Original article:

Using Two-Layered Feed-Forward Neural Networks to Model Blood Uric Acid Among Diabetic Patients

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Abstract:

Introduction: The end product of purine metabolism in humans is uric acid (UA). Although uric acid can function as either an antioxidant or an oxidant depending on the surrounding environment, the chemical environment can also impact uric acid.The uric acid level in the serum can predict the development of diabetic nephropathy in type 1 diabetes. ***Objective:*** This study aims to determine factors that are perhaps having an association with acid uric. ***Method:*** Variables selection is basedon clinical importance. The most significant variable will be assigned and analyzed using Artificial Neural Network (ANN) through multilayer feed-forward and contour plot. ***Results:*** Through the architecture of MLFF with two hidden layers, it was found that Creatinine level, Urea level, Systolic Blood Pressure reading, Waist circumference reading, Gender play an essential role toward uric level with an accuracy of 97.7% and the predicted mean squared error (MSE.net) is 0.005. The combination of the selected variable showing the highest significance in predicting the level of uric acid. ***Conclusion:*** These findings offer useful future management action plans for patients with diabetes.By controlling these four variables can improve the level of health among diabetic patients.

Keywords: Multilayer Feed Forward Neural Network (MLFFNN), Uric Acid,

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1.0 INTRODUCTION

Serum uric acid has become one of the essential parameters in clinical and researches throughout the world. Monitoring and controlling the serum urate is shown to prevent diabetes mellitus, especially in women patients[1]. Besides, low urate level contains increased blood pressure, abnormal serum lipid, and chronic renal disease. Cardiovascular disease prevention has included serum uric acid as an essential factor. Serum uric acid level can be used as a prediction for the mortality rate among cardiovascular patients. The serum level of uric acid ≥4.7mg/dl increases death risk in this group[2]. Another study showed serum urate ≥7.0 in males and ≥ 5.0 in females are essential in recognizing the mortality rate related to cardiovascular disease[3]. Therefore, the monitoring of serum uric acid level and its treatment is critical for controlling the prognosis.

Even though uric acid is associated with men, more information about uric acid's role in female

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pathologies is becoming available. Serum uric acid, for example, has been linked to female obesity and metabolic syndrome[4]. Type 2 diabetes-related conditions such as cholesterol, fasting blood sugar, glycosylated hemoglobin (HbA1c), and serum uric acid have all been shown to have a positive correlation[5]. The reduction of serum uric acid in this group may reduce the risk for cardiovascular morbidity and other related diseases. At the age of 50, comparably, females have higher waist circumference than males, which speculatively influences the serum uric acid level[6]. The waist circumference should be routinely noted in females above 40, which might be an indicator of abnormal serum uric acid reading.

Interestingly, male waist circumference is not significantly influenced by the serum's uric acid level [7]. This male/waist circumference ratio may be due to the male abdomen's lack of fat storage. Female patients are more likely to develop prehypertension and hypertension due to elevated serum uric acids linked to systolic and diastolic blood pressure [7][1]. A similar finding was also recorded among overweight female patients where their systolic blood pressure is independently related to uric acid [8]. Urea and uric acid are known to increase synergically in both obese males and females [9]. Those patients with elevated uric acid havea higher chance of getting obesity condition[10]. Uric acid influences the dental problem in cardiovascular disease. Elevated serum uric acid/creatinine ratio is found in ischemic heart disease with caries patients [11].

2.0 MATERIALAND METHOD

2.1 Modelling MLFF With Two Hidden Layers Approach

Artificial Neural Networks (ANN) is a computational model based on biological neural networks' structure and functions, also known as neural networks (NNs). An MLFF is a feed-forward artificial neural network with layers between the input, hidden, and output layers. As there is only one dependent variable in this study, this analysis's output node is set at one in the MLFF model. The MLFF with N input nodes, H hidden nodes, and one output node is given in Figure 1.

The values of the hidden node h_j, j =1…3 are given by $h_j = g_1\left(\sum_{j=1}^{3} v_j x_i + E_1\right)$ where v_{ji} the output *weight*, E_1 is the bias[20-23]. The hidden node n_j, j =1…3 are given by $n_j = g_2\left(\sum_{j=1}^{3} v_j h_i + E_2\right)$ where v_{ji} the output *weight* ,E_2 is the bias.

