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Wan Muhamad Amir W Ahmad
School of Dental Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian 16150, Malaysia, wmamir@usm.my

Mohamad Nasarudin Bin Adnan
School of Dental Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian 16150, Malaysia

Norhayati Yusop
School of Dental Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian 16150, Malaysia

Hazik Bin Shahzad
School of Dental Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian 16150, Malaysia, hazikshahzad@hotmail.com

Farah Muna Mohamad Ghazali
School of Dental Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian 16150, Malaysia

See next page for additional authors

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Prediction of Factors for Patients with Hypertension and Dyslipidemia Using Multilayer Feedforward Neural Networks and Ordered Logistic Regression Analysis: A Robust Hybrid Methodology

Wan Muhamad Amir W Ahmad[1*], Mohamad Nasarudin Bin Adnan[1], Norhayati Yusop[1], Hazik Bin Shahzad[1], Farah Muna Mohamad Ghazali[1], Nor Azlida Aleng[2], Nor Farid Mohd Noor[3]

[1]School of Dental Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian 16150, Malaysia

[2]Faculty of Ocean Engineering Technology and Informatics, Universiti Malaysia Terengganu, Kuala Nerus 21030, Malaysia

[3]Faculty of Medicine, Universiti Sultan Zainal Abidin, Medical Campus, Kuala Terengganu 20400, Malaysia

Abstract

Background: Hypertension is characterized by abnormally high arterial blood pressure and is a public health problem with a high prevalence of 20%–30% worldwide. This research combined multiple logistic regression (MLR) and multilayer feedforward neural networks to construct and validate a model for evaluating the factors linked with hypertension in patients with dyslipidemia.

Methods: A total of 1000 data entries from Hospital Universiti Sains Malaysia and advanced computational statistical modeling methodologies were used to evaluate seven traits associated with hypertension. R-Studio software was utilized. Each sample's statistics were calculated using a hybrid model that included bootstrapping.

Results: Variable validation was performed by using the well-established bootstrap-integrated MLR technique. All variables affected the hazard ratio as follows: total cholesterol (β_1: −0.00664; $p < 0.25$), diabetes status (β_2: 0.62332; $p < 0.25$), diastolic reading (β_3: 0.08160; $p < 0.25$), height measurement (β_4: −0.05411; $p < 0.25$), coronary heart disease incidence (β_5: 1.42544; $p < 0.25$), triglyceride reading (β_6: 0.00616; $p < 0.25$), and waist reading (β_7: −0.00158; $p < 0.25$).

Conclusions: A hybrid approach was developed and extensively tested. The hybrid technique is superior to other standalone techniques and allows an improved understanding of the influence of variables on outcomes.

Keywords: dyslipidemia, hypertension, multilayer feedforward neural networks, ordinal logistic regression

INTRODUCTION

High blood pressure, or hypertension, is a well-known, important public health chronic disease due to its concomitant risks for cardiovascular diseases, such as stroke and coronary heart disease (CHD).[1–3] Hypertension has been identified as a major risk factor leading to mortality and is a leading contributor to disability-adjusted life years.[4] According to studies on the clustering of the cardiac disease burden in the Asia–Pacific region, approximately 40% of adults over 25 have a clinical diagnosis of hypertension, resulting in more than 9 million fatalities.[5,6] Hypertension is responsible for approximately 7.4 million deaths from CHD and 6.7 million deaths from stroke.[5,7] Studies conducted across India have provided evidence of the rapid spread of the hypertension epidemic. According to the Indian National Nutrition Monitoring Bureau, which keeps track of the nutritional status of the people in the nine states of India, 25% of rural adults (aged 18 and over) have been diagnosed with hypertension.[8] Likewise, according to the NCD Risk Factor Collaboration's research on global blood pressure trends between 1975 and 2015, which comprised 1479 population-based studies, the prevalence of hypertension in adults rose from 594 million in 1975 to 1.13 billion in 2015.[9] Furthermore, the WHO predicted that by 2025, nearly 1.5 billion people (or 29.2% of the world's population) will have hypertension, up from the approximately one billion adults who had it in 2000.[10] In China, over 180 million people had hypertension in 2000 and another 100 million are projected to have this condition by 2025. Over 40% of the 1.13 billion adults with hypertension in 2015 resided in Asia, with China accounted for 226 million of these cases.[11] Worldwide, the prevalence of hypertension varies, with rates as low as 5.2% in rural North India and as high as 70.7% in Poland.[10] Blood pressure varies even within communities within the same nation, depending on the level of economic development and wealth.[10] In economically developed countries, between 20% and 50% of people have

