ORIGINAL ARTICLE

Cost prediction of antipsychotic medication of psychiatric disorder using artificial neural network model

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Background: Antipsychotic monotherapy or polypharmacy (concurrent use of two or more antipsychotics) are used for treating patients with psychiatric disorders (PDs). Usually, antipsychotic monotherapy has a lower cost than polypharmacy. This study aimed to predict the cost of antipsychotic medications (AM) of psychiatric patients in Iran. **Materials and Methods:** For this purpose, 790 patients with PDs who were discharged between June and September 2010 were selected from Razi Psychiatric Hospital, Tehran, Iran. For cost prediction of AM of PD, neural network (NN) and multiple linear regression (MLR) models were used. Analysis of data was performed with R 2.15.1 software. **Results:** Mean ± standard deviation (SD) of the duration of hospitalization (days) in patients who were on monotherapy and polypharmacy was 31.19 ± 15.55 and 36.69 ± 15.93, respectively ($P < 0.001$). Mean and median costs of medication for monotherapy ($n = 507$) were $8.25 and $6.23 and for polypharmacy ($n = 192$) were $13.30 and $9.48, respectively ($P = 0.001$). The important variables for cost prediction of AM were duration of hospitalization, type of treatment, and type of psychiatric ward in the MLR model, and duration of hospitalization, type of diagnosed disorder, type of treatment, age, Chlorpromazine dosage, and duration of disorder in the NN model. **Conclusion:** Our findings showed that the artificial NN (ANN) model can be used as a flexible model for cost prediction of AM.

Key words: Linear regression, neural networks, psychiatric disorders, treatment cost

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INTRODUCTION

Over the past 40 years, antipsychotic monotherapy or polypharmacy medications have been used as treatment modalities for psychiatric disorders (PDs).[1-4] However, it seems that antipsychotic polypharmacy has increased for schizophrenia patients over time, especially when monotherapy fails to act as an effective mode of treatment.[4-6] According to the World Health Organization (WHO) estimates, schizophrenia affects approximately 24 million people worldwide.[7,8] This PD imposes great cost burden on the individual and society. The prevalence of antipsychotic polypharmacy has been reported to be between 13 and 70%.[4,9-12] Despite advantages or disadvantages of antipsychotic polypharmacy, it increases treatment costs at a time of increasing budget constraints.[4,12-17] In the United Kingdom, 20.0% of the total burden of disease was attributable to mental illness compared with 17.2% to cardiovascular diseases and 15.5% to cancer. The cost of treatment of mental health problems in the United Kingdom increased approximately from £42 billion in 2003 to £110 billion per annum in 2010.[18,19] The cost of treatment of mental health problems in the United States was approximately $193 billion per year.[20,21] In Iran there is no national registry for these patients. Therefore, the exact number of individuals with schizophrenia and the burden of cost are unknown, although in regional studies, the prevalence of the disease was estimated at 0.3-0.5% for the adult population.[22,23]

The analysis of PD data and its prediction was made by using statistical methods and, recently, artificial neural networks (ANNs).[24-28] ANNs are computer programs that model the capabilities of the human brain by simulating the structure and function of neurons in the brain. Usually, an ANN model has three layers that are called the input, middle, and output layers. The input and output layers contain the predictors and the outcomes, respectively. The hidden layer contains

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unobservable nodes and applies a nonlinear transformation to the linear combination of the input layer. These models are flexible, and nonlinear methods allow better fit to the data by exploring and modeling the relationships between input and output variables; this leads to accurate prediction.[29,30]

However, cost prediction of antipsychotic medication (AM) of psychiatric patients was not done in these studies. In the present study, the ANN model was used to predict the cost of AM of PD as an alternative approach and then its accuracy was compared to a multiple linear regression (MLR) model.

MATERIALS AND METHODS

In this study, we analyzed the data from 790 patients with PD who were discharged between June and September 2010, and were selected from Razi Psychiatric Hospital, Tehran, Iran. The Research Ethics Committee of University of social welfare and rehabilitation sciences (USWRS) approved the study (project number 92/801/1/10406). The natural logarithm of cost of AM (in US dollars) was considered as the outcome variable. The covariates for this outcome consisted of age (in years), gender (male/female), education (illiterate/primary/middle school/diploma and higher), duration of hospitalization (in days), duration of disorder (in years), type of psychiatric ward (educational/noneducational), type of treatment of psychiatric disorder (monotherapy/polypharmacy), chlorpromazine dosage, and type of diagnosed disorder.