The hidden node Y_j, j =1,2 are given bywhere $Y_i = g_3\left(\sum_{j=1}^{3} v_j n_i + E_3\right)$ v_{ji} the output *weight*, E_3 is the bias.

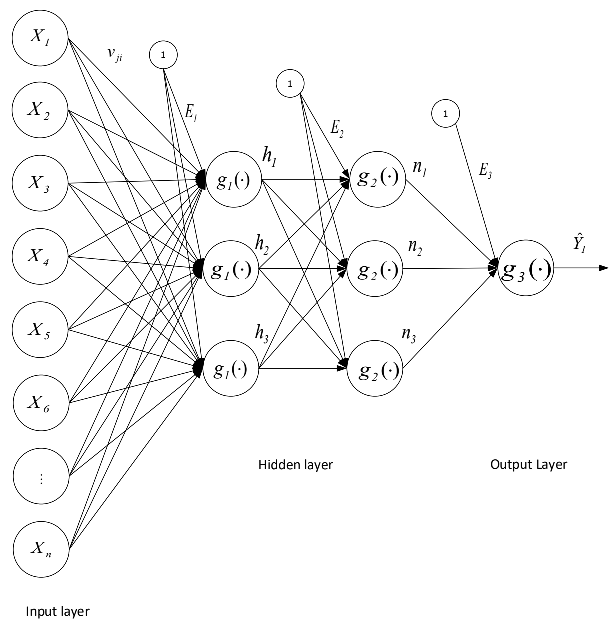

Figure 1.General architecture fortwo-layered feed-forward neural networks

2.2 Contour Plot Analysis Approach

The response can be represented graphically, either in the three-dimensional space or as contour plots that help visualize the response surface's shape. The equation given by ε represents the noise or error observed in the response y $f(X_1, X_2)$ represents the response surface. The response can be represented graphically in a three-dimension, $z = f(x,y)$ surface by plotting constant-z "slices" (contours) on a 2D format. Contours are curves of constant response drawn in the x_i, x_j plane, keeping all other variables fixed [20].

2.3 Data

Data were collected, reviewed, and extracted from the medical unit record, Hospital USM, and the related information. A list of patients diagnosed with hypertension and diabetes was included in the sample frame. In Table 1, all associated variables are collected and summarised.

Table 1. Data Description for the studied variable

Variable	Description
Uric	Reading of Acid Uric
Creatinine	Reading of Creatinine level
Urea	Reading of Urea
Systolic	Reading of Systolic Blood Pressure
Waist circumference	Reading of Waist Circumference
Gender	Patients Gender

3.0 RESULTS

3.1 Result for Modelling MLFFNN With Two Hidden Layers Approach

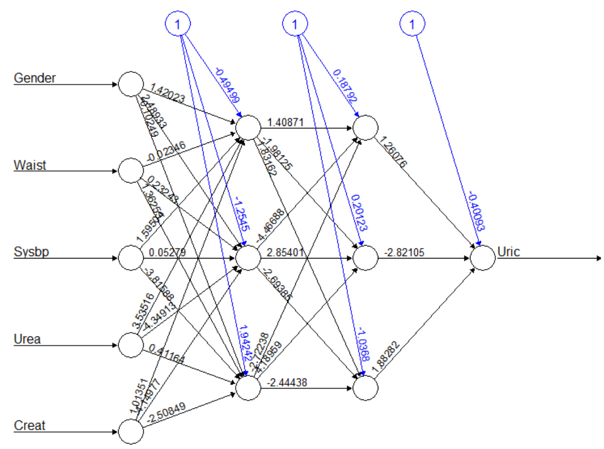

Figure 2.The Architecture of the MLFF with two hidden layers, five input nodes, two hidden nodes and one output node.

Table 2. The Result of Accuracy and Predicted Mean Squared Error.

No	Input Variable	Accuracy	MSE.net
1	Creatinine	0.919	0.203
2	Creatinine, Urea	0.932	0.211
3	Creatinine, Urea, Systolic Blood Pressure	0.900	0.056
4	Creatinine, Urea, Systolic Blood Pressure, Waist circumference	0.904	0.106
5	Creatinine, Urea, Systolic Blood Pressure, Waist circumference, Gender	0.977	0.005

3.2 Result for Male: Countour Plot Analysis Approach.

Part I: Plotting Analysis of Uric Acid vs. Urea Level; Creatinine Level.

