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Research Article

RELATION BETWEEN POLYCYSTIC OVARY SYNDROME (PCOS) AND BULIMIA NERVOSA: CASE STUDY, RESPONSE SURFACE METHODOLOGY AND ARTIFICIAL INTELLIGENCE NEURAL NETWORKS (ANNS)

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Abstract:

Objective To examine the relation between polycystic ovary syndrome (PCOS) patients and bulimia represented in age, social status, national residency, chronic diseases, current medication, depression diagnosis and GAD diagnosis for the non-pregnant and non-breastfeeding patient.

Methods using dot plot curve to explore the relationship between patient parameter and bulimia nervosa disease (n=217), detecting significant variables by using linear regression analysis and make RSM relation equation between bulimia nervosa and other variables and to build the networks architecture between input covariables and output bulimia nervosa results multi-layer perceptron (MLP) neural networks.

Results indicated that about 8.8% of polycystic ovary syndrome (PCOS) patients suffering from bulimia nervosa. Age parameter is a significant variable for bulimia nervosa with an average age of 29.8947 ± 6.4227 . status and Diagnosis Date for PCOS patients are non-significant for bulimia nervosa investigations (p-value > 0.05). All positive bulimia nervosa patients came from Buraydah and Unayzah residency. The results indicated that chronic diseases represented in Diabetes, thyroid disease and hypothyroidism have a relation with bulimia nervosa disease. Also, Duphaston, thyroxin and diabetes medication have a relation with bulimia nervosa disease. About 26.3% of depressed patients and 73.7% of GAD patients have bulimia nervosa.

Conclusion RSM and ANN results indicated that the Age variable is the most significant variable for bulimia nervosa prediction followed by Residency, medication, Chronic Type and Depression Diagnosis with moderate significance. Finally, PCOs Diagnosis Date and GAD Diagnosis are not significant for bulimia nervosa disease.

Keywords: Bulimia nervosa; polycystic ovary syndrome; neural networks; chronic diseases; Age; Sex; Eating disorders

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INTRODUCTION:

Bulimia Nervosa (BN) and polycystic ovary syndrome (PCOS) are commonly found in a quarter of the women population [1]. About 21% of the females have bulimia nervosa diagnosis [2]. About 1.5% of teenage women have Bulimia Nervosa [3] Bulimia nervosa affects teenage women and can be fully recovered after 5 to 10 years from initial diagnosis by a rate of 50% [4, 5]. About 26% of the females have polycystic ovary syndrome (PCOS) [6]. There is a strong relationship between polycystic ovary syndrome (PCOS), eating disorders and lifestyle. Thannickal et al 2019 studied the relation between PCOS with sleeping, eating and sexual disorders in women and the obtained results indicated that the PCOS women were more expected to have sleep disorders, lower sexual satisfaction and may be affected on bulimia nervosa [7]. Different researches have reported an enlarged the frequency of PCOS patients with bulimia nervosa, but these studies have not been verified on a large scale [8, 9]. Studies including 212 and 269 patients proved significant association between bulimia nervosa and PCOS [7]

The aim of this study to overcome of the existing limitations of polycystic ovary syndrome (PCOS) and bulimia nervosa by addressing the relation between bulimia nervosa and age, social status, national residency, chronic diseases, current medication, depression diagnosis and GAD diagnosis for the non-pregnant and non-breastfeeding PCOS patients. Also, to arrange the previous variables according to its importance. Finally, to estimate the predicted bulimia nervosa estimated equation by applying the value of previous parameters.

METHOD:**Design:**

The study was carried out at Maternity and Children Hospital in Buraydah, Qassim, Saudi Arabia. MCH provides specialized medical care in the field of Obstetrics and Gynecology, which is not available in other hospitals in Buraydah city. All patients who are diagnosed clinically by endocrinologists or gynecologists using Rotterdam Criteria with polycystic ovary [PCOS] and who are enrolled in MCH hospital were included in this study. This is a hospital-based cross-sectional study involved 217 patients with PCOS, attending the outpatient department [OPD] of oby-gyne clinics from March to June 2018. A valid and reliable Questionnaire Arabic version of PHQ-Eating Disorder self-administrative was used in data collection.

Ethics statement:

All patients provided oral informed agreement and the studies were accepted by the regional research ethics committee of Qassim province.

Sample selection and interview procedure:

Inclusion criteria included PCOS patients in reproductive age from 18 to 45 years old. We excluded patients suffering from autoimmune illnesses, major cardiovascular, liver, kidney or digestive diseases, and patients who had received oral medications [oral steroids, androgens, or anti-epileptics], pregnant and lactating females, and patients with a family history of psychiatric disorder.

We evaluated the patients using Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition [DSM-V] criteria. We used a self-administered Patient Health Questionnaire, The Arabic Version, because it is a valid and reliable tool to screen for depression, anxiety, eating, and panic disorders in a Saudi sample based on a study called, An Arabic translation, reliability, and validation of Patient Health Questionnaire in a Saudi sample.

