesterol) the simple coefficient of variation is C_v = 22.699% and we conclude that the series considered: cholesterol is a non-homogeneous series. The same can be said for creatinine, glycemia and urea.

For the variable Y (TG) the simple coefficient of variation is Cv = 42.182%> 40% and we conclude that the series considered: TG is a non-homogeneous series. The same can be said in case of calculations, TGO, TGP and ESR.

Skewness coefficient of assimetry

The coefficient of assimmetry (Skewness) is calculated by the relationship[3]:

$$\alpha = \frac{\bar{X} - Mo}{\sigma_X}$$

We can study the variation of the asymmetry of the series considered:

- If $\alpha < 0$ - we have a negative asymmetry
- If $\alpha = 0$ the series is symmetrical
- If $\alpha > 0$ the asymmetry is positive, which is even more pronounced as á is further than 0.

For the X - uric acid variable, using the software, the value is obtained. $\alpha = 0.724 > 0$

We are dealing with a positive asymmetry

For the Y (cholesterol) variable, using the software, the value is obtained. $\alpha = -1.0318 < 0$

We are dealing with a negative asymmetry. All other Y variables considered have positive values, so we have in each case the positive asymmetries.

The results obtained from the software calculations give the values recorded in table 2 on line 7 (Cv%).

Kurtosis coefficient

The coefficient of curvature (Kurtosis) is calculated with the relationship[19]:

$$\beta_4 = \frac{M(X - \bar{X})^4}{\sigma_X^4} - 3$$

The following interpretation can be made:.

- If $\beta 4 > 3$-Gauss's bell is smaller than the histogram obtained with the Eviews software, the variable considered is Leptocurbal
- $\beta 4 < 3$ - Gauss's bell is higher than the histogram - the variable is Platicurbive

With the EViews software the value is obtained

- for the variable X (uric acid) the obtained value $\beta 4 = 4.716 > 3$ - we have the case of a leptocurbal variable
- for the variable Y (cholesterol) the value obtained $\beta 4 = 6.113 > 3$ - we have the case of a leptocurbinal variable. We can also say about blood glucose, TG, TGO, TGP, urea and ESR
- for the Y variable (creatinine) the value obtained $\beta 4 = 1.5 < 3$ - we have the case of a platicurbive variable. We can also say about calcium.

Tabel 2

THE CALCULATING STATISTICS FOR SELECTED VARIABLES :MEAN, MEDIAN, STANDARD DEVIATION (STD. DEV) AND COEFFICIENT OF SIMPLY VARIATION , SKEWNESS AND KURTOSIS FOR X INDEPENDENT VARIABLE URIC ACID AND Y DEPENDENT VARIABLE: UREA , CREATININE, GLUCOSE, CHOLESTEROL, TRIGLYCERIDES AND ESR

	URIC ACID	CHOLESTEROL	CREATININE	GGT	GLUCOSE	TG_35_160_	TGO	TGP	UREA	ESR
Mean	6.961	214.895	2.000	71.420	92.254	192.441	58.942	73.004	37.179	23.231
Median	6.750	212.500	1.800	71.420	88.000	156.500	48.230	52.405	35.500	20.000
Maximum	14.100	307.560	2.700	71.420	167.220	506.450	130.000	267.000	76.470	85.000
Minimum	2.300	39.569	1.500	71.420	20.882	81.263	31.830	37.970	11.491	2.000
Std. Dev.	2.406	48.781	0.624		23.682	81.176	30.598	69.046	11.996	16.728
Cv(%)	34.563	22.699	31.20	-	25.67	42.182	51.912	94.578	32.265	72.00
Skewness	0.724	-1.0318	0.528		0.570	2.0136	1.603	2.544	1.358	1.667
Kurtosis	4.716	6.113	1.500		6.305	7.7045	4.302	7.717	6.011	6.702
Observations	36	36	3	1	36	36	9	10	36	36

Analysis of points cloud

Analysis of Points cound give us the form of connection.