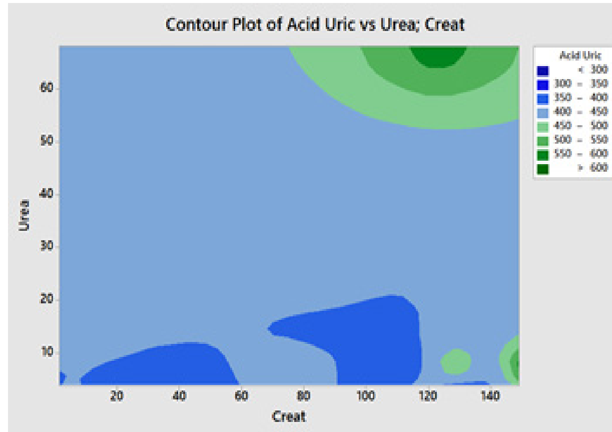

Figure 3. Contour plot of acid uric vs. urea; creatinine male

Figure 3 shows the contour plot of Uric Acid vs. Urea level; Creatinine level. Contour and surface plots indicate that the Uric Acid reading's highest value is achieved when Urea levels and creatinine are high. This area appears in the upper right corner of the contour plot as well as the surface plot. These two factors are Urea levels and creatinine and contribute to the uric acid level in this case.

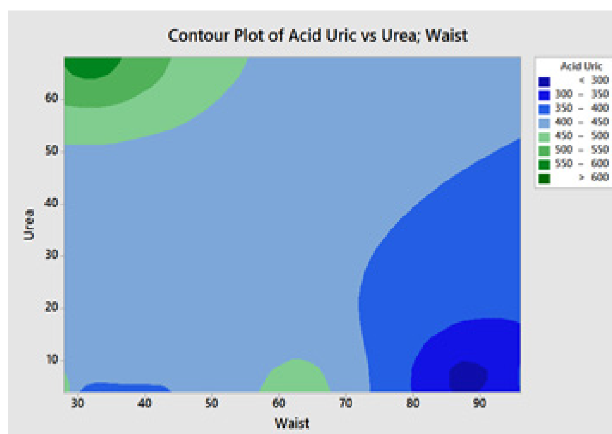

Figure 4. Contour plot of acid uric vs. urea; waist reading male

Figure 4 shows the contour plot of uric acid vs. Urea Level; Waist reading. The contour and surface plots indicate that urea reading's highest value is obtained when Urea Level increases. Waist circumference does not have a relationship with uric acid. This area appears at the upper left corner of the contour plot as well as the surface plot. Among these two factors,the urea level, and waist circumference, the urea level seems to contribute to the uric acid level in this case.

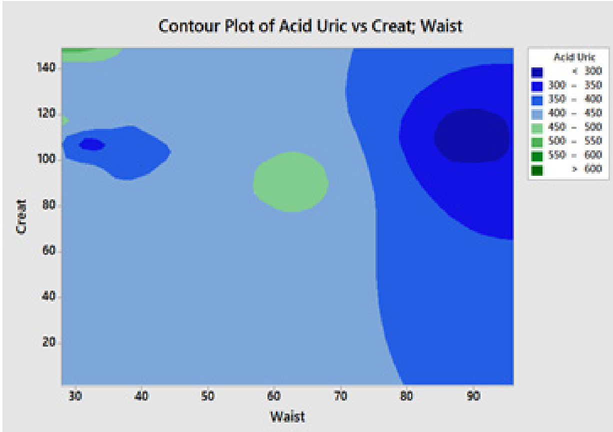

Figure 5. Contour plot of acid uric vs. creatinine; waist reading among male

The contour plot of uric acid vs. creatinine is demonstrated in Figure 5; waist reading.The contour and surface plots indicate that uric acid level does not impact the level of creatinine or the reading of the waist. The waist circumference contour obtained has been studied, and it has been found that the contour does not have a relationship to uric acid level. There is no specific pattern for the particular characteristic of acid uric that can be explained. It can be concluded from this contour plot that these two variables do not associate the acid uric with waist circumference and creatinine level.