Statistical analysis:**Neural network structure:**

Artificial neural networks (ANNs) were developed to predict Bulimia Nervosa, which consists of (10) input layers, (2) hidden, and (3) output layers. The network structures were expressed as 10 – 2 – 1. The data from the ten independent variables are transferred to the input layer and typically divided into standard results for training, testing and validation procedures. The network type is “Multilayer perceptron backpropagation”. The multilayer perceptron uses a feedforward architecture and can have multiple hidden layers and It is one of the most commonly used neural network architectures.

Response surface methodology:

The RSM plots show a simultaneous confidence band for the fitted response surface. A chart was plotted that displaying a contour of RSM for Bulimia Nervosa prediction against the independent variables for non-pregnant and non-breastfeeding PCOs Patients. A pure-linear regression model was employed to describe the RSM plots by fitting the experimental data.

$$Y = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_3x_3 + \beta_4x_4 + \beta_5x_5 + \beta_6x_6 + \beta_7x_7 + \beta_8x_8 \quad \text{Eq. 1}$$

Where, Y is the predicted Bulimia Nervosa [(1) yes and (2) No]; x_1 is Age [(14 – 45)]; x_2 is Residency [(Buraydah(1), Unayzah(2), Uyun Al Jawa(3), Afif(4), alrass(5), Al Mithnab(6), Al Bukayriyah(7), Uglat

Asugour(8), Dariyah(9), Al Asyah(10), Hail(11), Al Quwarah(12) and Al Rubayiyah(13)]; x_3 is Status [(1) Single, (2) Married and (3) divorced]; x_4 is Chronic Diseases [(1) yes and (2) No]; x_5 is Current medication[(1) yes and (2) No]; x_6 is Diagnosis Date [(0 - 248 month)]; x_7 is Depression Diagnosis [(1) no depression, (2) moderate, (3) severe to moderate depression and (5) mild depression, (6) severe depression]; x_8 is GAD Diagnosis [(1) mild GAD, (2) sever GAD, (3) moderate GAD and (4) No GAD]. β_0 is the model intercept; $\beta_1, \beta_2, \beta_3, \beta_4, \beta_5, \beta_6, \beta_7$ and β_8 are the linear coefficients of $x_1, x_2, x_3, x_4, x_5, x_6, x_7$ and x_8 , respectively.

RESULTS AND DISCUSSION:

Case studies for PCOS patients on bulimia nervosa disease:

Effect of age and social status:

Numerous ages and social status from PCOS patients were selected for bulimia investigation $n=217$ represented in Table 1. The results of the bulimia investigation test indicated that only 19 patients were positive bulimia nervosa within ages of 29.89 ± 6.42 years. Figure 1 shows the relation between PCOS patient ages and social status against bulimia nervosa disease. Jahanfar et al 1995 studied the connection between bulimia nervosa and patients with PCOS and without PCOS into two groups using different parameters. The obtained results indicated that the age parameter was 30.42 ± 8.59 years for non-PCOS and 27.55 ± 9.31 years for PCOS showing an agreement with the obtained results [1].

Table 1. The percent of PCOS patient ages and status for positive bulimia investigation test

Ages	Count	%	Ages	Count	%	Ages	Count	%
14	2	0.92	26	13	5.99	36	9	4.15
16	1	0.46	27	7	3.23	37	9	4.15
18	7	3.23	28	14	6.45	38	9	4.15
19	3	1.38	29	10	4.61	39	6	2.76
20	5	2.30	30	15	6.91	40	9	4.15
21	3	1.38	31	8	3.69	41	4	1.84
22	8	3.69	32	12	5.53	42	2	0.92
23	9	4.15	33	10	4.61	43	2	0.92
24	6	2.76	34	9	4.15	44	1	0.46
25	10	4.61	35	10	4.61	45	4	1.84
Positive bulimia investigation test (Ages)								
29	40	26	28	41	27	21	36	37
20	27	28	33	25	19	34	28	30
40								
Average age				29.8947				
Standard deviation				6.4227				
Status								
Status			Count			%		
Married			145			66.8		
Single			64			29.5		
Divorced			8			3.7		
Positive bulimia investigation test								
Married			Single			Divorced		
63.15%			31.57%			5.26%		