***Corresponding author:**
Wan Muhamad Amir W Ahmad
School of Dental Sciences, Health Campus,
Universiti Sains Malaysia, Kubang Kerian, Malaysia
E-mail: wmamir@usm.my

hypertension.[12] In the Asia–Pacific region, the prevalence of hypertension varies, ranging from 5% to 47% in men and from 7% to 38% in women.[5] A meta-analysis by Soo *et al*. demonstrated that the prevalence of hypertension in Malaysia is 29.7%.[13]

Analyzing the association of hypertension and cardiovascular diseases shows that patients with prehypertension are at 1.5 times higher risk of developing cardiovascular diseases than those with normal blood pressure.[14] The Framingham Heart Study cohort's 34-year follow-up revealed that the risk of people with higher blood pressure for congestive heart failure is twice that of those with lower blood pressure.[15] Some risk factors, such as age, sex, race, physical activity, and socioeconomic class, have been linked to hypertension. People older than 60 years old account for the vast majority of cases of uncontrolled hypertension.[16] Additionally, anthropometric indices of obesity, such as waist:hip ratio and body mass index, have been linked to hypertension in population studies.[17] In the Framingham Study, excess body fat was linked to 70% of new cases of hypertension.[15] Of the known risk factors for primary hypertension, age, gender, and genetics cannot be changed. In contrast, the majority, including smoking, drinking, unhealthy diet, physical inactivity, excess weight, and obesity, can be effectively controlled.[18] In general, hypertension, particularly uncontrolled hypertension, is associated with an increased risk of cardiovascular death.[18]

Dyslipidemia, now referred to as hyperlipidemia, pertains to abnormal alterations in body composition, particularly in body fat and lipid profiles. Diabetes mellitus is linked to dyslipidemia and is characterized by reduced levels of high-density lipoprotein cholesterol, elevated plasma triglycerides, and increased levels of small dense particles of low-density lipoprotein cholesterol.[10,19] It is associated with lipid abnormalities because insulin resistance affects critical enzymes and pathways involved in lipid metabolism.[20] Furthermore, the lipid molecules in diabetic dyslipidemia have been proposed to be atherogenic. This situation indicates that even normal lipid levels may be more atherogenic in diabetics than in nondiabetics. The link between atherosclerosis and dyslipidemia is well established. Diabetes-related hyperglycemia, obesity, and insulin changes all hasten the progression of atherosclerosis.[21]

Machine learning in the medical field has created new techniques for the early prediction of hypertension. Neural networks have proven to be a powerful tool and shown great results in disease prediction.[22] Previous research has investigated the use of anthropometric, demographic, and lifestyle indices as estimators for hypertension with mixed results.[23] Therefore, this research gap can be reasonably addressed by identifying the association of selected variables with hypertension and the clinical benefit of the developed models. Multilayer perceptron with ordinal regression models could serve as an essential tool assisting health professionals because it uses clinically relevant factors. The objectives of this research include investigating the variables that are associated with hypertension, developing a feedforward neural network model with ordinal regression activators and R syntax for future researchers, and analyzing the reliability of hypertension prediction using mean squared error calculation. This programming is expected to enable researchers to obtain optimal decision-making outcomes in the future.

METHODS

Data collection

A total of 1000 data entries were collected from the Hospital Universiti Sains Malaysia (USM). This study received approval from the USM Research Ethics and Human Research Committee (USM/JEPeM/16050184). The patient's privacy and medical condition were protected. Several variables were recorded. They included hypertension, total cholesterol, diabetes status, diastolic reading, height, CHD incidence, triglyceride, and waist measurements. Hypertension data had three ordinal categories: normal blood pressure, borderline high blood pressure, and high blood pressure. Similarly, diabetic status had three categories: normal, prediabetic, and diabetic. All other variables were continuous and used without any dichotomization.