3.3. Result for Female: Countour Plot Analysis Approach

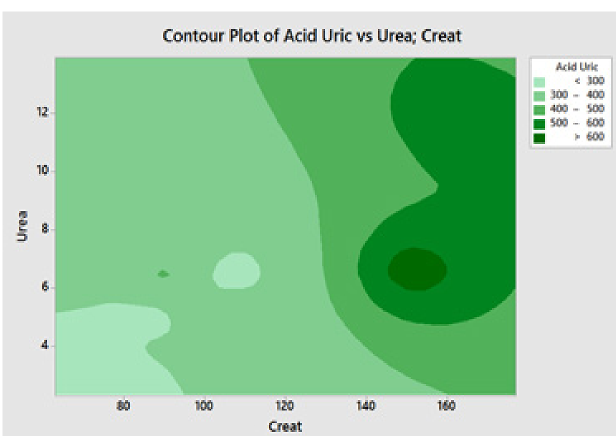

Figure 6. Contour plot of acid uric vs. urea; creatinine level among female

Figure 6 shows the contour plot of uric acid vs. urea level; creatinine level among female patients. The contour plots indicate that when the level of creatinine is high, the highest value of uric acid reading is achieved. On the right side of the outline plot and the surface plot, this area appears. When the urea level increases, it can be seen that uric acid also increases slowly and slowly, spreading the contour width. In this case, both of the factors studied seem to contribute to the uric acid level.

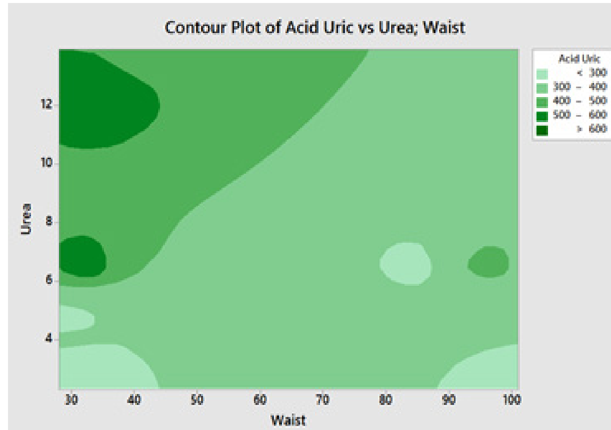

Figure 7. Contour plot of acid uric vs. urea; waist reading female

Figure 7 shows the contour plot of uric acid vs. urea level. Contour and surface plots indicate that the highest uric acid value is obtained when Urea Level is increased. The waist circumference characteristic suggests that uric acid decreased as waist circumference increases. This area appears at the contour plot's upper left corner and the surface plot. In conclusion, uric acid increases when urea levels increase and waist circumference is low. Contour plot characteristics can be seen through the contour plot in Figure 7.

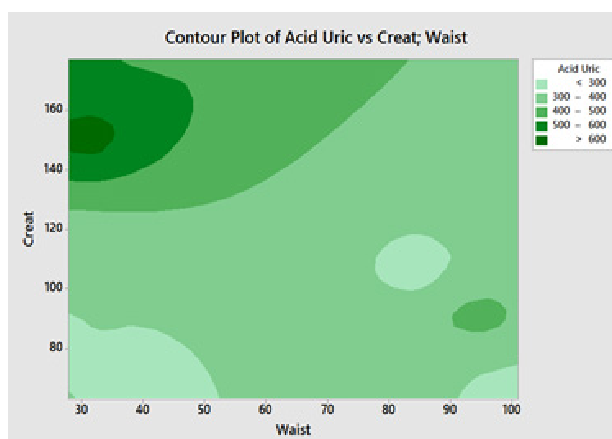

Figure 8. Contour plot of acid uric vs. creatinine; waist reading among male

Figure 8 displays the contour plot of uric acid vs. creatinine; waist circumference reading. The contour and surface plots indicate that if the creatinine level increases, the level of uric acid increases. The characteristic of uric acidshows a decrease when the circumference of the waist increases. The circumference of the waist and the creatinine contour have been studied, and it has been found that the contour has a relationship to the uric acid level. For the particular feature of acid uric, there is a specific pattern that can be explained.The acid uric, with waist circumference and creatinine level having a relationship, can be concluded.