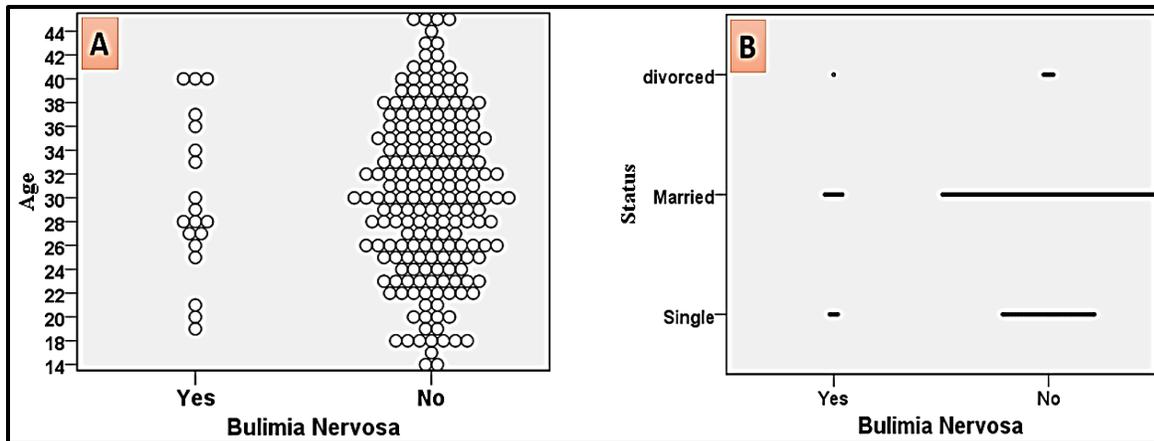


Figure 1. A) Relation between PCOS patient ages and bulimia nervosa disease, B) Relation between PCOS patient social status and bulimia nervosa disease.

Effect of national residency:

The effect of national residency from 13 places from Saudi Arabia and the participated patients were 76.6% from Buraydah, 14.8% from Unayzah, 3.6% from Alrass and Al Asyah, 1.9% from Uyun Al Jawa and Hail, and 3.1 % from Afif, Al Quwarah, Al Bukayriyah, Dariyah, Uglat Asugour and Al Mithnab. The obtained results indicated that residency was a significant variable for bulimia investigation and all

PCOS with bulimia nervosa patients were condensed in Unayzah and Buraydah as shown in Figure 2. That is may occur because of the variety of lifestyle and eating disorder behaviors. Deborah et al 2014, studied eating disorder behaviors with demographic profile changing by collecting different data of age, sex, residency and the obtained results indicated a significant relationship between residency and Quality of life which is reflected in Nervosa diseases [10].

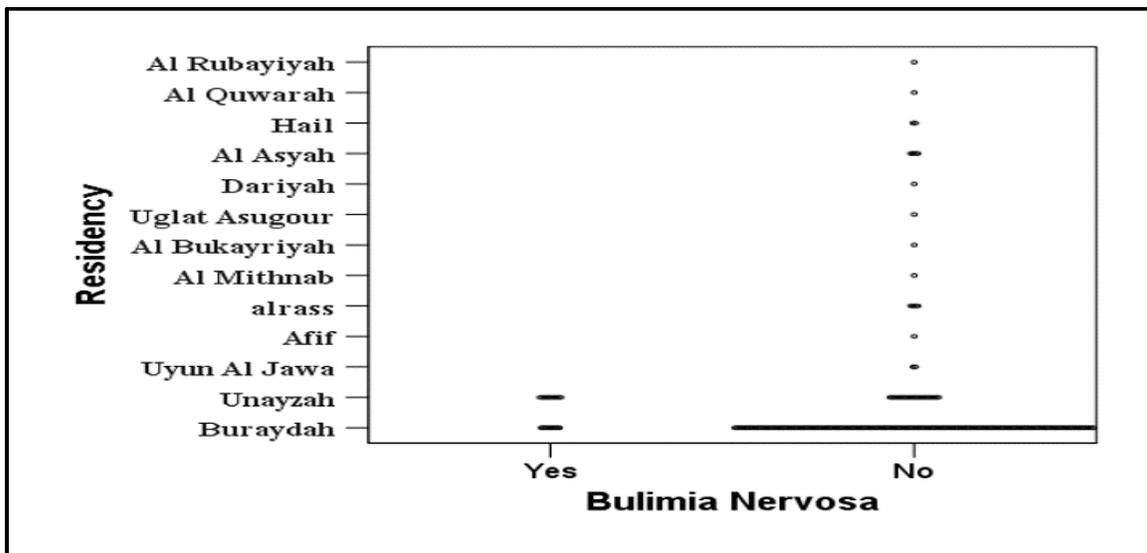


Figure 2. The relation between PCOS patient national residency and bulimia nervosa disease

Effect of chronic diseases and chronic type:

The effect of chronic diseases and chronic type were studied. The results indicated that 15% from total PCOS patient have chronic diseases as hypothyroidism 41.2%, thyroid disease 14.7%, Hypertension 8.8%, Asthma 8.8%, Anemia 2.9%, Diabetes 11.8%, Diabetes associated with Hypertension 5.9%, thyroid disease associated with

anemia 2.9% and other 2.9 %. The results indicated that Diabetes, thyroid disease and hypothyroidism have a relation with bulimia nervosa disease. Figure 3 describes the relationship between chronic diseases and bulimia nervosa disease and the relation between the type of chronic disease and bulimia nervosa disease.