Statistical analysis

Figure 1 shows the step-by-step process of statistical analysis. Here, $p < 0.25$ was selected as the significance level by Mickey and Greenland's work on logistic regression and used to identify variables of importance.[24,25]

Modeling of computational biometry

In this study, the multilayer perceptron model with ordinal regression was constructed using an advanced computational statistical modeling methodology. The advanced method is a hybrid model that employs approaches, such as bootstrapping, multilayer feedforward neural networks (MLFFNs), and ordinal regression. In this methodology, the data were randomly divided into two groups: the testing and training datasets. The developed methodology relied on the testing and training datasets, predicted mean squared error (MSE), and the accuracy value of the mean absolute deviance (MAD). In phase 1, the training data were used for modeling purposes and the multilayer neural networks were fitted. In phase 2, the testing data were used for validation and ordinal regression models were utilized to investigate the underlying association between hypertension and the selected explanatory variables.

MLFFNN

MLFFNN is the most extensively used artificial neural network technology for pattern recognition, classification,

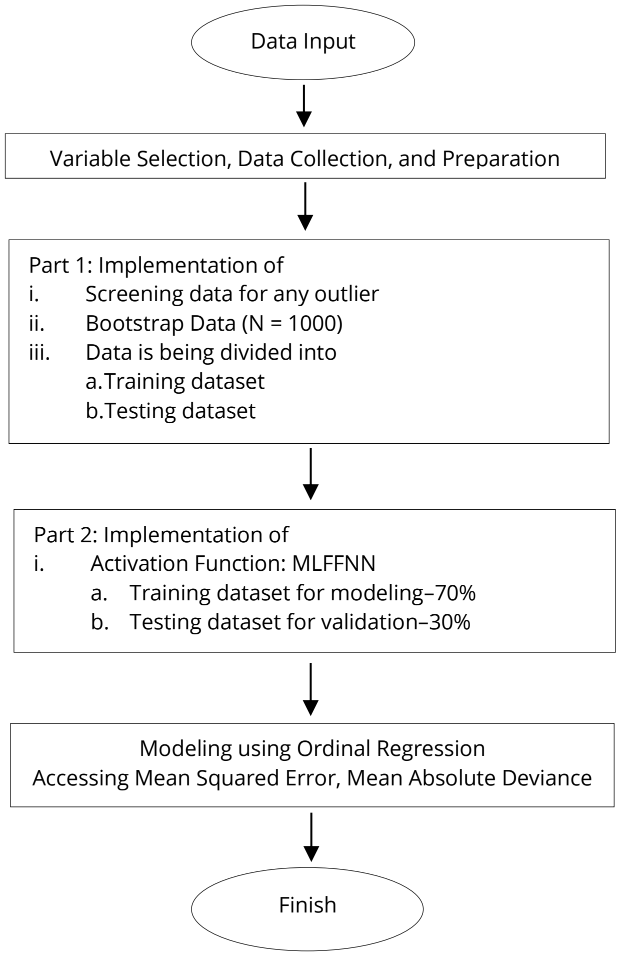

FIGURE 1. Flowchart of the proposed statistical approach

and prediction. It is a type of feedforward artificial neural network containing one or more layers between the input, hidden, and output layers. Given that the MLFFNN model contains only one dependent variable, the analysis of the output node is fixed at 1. The variable chosen from the MLFNN procedure was used as input for ordinal logistic regression (OLR).[26]

Ordinal Logistic Regression

Ordinal regression becomes useful when addressing a categorical dependent variable with more than two categories. OLR is a specific type of logistic regression that is applied when a response variable has more than two categories with a natural rank or order. For analysis, hypertension readings, which are measured on a ratio scale, were transformed into a three-category ordinal variable to capture graded risk levels and align with clinical practice.[27] The maximum likelihood method was employed to estimate regression parameter values. The ordinal model is given by $y_i^* = x_i\beta + \varepsilon_i$. However, given that the dependent variable is categorical, the following must be used:

$$C_x(x) = \ln\left[\frac{P(Y \le j \mid x)}{P(Y > j \mid x)}\right] \text{ and } \ln\left(\frac{\Sigma \mathrm{pr}(\text{event})}{1 - \Sigma \mathrm{pr}(\text{event})}\right) =$$

$$\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 +, \ldots, + \beta_k X_k.$$