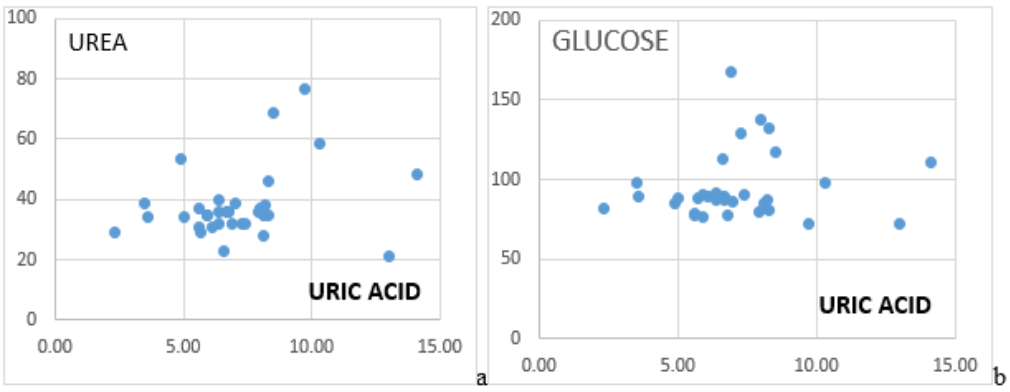

Fig. 1a,b: POINTS CLOUD FOR RELATIONSHIP BETWEEN: URIC ACID, UREA, AND GLUCOSE

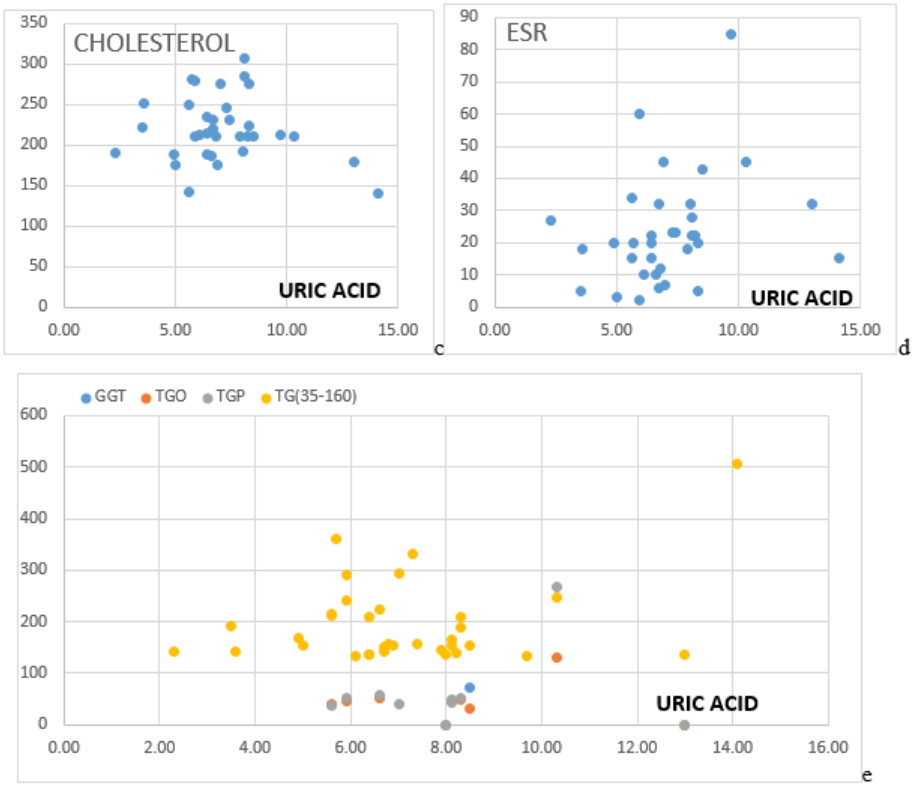

Fig. 1c,d,e : POINTS CLOUD FOR RELATIONSHIP BETWEEN: URIC ACID, CHOLESTEROL, TRIGLYCERIDES AND ESR.