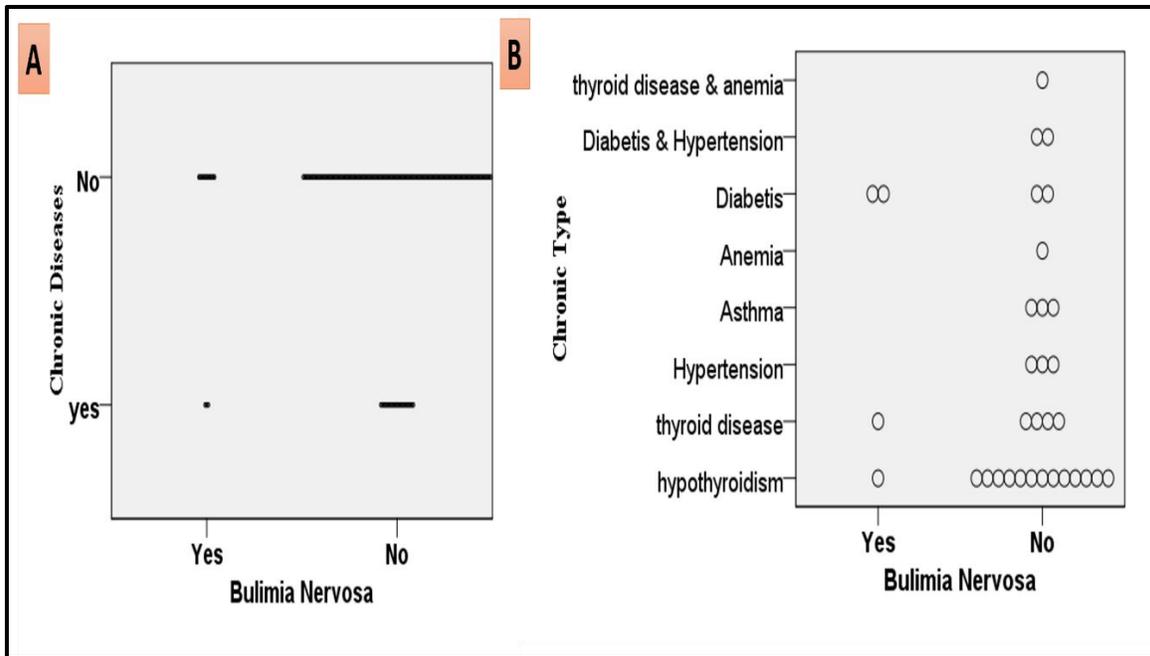


Figure 3. A) The relation between chronic diseases and bulimia nervosa disease, B) The relation between chronic diseases type and bulimia nervosa disease.

Effect of current medication:

The effect of current medication on bulimia nervosa disease was studied. The result indicated that there was about 35 type of medications used by PCOS patients and the medication which have relation was Duphaston, thyroxin and diabetes medication as shown in Figure 4.

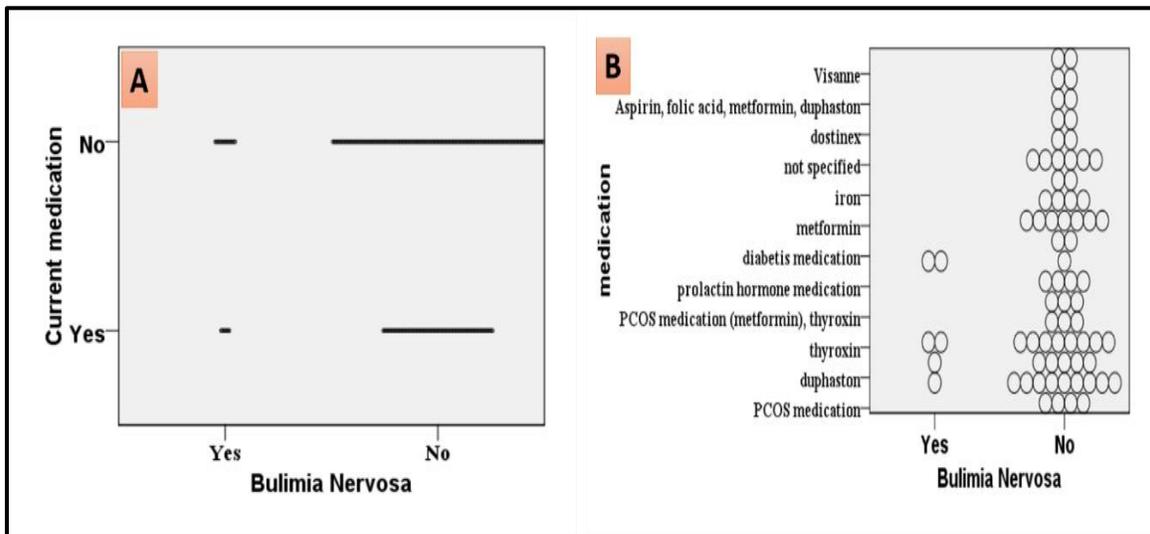


Figure 4. A) The relation between current medication and bulimia nervosa disease, B) The relation between medication type and bulimia nervosa disease.