This can be summarized as

$$\ln\left(\frac{P(Y \le j \mid x)}{1 - P(Y \le j \mid x)}\right) = \alpha_j + \beta_i X_k$$

$$i = 1 \ldots k, \quad j = 1, 2, \ldots, p-1,$$

where α_j = called threshold or intercept, β_i = parameter in the model, and X_{i1} = set of factors or independent variables. The equation $\ln\left(\frac{P(Y \le j \mid x)}{1 - P(Y \le j \mid x)}\right) = \alpha_j + \beta_i X_k$ is an ordinal logistic model for *k* predictors with *p* − 1 levels as the response variable.[28]

Bootstrapping

Bootstrapping involves selecting a random sample from a population and then calculating sample statistics. Through the multiple substitution of samples, a pseudo-population is created by repeatedly copying original samples. This process generates samples that differ from the original samples. Statistics were computed for each sample drawn with replacement during bootstrapping.[29]

R syntax

Statistical analysis was performed with R-Studio software package (4.2.1, R Core Development Team) by using the neuralnet package. This study examined a model that incorporated clinically relevant factors, which is one of its strengths.

```
# Dataset for the Biometry Modeling Study
Input = ("
choltot diabetes diabbp height hyper incchd trig waist
209 2 81 178.0 2 0 168 119.0
175 1 81 181.0 1 1 332 114.0
228 3 79 183.0 2 0 304 104.0
194 1 69 178.5 0 0 81 91.5
156 1 65 175.5 0 0 98 97.0
239 1 72 183.0 2 0 471 106.0
222 1 94 181.9 2 0 145 92.5
⋮        ⋮        ⋮
169 3 64 177.5 0 0 70 80.5
203 1 77 161.0 1 0 82 78.2
219 1 66 166.6 0 0 102 116.8
")
data1 = read.table(textConnection(Input),header = TRUE)
# Part 1: Multilayer Perceptron Model
# Step 1: Perform 1000 Bootstraps
mydata <- rbind.data.frame(data1, stringsAsFactors = FALSE)
iboot <- sample(1:nrow(mydata),size = 100, replace = TRUE)
data <- mydata[iboot,]
# Install the Neuralnet Package
library("neuralnet")
# Step 2: Check for Missing Values
```