The appearance of the cloud of points gives us the way the points are placed on the graph because there is a link between the variables.

The more clustered the points are, the stronger the link. The closer the points are, the weaker the link.

If the width of the cloud is small, the intensity is large between the variables

If the cloud width is large, the intensity is small between the X and Y variables

The meaning of the link are as follows:

The link can be direct: if Y increases with X's growth

The link can be inverse: if the cloud is oriented right up and down

Fisher test

Fisher test is done to determine the type of the relashionship which can be low, medium or strong intensity.

The characteristic equation for the relashionship can be a polinom of 6-th degrees

$Y = Ax^6 + Bx^5 + CX^4 + DX^3 + Ex^2 + Fx + G$

And the coefficients A,B, …G are given in table 3.

The characteristic equation have the corelation coefficients R2 placed in 3 posible intervals as follows:

- $R^2 \in [0; 0.5]$ - RELATIONSHIP IS LOW (LS)
- $R^2 \in [0, 5; 0.75]$ - RELATIONSHIP IS MEDIUM INTENSITY (LIM)
- $R^2 \in [0.75; 1]$ - RELATIONSHIP IS STRONG (LP)
- The Fisher test involves two stages of work:
- Step 1: Determination of $F_{calc} = \frac{R^2}{1-R^2} \cdot \frac{T-k}{k-1}$
- Step 2: Comparison between Fcalc and Ftab
- Ftab = 4 - for 95% probability data [I.Master, 2008].
- T = 34; 10; 9; 3-is the number of observables and k = 2 the number of estimated parameters
- If Fcalc <Ftab - there is no link between variables at the total data
- Fcalc> Ftab - there is a link between variables at the total data level.

	TYPE OF INTERACTION	A	B	C	D	E	F	G
1	ESR – URIC ACID :	0.0072	-0.3469	-6.6034	-62.839	+314.35	-779.16	757.69
2	UREA – URIC ACID:	0.0062	-0.279	+4.858	-41.364	+179.98	-374.1	+321.47
3	GLUCOSE – URIC ACID:	-0.0041	+0.2132	-4.2901	+42.547	-217.44	+540.18	-419.73
4	CHOLESTEROL - URIC ACID	-0.011	0.5475	-10.819	+107.21	-556.57	1424.1	-1175
5	CREATININe – URIC ACID T=3	-	-	-	-	-	0.678	-3.9036

Table 3
VALUES OF THE COEFFICIENTS A, B, ..., G, CORRESPONDING TO THE CHARACTERISTIC EQUATIONS

6	TG- URIC ACID	0.0294	-1.3698	+25.289	-234.43	+1135.1	-2670.4	+2512.8
7	TGO – URIC ACID: T=9	0.3567	-17.897	+365.54	-3891.3	+22783	-69616	+86850
8	TGP- URIC ACID T=10	1.2652	-63.208	+1287.4	-13692	+80280	-246306	309326

Table 4

DW, R^2, F CALC AND DECISIONS FOR THE CONSIDERED MODEL

	Type of interraction	DW	DW DECISION	R^2	R^2 DECISION	Fcalc	Fcalc DECISION
1	ESR– URIC ACID:	2.298	Negative autocorrelation - good model in forecasting	0.3693	LS	18.753	There is a link between the calculated data
2	UREA – URIC ACID	2.335	Negative autocorrelation - good model in forecasting	0.6273	LIM	53.859	There is a link between the calculated data
3	GLUCOSE –URIC ACID:	2.458	Negative autocorrelation - good model in forecasting	0.1599	LS	6.090	There is a link between the calculated data
4	CHOLESTEROL - URIC ACID:	2.299	Negative autocorrelation - good model in forecasting	0.2557	LS	10.993	There is a link between the calculated data
5	CREATININE – URIC ACID T=3	-	-	0.9918	LP	120.9012	There is a link between the calculated data
6	TG- URIC ACID	2.114	Independent Errors Indecision in forecasting	0.5192	LIM	34.35	There is a link between the calculated data
7	TGO – URIC ACID: T=9	0.059	Positive autocorrelation - the model is not good in predicting	0.8879	LP	55.444	There is a link between the calculated data
8	TGP- URIC ACIDT=10	0.080	Positive autocorrelation - the model is not good in predicting	0.9818	LP	431.5604	There is a link between the calculated data