Effect of depression and GAD diagnosis:

The effect of depression diagnosis on PCOS patients (n=217) was studied and classified into five categories no depression, moderate, sever to moderate and severe depression. The result indicated that only 23.5% have

depression diagnosis (n=51). The patients have depression diagnosis with bulimia nervosa disease was 9.8% from total depressed patients (n=5) and 26.3% from bulimia nervosa patients (n=19) as shown in Figure 5A. The difficulties of depression diagnosis

associated with bulimia nervosa patients was 21.1% find very difficult (n=4), 52.6% find not difficult at all (n=10), 26.3% find it somewhat difficult (n=5).

The effect of GAD diagnosis on PCOS patients was studied and classified into four categories mild, sever, moderate and no GAD. The result indicated that 66.4% of total PCOS patients have GAD diagnosis (n=140). The GAD diagnosis patients associated with bulimia nervosa disease was 10% of total GAD

diagnosis patients (n=14) and 73.7% of associate bulimia nervosa patients (n=19), as shown in Figure 5B. The GAD diagnosis with bulimia nervosa patients has 21.1% moderate GAD, 10.5% sever GAD, 42.1% mild GAD and 26.3% no GAD. The difficulties of GAD diagnosis associated with bulimia nervosa patients was 52.6% find somewhat difficult (n=10), 36.8% find not difficult at all (n=7), 10.5% find it very difficult (n=2).

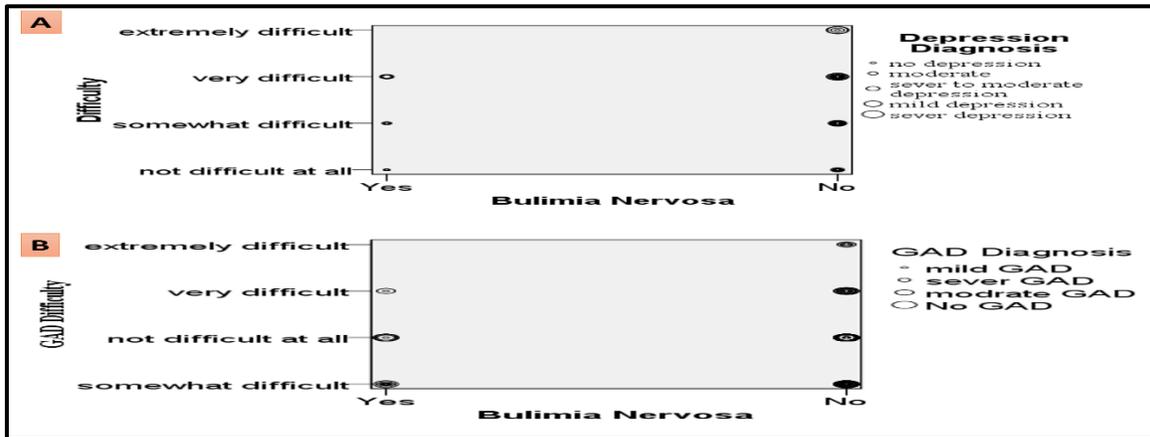


Figure 5. A) The relation between depression diagnoses and bulimia nervosa disease, B) The relation between GAD diagnosis and bulimia nervosa disease.

Response surface methodology (RSM):

Linear regression analysis was conducted for bulimia nervosa disease as a dependent parameter with GAD Diagnosis, Chronic Diseases, Depression Diagnosis, Diagnosis Date, Residency, Status, Current medication, Age as Predictors by using Enter methods[11]. The obtained results indicated that the model was significant (p-value <0.05) to describe the relation between bulimia disease and other variables as shown in Table 2.

Table 2. ANOVA test between Bulimia Nervosa as Dependent Variable and predictors.

ANOVA ^a						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	17.765	8	2.221	29.174	.000 ^b
	Residual	501.315	6586	.076		
	Total	519.081	6594			

a. Dependent Variable: Bulimia Nervosa

b. Predictors: (Constant), GAD Diagnosis, Chronic Diseases, Depression Diagnosis, Diagnosis Date, Residency, Status, Current medication, Age

The significance test indicated that Age, Residency, Chronic Diseases, Current medication, Diagnosis Date and Depression Diagnosis were significant variable (p-value < 0.05) for positive Bulimia Nervosa test while Status and GAD Diagnosis were not significant for positive Bulimia Nervosa test as shown in Table 3.

Table 3. The B statistics, t-value and p-value for case study variables and Bulimia Nervosa disease.