To predict cost of AM by MLR, the stepwise selection method was used and *P* values less than 0.05 were considered significant. In the ANN strategy, initially, the data was divided into two subsets: Training/learning (60%) and testing/validation (40%) subsets. The model-building process was made on training dataset based on a three-layer multilayer perceptron (MLP) with eight variables in the input layer, 4 to 14 nodes in the middle layer, and one node in the output layer. In addition, a back propagation learning algorithm was used and activation function was considered as sigmoid and identity in middle and output layers, respectively. Afterward, the model was validated by testing dataset. Here, the mean squared error of prediction (MSPR) was used for comparing the prediction ability of the described models. Data were analyzed using the R 2.15.1 software.[31]

RESULTS

Six hundred and twelve (77.5%) of the psychiatric patients were men and the rest were women; 33.4% of the diagnosed disorders were schizophrenia. In addition, 519 (65.7%) of the patients were on monotherapy [Table 1]. For 75% of the patients, the prescribed chlorpromazine equivalent dosage was 250 to 1000 mg. Median of chlorpromazine dosage in monotherapy and polypharmacy was 600 and 900 mg, respectively. Mean ± standard deviation (SD) age for patients on monotherapy and polypharmacy was 35.64 ± 11.96 and 34.81 ± 11.34 (in years), respectively. In addition, median age of these patients was 34. Mean ± SD of duration of hospitalization for patients on monotherapy and polypharmacy was 31.19 ± 15.55 and 36.69 ± 15.93 (in days), respectively. Mean and median costs of medication for monotherapy (n = 507) were \$8.25 and \$6.23, and for polypharmacy (n = 192) were \$13.30 and \$9.48, respectively. In addition, 67.0 and 79.2% of the patients were on monotherapy in educational and noneducational wards, respectively, and others on polypharmacy. Median costs of medication in the educational and noneducational wards were \$6.02 and \$7.89, respectively.

Table 1: General characteristics of the patients with PDs

Variables	No	%
Gender		
Male	612	77.5
Female	178	22.5
Educational status		
Illiterate	65	8.2
Primary	435	55.1
Middle school	128	16.2
Diploma	112	14.2
Other	48	6.1
Treatment		
Monotherapy	519	65.7
Polypharmacy	197	24.9
Unknown	74	9.4
Type of ward		
Educational	390	49.4
Noneducational	392	49.6
Unknown	8	1.0
Type of diagnosed disorder		
Schizophrenia	264	33.4
Bipolar I	211	26.7
Bipolar Schizoaffective disorder	64	8.1
Other disorders	251	31.8

PD=Psychiatric disorder

Based on importance analysis in the ANN strategy, duration of hospitalization, type of diagnosed disorder, type of treatment, age, chlorpromazine dosage, and duration of disorder were determined as ordered important factors for the cost prediction of the patients [Table 2].

For comparing the prediction ability of the models, we used MSPR for the testing subset. The results are presented in Table 3. The MSPR showed that the ANN prediction was better than MLR model (MSPR was 1.147 vs. 1.652 for first-order and 1.590 for second-order model).

Table 2: ANN and MLR modeling results to determine the important factors for PD patients

ANN model		MLR model	
Ordered* variables	Importance	Ordered** variables	*P*-value
Duration of hospitalization	0.286	Duration of hospitalization	0.000
Type of diagnosed disorder	0.139	Type of treatment	0.003
Type of treatment	0.124	Type of ward	0.045
Age	0.110	Type of diagnosed disorder	0.065
Chlorpromazine dosage	0.102	Chlorpromazine dosage	0.151
Duration of disorder	0.100	Duration of disorder	0.172
Educational status	0.075	Age	0.253
Gender	0.038	Educational status	0.321
Type of ward	0.026	Gender	0.921

ANN=Artificial neural network; MLR=Multiple linear regression; PD=Psychiatric disorder, *According to importance column; **According to *P*-value column

Table 3: Comparison of results for ANN model with MLR

		MLR	
	ANN	First-order model	Second-order model
Number of parameter	119	9	54
MSE	0.498	0.613	0.654
MSPR	1.147	1.652	1.590

ANN=Artificial neural network; MLR=Multiple linear regression

DISCUSSION

During the past decade, prescriptions of antipsychotic polypharmacy medications have increased, especially for adult patients with PDs.[32] In addition, fees for the services are enormous, especially for individuals with severe PDs.[32,33] However, some studies reported predictors of hospitalization and the cost burden of schizophrenia.[13,16,17,24-28,34] Among these studies, the ANN model has been used to predict length of hospital stay for psychiatric diagnosis-related groups,[24] to determine the number of state psychiatric hospital beds,[25] to identify patients with schizophrenia,[26] and to identify metabolic syndrome in patients treated with second-generation antipsychotics.[27] These studies showed that the ANN model can be used as a powerful predictive tool.

The applications of NNs were reported in different medical fields such as cancer, clinical decision support, telemedicine, and self-care. It is mentioned that their accuracy in predictions depends on better integration with data, information, and clinical protocols.[35] As a result, in many applications, NNs have shown better prediction ability compared to traditional statistical methods.[36] In a review study, application of ANNs and statistical methods was compared. Of 96 studies, ANN performed better than regression models in 58% of the cases, and in 24% of the cases, ANN performed equal to statistical methods.[37] Generally in prediction or classification problems, ANN models are better than the usual statistical models. In this sense, with acceptable training process, an ANN will be able to predict new data correctly. In this study, we used the ANN and MLR models for prediction of the cost of ATM. The results showed that the prediction of the ANN model was better than that of the MLR model. So, the ANN model can be used as a powerful and flexible model for the cost prediction of AM. Given that most of the cost of care for the mentally ill in the public or private sector is thrust on the patient's family, prediction of the cost of treatment is beneficial. In addition, PDs usually require frequent or prolonged hospitalization. Consequently, accurate prediction of the cost of treatment would be helpful for the patients and their families.

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