apply(data, 2, function(x) sum(is.na(x)))
 # Step 3: Max–Min Data Normalization
normalize <- function(x) [return ((x − min(x))/(max(x) − min(x)))]
maxmindf <- as.data.frame(lapply(data, normalize))
 # Step 4: Determine the Training and Testing Datasets: 70% for Training and 30% For Testing
index = sample(1:nrow(data),round(0.60*nrow(data)))
Training <- as.data.frame(data[index,])
Testing <- as.data.frame(data[−index,])
 # Step 5: Plot the Architecture of the MLP Neural Network
nn <- neuralnet(hyper~choltot + diabetes + diabbp + height + incchd + trig + waist,data = Training,
hidden = c(6),act.fct = "logistic,"
linear.output = FALSE, stepmax = 1000000)
plot(nn)
options(warn = −1)
nn$result.matrix
 # Step 6: Test the Accuracy of the Model-Predicted Results—Comparison of the Predicted and Actual Results
Temp_test <- subset(Testing, select = c("choltot,""diabetes,""diabbp,""height"
,"incchd,""trig,""waist"))
head(Temp_test)
nn.results <- compute(nn, Temp_test)
 # Step 7: Results
results <- data.frame(actual = Testing$hyper,
prediction = nn.results$net.result)
results
 # Step 8: Use the Predicted Mean Squared Error NN (MSE-Forecasts the Network) as a Measure of the Distance of Predictions from Real Data
predicted <- compute(nn,Testing[,1:8])
MSE.net <- sum((Testing$hyper - predicted$net.result)^2)/nrow(Testing)
 # Step 9: Print the Predicted Mean Square Error
MSE.net
 # Step 10: Neural Network Parameter Output
nn <- neuralnet(hyper~choltot + diabetes + diabbp + height + incchd + trig + waist,data = Training,
hidden = 6,act.fct = "logistic," linear.output = FALSE,
stepmax = 1000000)
nn$result.matrix
 # Step 11: Model Validation
results <- data.frame(actual = Testing$hyper,prediction = nn.results$net.result)
results
summary(results)
 # Step 12: Model Accuracy
predicted1 = results$prediction*abs(diff(range(data$hyper))) + min(data$hyper)
 # Step 13: Print(Predicted)
actual1 = results$actual*abs(diff(range(data$hyper))) + min(data$hyper)
 # Step 14: Print(Actual1)
deviation = ((actual1-predicted1))
Print(deviation)
 # Step 15: MAD
value = abs(mean(deviation))
print(value)
accuracy_in_percent = (1-value)*100
accuracy_in_percent
 # Part 2: Model the Ordinal Model
 # Step 1: Build the OLR Model
library("MASS")
polr(formula = as.factor(hyper) ~ choltot + diabetes + diabbp +
height + incchd + trig + waist, data = data, Hess = TRUE,
method = c("logistic"))
m<-polr(formula = as.factor(hyper) ~ choltot + diabetes + diabbp +
height + incchd + trig + waist, data = data, Hess = TRUE,
method = c("logistic"))
 # Step 2: Store the Table
(ctable <- coef(summary(m)))
 # Step 3: Calculate and Store *p* Values
p <- pnorm(abs(ctable[, "t value"]), lower.tail = FALSE)*2
 # Step 4: Combine Tables
(ctable <- cbind(ctable, `*p* value` = *p*))
 # Step 5: Odds Ratios
exp(coef(m))

RESULTS

This study aims to investigate the performance of a MLFFNN, which is based on the activation function: ordered logistics model. This MLFFNN considered training and testing datasets. The optimal model for ordered logistic regression was identified by the MLFFNN algorithm by choosing variables that were clinically important and able to generate the lowest predicted MSE.

Results of MLFFNN modeling

Table 1 shows the results of ordered logistic regression using a training dataset wherein hypertension status is a dependent variable. The MAD of 0.00724 for the ordered logistic model indicates the distribution of the available data. A small value indicates the effectiveness of the obtained analysis in demonstrating the similarity between the predicted and actual data. Our study followed the industry standard train-to-test split of 70:30, meaning that 70% of the data are available for modeling and 30% for testing.[30] Given this situation, it is appropriate to show the accuracy and dependability of our predicted data. Figure 2 shows the network architecture of the best MLFFNN model with seven input variables, one hidden layer, and one output node.

As discussed in this section, the established bootstrap method for integrated ordered logistic regression was employed to validate variables. In this case, seven variables were chosen for analysis as follows: total cholesterol (β_1: −0.00664; $p < 0.25$), diabetes status (β_2: 0.62332; $p < 0.25$), diastolic reading (β_3: 0.08160; $p < 0.25$), height measurement (β_4: −0.05411; $p < 0.25$), CHD incidence (β_5:

1.42544; $p < 0.25$), triglyceride reading (β_6: 0.00616; $p < 0.25$), and waist reading (β_7: −0.00158; $p < 0.25$). Table 1 summarizes the results of multiple regression analysis, which found that all seven factors had a significant effect on hypertension.

Evaluation of the model

The forecast value was used for model evaluation. Prediction accuracy was determined by comparing actual and predicted values. The testing dataset was employed to evaluate the model constructed from the training dataset. The difference between the actual and predicted data was measured by using the distance prediction method. R syntax provides a model evaluation approach for the subsequent assessment. Table 2 displays the actual and predicted values obtained using the proposed methodology.

As shown in Table 3, the mean squared value for the actual data was 1.27 (SD = 0.905) and that for the predicted data was 0.98 (SD = 0.158). A paired t-test was conducted to examine the difference between these means, resulting in $p > 0.05$. This result indicated that the actual and predicted values did not significantly differ.