		Coefficients ^a				
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
	(Constant)	1.745	.030		59.012	.000
	Age	.004	.001	.100	6.663	.000
	Residency	.004	.002	.030	2.423	.015
	Status	-.014	.008	-.024	-1.712	.087
1	Chronic Diseases	.067	.010	.091	6.442	.000
	Current medication	-.037	.008	-.064	-4.540	.000
	Diagnosis Date	-.001	.000	-.159	-12.533	.000
	Depression Diagnosis	.017	.003	.063	5.085	.000
	GAD Diagnosis	.001	.003	.005	.380	.704

a. Dependent Variable: Bulimia Nervosa

Equation 2 showed the all-regression models (significant and insignificant). For simplicity, the insignificant factors were excluded, and a new regression model was obtained (**Equation 3**):

$$Y = 1.745 + 0.0048x_1 + 0.0046x_2 - 0.014x_3 + 0.067x_4 - 0.037x_5 - 0.001x_6 + 0.017x_7 + 0.001x_8 \quad \text{Eq.2}$$

$$Y = 1.745 + 0.0048x_1 + 0.0046x_2 + 0.067x_4 - 0.037x_5 - 0.001x_6 + 0.017x_7 \quad \text{Eq.3}$$

Where, Y is the predicted Bulimia Nervosa [(1) yes and (2) No]; x_1 is Age [(14 - 45)]; x_2 is Residency [(Buraydah(1), Unayzah(2), Uyun Al Jawa(3), Afif(4), alrass(5), Al Mithnab(6), Al Bukayriyah(7), Uglat Asugour(8), Dariyah(9), Al Asyah(10), Hail(11), Al Quwarah(12) and Al Rubaiyah(13)]; x_3 is Status [(1) Single, (2) Married and (3) divorced]; x_4 is Chronic Diseases [(1) yes and (2) No]; x_5 is Current medication[(1) yes and (2) No]; x_6 is Diagnosis Date [(0 - 248 month)]; x_7 is Depression Diagnosis [(1) no

depression, (2) moderate, (3) sever to moderate depression and (5) mild depression, (6) severe depression]; x_8 is GAD Diagnosis [(1) mild GAD, (2) sever GAD, (3) moderate GAD and (4) No GAD]. β_0 is the model intercept; $\beta_1, \beta_2, \beta_3, \beta_4, \beta_5, \beta_6, \beta_7$ and β_8 are the linear coefficients of $x_1, x_2, x_3, x_4, x_5, x_6, x_7$ and x_8 , respectively.

Artificial intelligence Neural Networks (ANNs):

ANNs were trained using the back-propagation algorithm using sample training 78.6 % and testing 21.4 % for 28 valid results with a total number of 28 runs. The network trained by making a continuous process connection between weight and bias in which the network is implanted as shown in Figure 6 with Rescaling Method for Covariates Standardized test, activation Function -Hyperbolic tangent-test, the sum of squares error was 1.977 and relative error 0.188.