Conclusion: In our case, it seems that there is always a link between the data considered, and the intensity of the link increases Fcalc. In table 4 are the values of Fcalc.

Table 3 gives the coefficients A, B, ..., G for the regression equations attached to the variables considered.

Durbin watson test

Durbin Watson test is done to verify the independence assumptions.

All the results obtained by applying the Durbin Watson test are in table 4.

Durbin Watson Test is Used to stop if the dependency model of the variables considered, obtained by simulation can be used in predictions or not.

The hypotheses emitted are:

H0: Errors are independent

H1: Errors are dependent

DWcal for each variable: uric acid, urea, compares with $d_1 = 1.72$ and $d_2 = 1.75$ of the Durbin-Watson distribution table depending on a convenient choice between 0.05 and 0.01, depending on the exogenous number of k = 1 And the observed values T = 34. The rule for decision after applying the Durbin Watson Test is presented in table 5.

When we have positive autocorrelated errors, the considered model can not be used in Forecasts

When the errors are neglected, the considered model can be used in the forecasting

Table 5
DECISION MODE FOR THE DURBIN WATSON TEST

$0 \le DW_{calc} \le 1.72$	$1.72 \le DW_{calc} \le 1.75$	$1.75 \le DW_{calc} \le 2.25$	$2.25 \le DW_{calc} \le 2.28$	$2.28 \angle DW_{calc} \angle 4$
Positive Autocorrelation	Indecision	Independent errors	Indecizie	Negative Autocorrelation

Discussions and conclusions

In this paper we presented a study on the biostatistical analysis of URIC ACID, CREATININE, UREA, GLICEMIA, COLESTEROL, TRIGLICERIDE AND ESR and their association with gout arthritis. We calculated and explained for the selected data set the Average value, Median value, Average square deviation, Simple variation coefficient, Skewness and Kurtosis coefficient and was done a Point cloud analysis.Some statistical models have been created.

ESR-URIC ACID, UREA- URIC ACID:, GLUCOSE - URIC ACID:, CHOLESTEROL - URIC ACID:, CREATININE - URIC ACID, TG-URIC ACID, TGO-URIC ACID, TGP-URIC ACID.

It has come to the conclusion that there is a strong link between TGO, TGP and creatinine and uric acid. Also, there are average concentrations of urea, TG and uric acid and TG and uric acid. There are weaknesses between ESR, blood glucose and cholesterol and uric acid, which can also be seen in figure 1 where the cloud of dots is represented. Some statistical models have been created that are good for future forecasting purposes.

The Durbin Watson test was performed and conclusions were drawn regarding the positive or negative autocorrelation mode of the errors and the possibility that the considered model can be used in predictions.

The study concluded that ESR -URIC ACID, UREA- URIC ACID: GLUCOSE- URIC ACID: CHOLESTEROL URIC ACID: are models that have been imposed in the present study as polynomial addicts of the 6th order.

There are strong connection between hyperuricaemia, gout and type 2 diabetes, insulin resistance and metabolic syndrome. This demonstrates the colossal importance for doctors and patients alike to assign gout a *red flag* for increased cardiovascular risk.

The therapy management in gout targets all three stages of the disease, the acute attack, decreasing excessive uric acid levels to prevent burns of gout arthritis and prevent the deposition of urate tissue and also the prophylaxis of acute flares. It is essential to make the difference between the specific therapy needed in order to reduce acute inflammation and the therapy which controls levels of hyperuricaemia in patients with chronic gouty arthritis [23].