TABLE 1. Results of ordered logistic regression integrating bootstrapping method for training and testing datasets

Variable	Estimate	Std. Error	Z-Value	*p*
Total Cholesterol	−0.00664	0.007286	−0.91145	0.362055 e−01*
Diabetes Status	0.62332	0.315388	1.97636	0.048114 e−02*
Diastolic Reading	0.08160	0.023740	3.43725	0.000588 e−04*
Height Measurement	−0.05411	0.016238	−3.33211	0.000862 e−04*
Incidence of CHD	1.42544	0.664793	2.14418	0.032018 e−02*
Triglycerides Reading	0.00616	0.003458	1.78036	0.075016 e−02*
Waist Reading	−0.00158	0.022606	−0.06968	0.944442 e−01*
Cut 2	−3.41740	0.003816	−895.554	0.000000 e−00*
Cut 1	−2.53853	0.199198	−12.744	0.000000 e−37*

*Significant at the level of 0.25

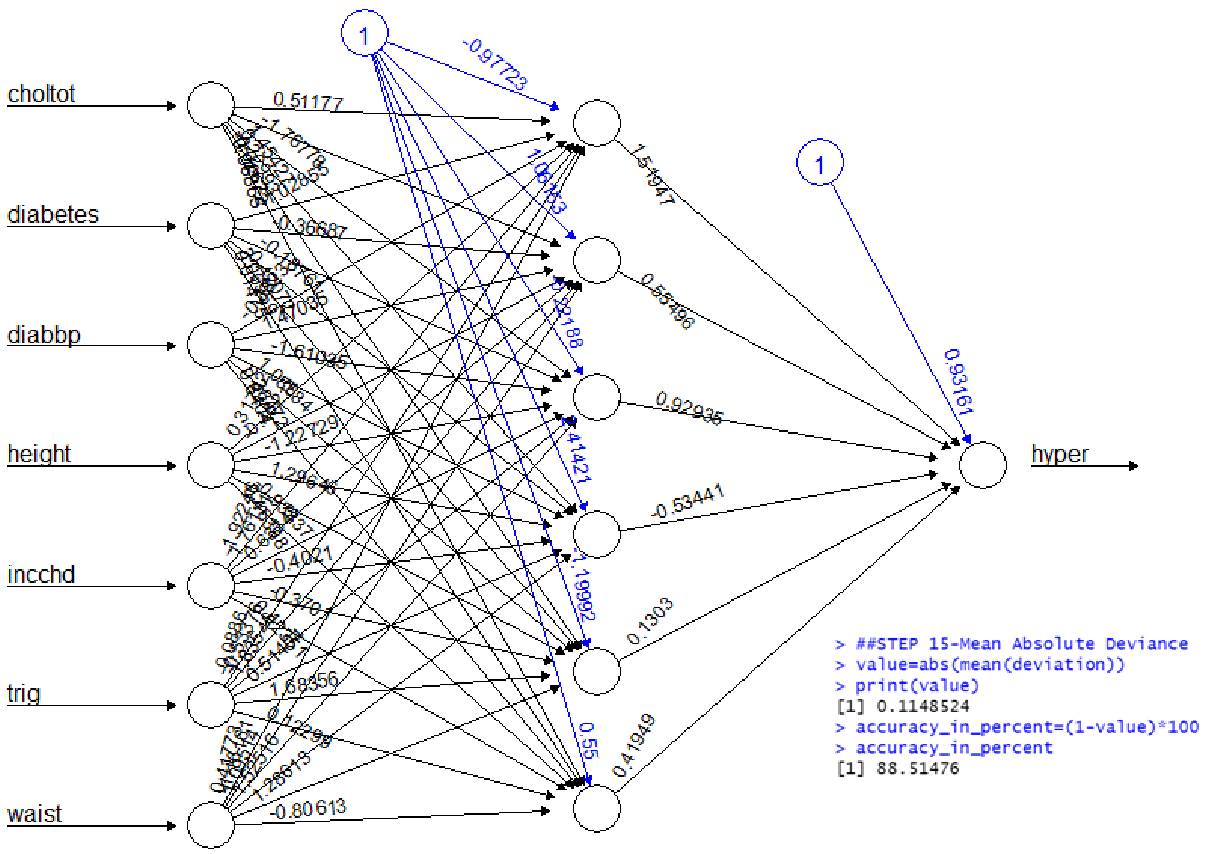

FIGURE 2. Architecture of the best MLFFNN model with seven input variables, one hidden layer, and one output node