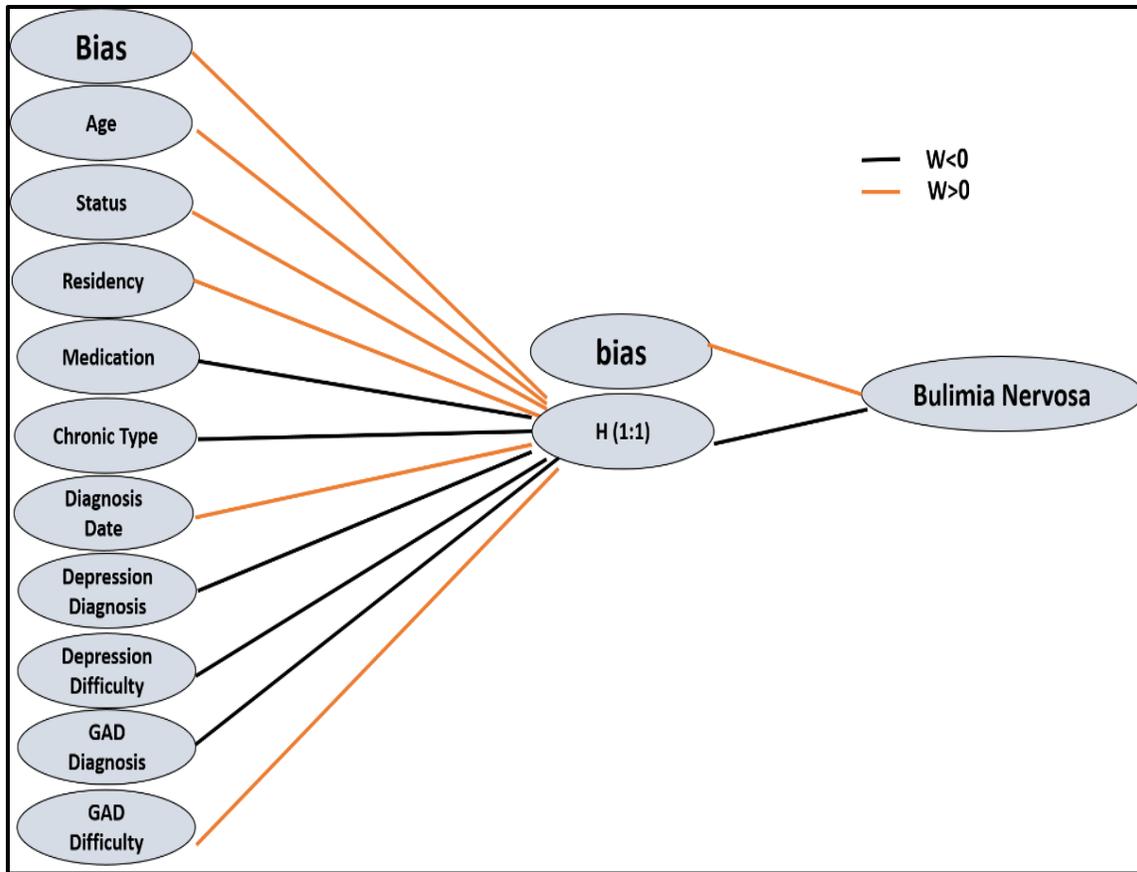


Figure 6. Neural Network structure between variables and Bulimia Nervosa

Results showed that there is small deviation between the predictive values and normalized value as shown Figure 7.

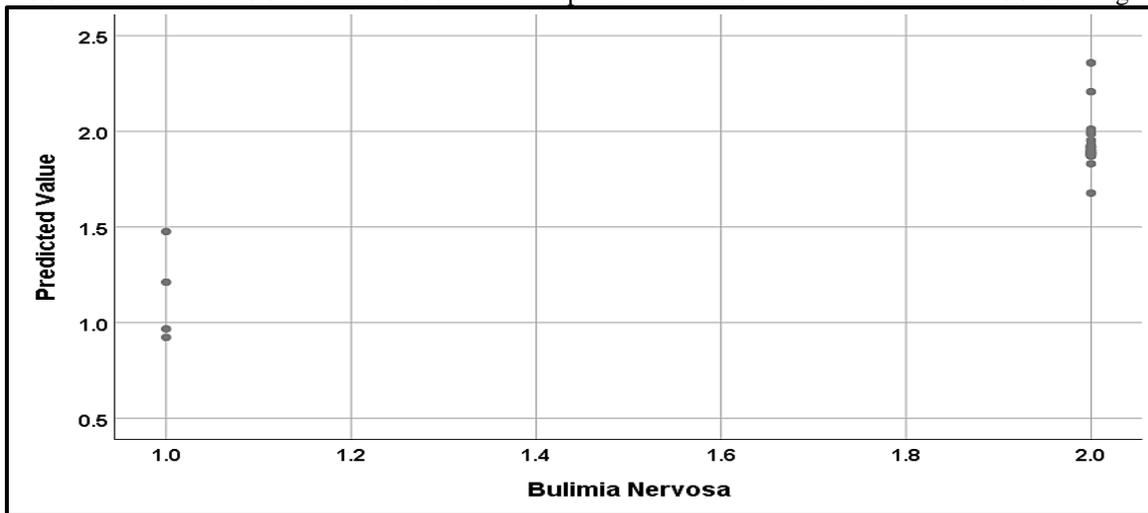


Figure 7. The relation between the predicted value and Bulimia Nervosa (1=yes and 2-No)

Also, there is a small deviation between the residual value and predictive value (-0.4, +0.2 %) indicating the reality of the result and the effectivity of model results to describe the relation between Bulimia Nervosa and other variables.