The main goal of long-term therapy is to lower the serum urate levels in order to help the dissolution of monosodium urate crystals, to reduce recurrent acute gout attack, to stop storage of sodium urate crystals monohydrate aggregates (tophi) deposited in and around the joints, to prevent joint damage and functional incapacity. According to the 2012 American College of Rheumatology (ACR) Guideline, ULT(urate lowering therapy) is indicated for the following conditions: 1) frequent gout attacks (two or more gout attacks/year), 2) clinically detectable tophi, 3) joint damage from gout, 4) concomitant urate nephrolithiasis, or 5) concurrent chronic kidney disease (stages 2–5, or end stage renal disease).A *treat- to-target* strategy to achieve serum urate level, 6 mg/dL is recommended for all the above patients who do not have clinically signs of tophi or erosive arthritis.Urate level , 5 mg/dL is recommended to improve the symptoms and signs of gout for patients with more severe gout.The ACR Guideline recommends monitoring serum urate level every 2–5 weeks during ULT dose escalation until the target level is achieved and at least once yearly thereafter (more frequently if the gout symptoms remain active).[20,22]

The European League Against Rheumatism (EULAR) established the recommendations for the management of gout for clinical practice published in 2016, which contain 3 general principles and 11 key recommendations as following:Patient education about the pathophysiology of the disease, about its treatment and comorbidities is essential. Understanding the principles of managing acute attacks and eliminating urate crystals by lifelong lowering of the serum urate (SU) below a target level is very important. Guidance about diet, weight, important risk factors, lifestyle, as well as the management of comorbidities is useful. For the treatment of flares, colchicine, nonsteroidal anti-inflammatory drugs (NSAIDs), and oral or intraarticular steroids, or a combination thereof, are recommended. For the patients which present frequent flares and have contraindications to colchicine, NSAIDs, and corticosteroids, an interleukin-1 blocker should be taken in consideration. Urate-lowering therapy (ULT) needs to be discussed from the first presentation and SU levels need to be maintained at levels under 6 mg/dL (360μmol/L), or under 5 mg/dL (300 μmol/L) for those with severe gout. Allopurinol is recommended as first-line ULT with dose adjustment according to renal function. If the SU target cannot be achieved with allopurinol, then febuxostat, a uricosuric, or combining a xanthine oxidase inhibitor with a uricosuric should be considered. All ULTs should be started at low dose and titrated upwards until the SU target is achieved. Unless contraindicated, flare prophylaxis with low-dose colchicine or with NSAIDs at low dosage is recommended during the first 6 months of ULT [21].

Although we have the ACR and EULAR guidelines which recommend the treat-to-target strategy for the management of hyperuricemia, there are different factors, such as patient compliance, inadequate patient education, lack of adherence or deficiency in primary care, that often contribute to poor monitoring and thereby treatment targets may not be achieved.

Gout arthritis is associated with important painful redness and swelling of the affected joints and thereby with reduced quality of life. During the acute gouty attack NSAIDs should be administrated immediately and are preferred associated withnon-pharmacological means such as topical ice andresting of affected joints. [23]

Data in literature shows that gout is associated with significant morbidity and often asymptomatic hyperuricemia has been shown that increases the risk for cardiometabolic and chronic kidney disease. In April 2017 a study made on Japanese adults showed that asymptomatic hyperuricemia (defined as >7 mg/dL in men and e”6 mg/dL in women) was associated with increased cumulative incidence of hypertension, dyslipidemia, chronic kidney disease and overweight/obesity [24].

In order to obtain improved outcome in patients with gout, it is needed to initiate prophylactic anti- inflammatory

medication when starting ULT, monitoring urate serum levels, frequent follow- ups and improved patient education, in order to give a better adherence to therapy.

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