4. 0 SUMMARY AND DISCUSSION

Hyperuricemia refers to a high level of uric acid in the blood. This can lead to gout, a disease in which urate crystals build up in painful joints. It can also cause our blood and urine to become too acidic [12]. A simple blood test can detect the amount of uric acid in our bodies, so it's essential to check on it regularly. Furthermore, the factors that cause high uric acid levels must be controlled, such as the type of food consumed, the amount of alcohol consumed, and so on. The factor contributing to uric acid will be used as input data in this study, and the uric acid level will be used as the study outcome [13]. This paper begins by highlighting the various variables and their possible combinations. The developed MLP methodology will assess the accuracy and predicted mean square error of the selected variables. The accuracy of diabetic patients' uric acid reading prediction was improved by combining creatinine level, urea level, systolic blood pressure reading, waist circumference reading, and Gender. With the smallest predicted mean squared error, the accuracy of prediction level acid uric had improved up to 97.7%. (the smallest value of PMSE, the better result is achieved). The R syntax algorithm was used to develop and coordinate the multilayer feed-forward neural network (MLNN) with two hidden layers. The combination of the variables at number 5 yields the best results. As a result, these five variables can be used to input the modeling procedure for modeling purposes. This technique, which was developed specifically for the decision-maker, resulted in successful research and the best decision-making outcomes.

Acid uric monitoring can adequately predict and help the patient manage any complications such as gout, kidney stones, and many more. The increase in uric acid was associated with an increase in serum creatinine level, which revealed decreased renal function. The serum creatinine and uric acid levels were found to have a significant relationship in this study (p = 0.001). It was observed that with the subjects' serum creatinine levels increasing, uric acid levels also increased [14]. Many studies, such as Barkha Goyal et al.,2017 have found a link between poor glycemic control and creatinine. Uric acid levels are also used as a predictor of cardiac risk, and when they are elevated in people with Type 2 diabetes, they add to the already existing cardiac risk [15]. Uric acid levels rise in women after menopause, increasing their chances of getting gout. The study's findings revealed that uric acid levels were significantly associated with Gender and uric acid excretion. The majority of our study participant males (65.22 percent) had uric acid levels of 7.4, while the rest (34.78 percent) had groups of 3-7.4. The uric acid of most of our study participant females (80.39 percent) had levels of 6.3, while the rest (19.61 percent) had levels of 2.1-6.3. Uric acid levels averaged 9.53 ± 04.38.

There was a significant correlation between serum uric acid and blood urea nitrogen and serum creatinine. Groups with a higher level of serum uric acid had an increased risk of renal function impairment. Serum uric acid levels correlated with linear pattern creatinine (F=159.470, P<0.001) and blood urea nitrogen (F=165.059, p<0.001), respectively. Overall, as expected, it was a positive correlation between the right serum uric acid and the serum urea levels in patients with chronic renal failure. The correlation coefficient, r, was 0.638 (with a significance level of 0.001) [16].

Prehypertensive individuals had the highest mean uric acid concentration, which was significantly higher than normotensives (p=0.0001).There was a significant positive correlation between the level of uric acid and both systolic and diastolic blood pressure (P<0.0001; P<0.0001), respectively. In conclusion, it observed a significant positive association between uric acid with both systolic and diastolic blood pressure after controlling for confounding factors. The association was most evident in people with hypertension. We also observed a significant negative association between uric acid and age on hypertension[17].

After adjusting for age and Gender, correlation analysis revealed that uric acid was positively correlated with height, weight, BMI, waist circumference, hip circumference, fat mass (FM), and free fat mass (FFM).In this study, the level of SUA was found to have a significant positive correlation with systolic and diastolic blood pressure in males. All measured obesity indices (waist circumference (WC), body mass index (BMI), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR)) were also significantly positively correlated. The serum uric acid level (SUA) is linked to both systolic and diastolic blood pressure and WHR. WHR had an independent relationship with uric acid among all obesity indices[18].In the Chinese population, the risk of prediabetes increased dramatically as SUA increased. This link was found to be stronger in older females (48 years old) than in younger females, possibly pointing to pathogenic mechanisms underlying gender differences in the association between SUA and prediabetes[19].

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Conflict of Interest: None

Data availability: All data are available within the manuscript. Raw data can be given upon reasonable request.

Author's contribution:

Data gathering and idea owner of this study:WMAWA, FMMG, NMMN,NAA.

Study design: WMAWA, FMMG, NMMN, NAA.

Data gathering: WMAWA, FMMG, NMMN, NAA.

Writing and submitting manuscript: WMAWA, FMMG, NMMN, NAA and MKA

Editing and approval of final draft:WMAWA, FMMG, NMMN, NAA and MKA

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