TABLE 2. Actual and predicted values from the proposed methodology

Actual	Predicted
0	0.82964129
2	0.99952417
2	0.99952417
1	0.82964129
0	0.85360592

TABLE 3. Summary statistics of the proposed methodology

Variables	Mean ± SD	*p*
Actual	1.27 ± 0.905	0.051
Predicted	0.98 ± 0.158	

Paired samples t-test was applied

DISCUSSION

This study used a harmonized hybrid methodology to examine a model that incorporated clinically relevant factors with a direct association with hypertension. The successfully implemented method is highly accurate and valuable for estimating event probabilities (predicting the odds of being a case). However, regression modeling has several limitations, including estimation. The calculation procedures for each predictor variable and outcome are complex with low accuracy and precision. The proposed method, which is based on a single syntax calculation, improves the accuracy and precision of ordered regression modeling. The findings revealed that total cholesterol, diabetes status, diastolic reading, height measurement, CHD incidence, triglyceride reading, and waist circumference are the most critical factors influencing hypertension.

Over the past decade, numerous studies have explored the risk factors associated with hypertension. A clinical application with increased robustness for identifying risk factors can be obtained by combining MLFFNN with ordered regression analysis. For example, Chang *et al*. employed a different mining tool and found significant results indicating that triglycerides, creatinine, age, and uric acid are linked to hypertension risk.[31] Akdag *et al*. utilized decision trees and identified BMI, waist:hip ratio, gender, and triglycerides as risk factors for hypertension.[32] A study conducted in Qatar by AlKaabi obtained similar results through random forest and logistic regression analysis. It highlighted age, physical activity, fruit and vegetable consumption, and diabetes history as crucial predictors of hypertension.[33] Furthermore, a longitudinal study by Dimitriadis demonstrated the significant association of hypertension with risk factors such as age, gender, and blood glucose levels.[34]

The main objective of this project is to combine bootstrapping, MLFFNN, and ordered logistic regression techniques to develop and implement medical statistic strategies. Variable selection involves incorporating clinical expert opinion. A "mega" file is created from the initial dataset to begin the bootstrap method. The bootstrap method iteratively repeats this procedure frequently thousands of times. The R syntax algorithm aids the integration of the application with the methodology and establishes a link between the application and the notion of the method-based methodology. Training and testing use different sets of data. In this work, 30% of the bootstrap data were categorized as a testing dataset, and 70% were categorized as a training dataset. Data from the training dataset were used to build and test the model. The successful model had the smallest MAD based on actual and predicted values.

The study findings will assist decision-makers in achieving the best possible outcome. The most challenging tasks involve selecting the appropriate input parameters, preparing the data for ordered logistic modeling, and standardizing the data. The performance of the developed model is promising, and its results can be utilized as an early warning tool by health professionals to alert patients to the possibility of being hypertensive. The insights obtained from designing, developing, implementing, testing, and analyzing the network model will be valuable for future endeavors to create an early warning tool for hypertension prediction. This tool could serve as an affordable, straightforward, and rapid screening method to help the public identify their risk of hypertension.

CONCLUSIONS

This study created a hybrid approach that included bootstrapping, multilayer neural networks, ordered logistic regression, and R syntax. It demonstrated that the abovementioned methodology outperformed in terms of the R-squared values for the predicted MSE. The hybrid technique is superior to other standalone techniques and allows an improved understanding of the influence of variables on outcomes. The statistical strategy showed that regression modeling outperformed other modeling techniques and had a mean absolute deviant error of 0.00297. The model revealed that the independent variables associated with hypertension were total cholesterol, diabetes status, diastolic reading, height, CHD incidence, triglyceride reading, and waist circumference.

CONFLICT OF INTEREST

The authors declare no conflict of interest in this research.

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