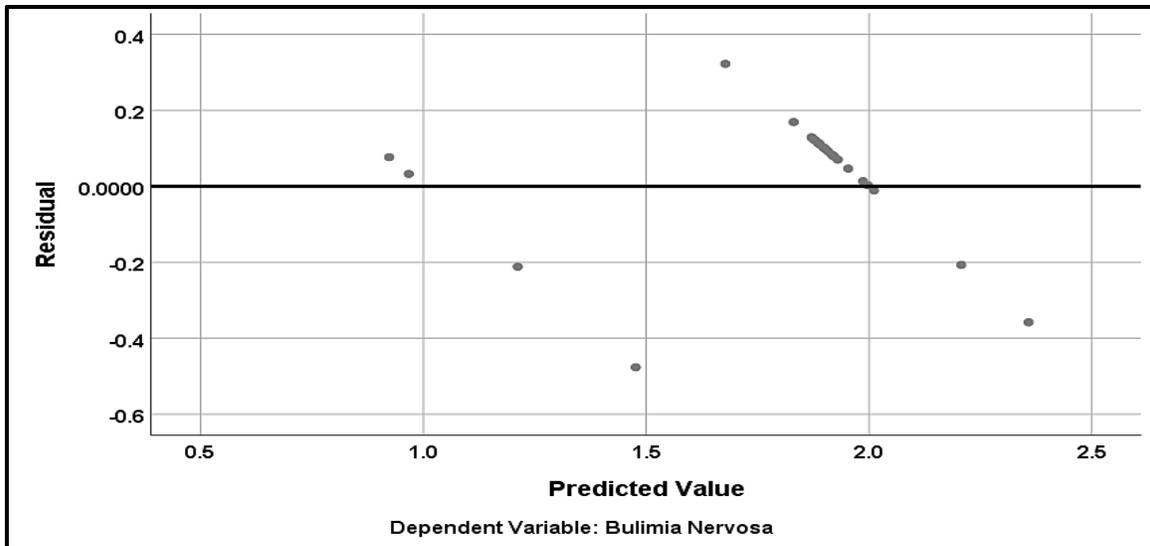


Figure 8. The relation between the predicted value of Bulimia Nervosa (1-yes and 2-No) and residual

Figure 9. ranks the importance of each variable indicating that the Age effect is the most effective parameter showed 100% importance, Residency, medication, Chronic Type and Depression Diagnosis showed about 50% importance. While the Diagnosis Date and GAD Diagnosis are not important as shown in Table 4 showing agreement with RSM results

Table 4. Importance and normalized importance variables against Bulimia Nervosa.

Independent Variable Importance		
	Importance	Normalized Importance
Age	.218	100.0%
Status	.063	29.0%
Residency	.121	55.6%
medication	.108	49.7%
Chronic Type	.111	51.1%
Diagnosis Date	.015	6.8%
Difficulty	.085	39.1%
Depression Diagnosis	.123	56.5%
GAD Diagnosis	.025	11.3%
GAD Difficulty	.132	60.4%

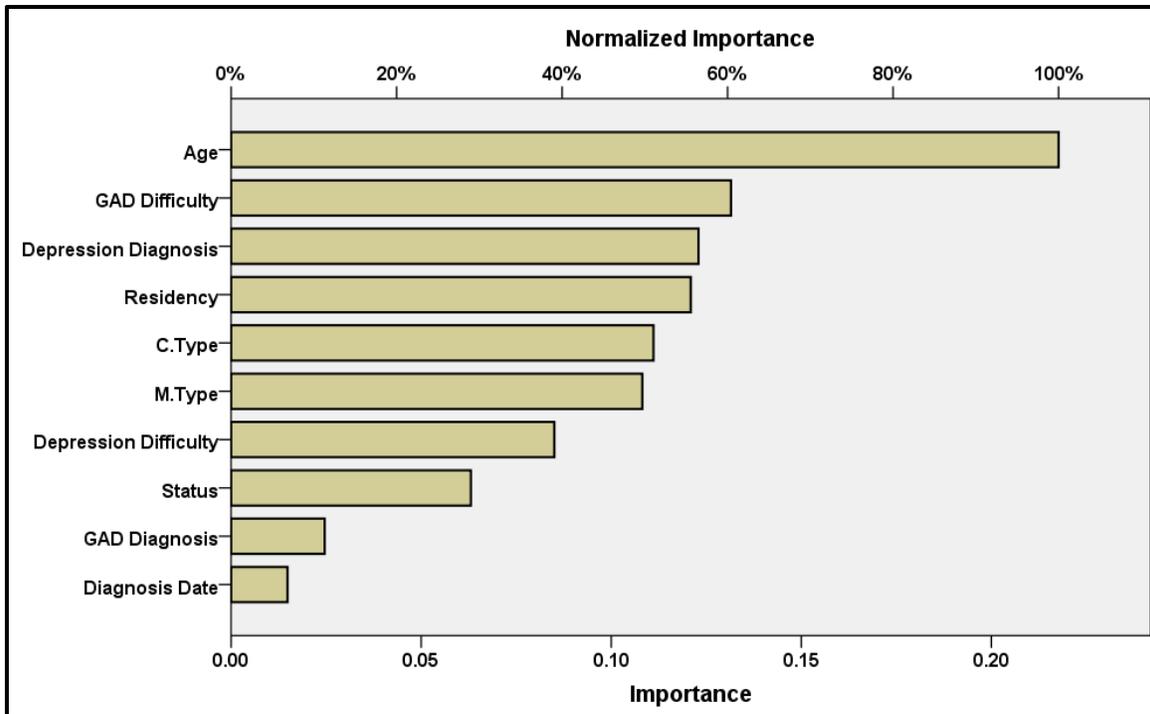


Figure 9. importance and normalized importance for each covariable

CONCLUSION:

The result concluded that, 8.8% of polycystic ovary syndrome (PCOS) patients suffering from bulimia nervosa within age 29.8947 ± 6.4227 , Mainly condensed in Buraydah and Unayzah residency, the most relative chronic diseases was Diabetes, thyroid disease and hypothyroidism, the relative medications was Duphaston, thyroxin and diabetes medication and 26.3% of depressed patients, 73.7% of GAD patients have bulimia nervosa. Finally, we can estimate the bulimia nervosa investigation test by applying the predicted RSM equation.

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