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Deep learning network for identification of Ischemia using clinical data

Varun Sapra, Madan Lal Saini

Abstract*: *Ischemic heart disease is amongst the foremost reasons of death and disability majorly because of atherosclerosis and other cardiovascular syndromes like cerebrovascular accidents and myocardial infarction. Ischemia can be diagnosed by using invasive & non-invasive methods. Invasive methods are generally expensive and always requires high level of technical and medical expertise. This paper focuses on a bio inspired optimization approach for the identification of effective biomarkers and deep learning based neural network technique on non-invasive clinical parameters to diagnose Ischemia with more accuracy. For experiment purpose, the clinical data of Coronary Artery disease (CAD) patients was collected from the cardiology department of Medical College, Shimla, India. The proposed method improves the prediction accuracy of Ischemia.

Index Terms*: *Neural Network, Ischemia Heart Disease, Non-Invasive, Angiography.

I. INTRODUCTION

Disordering in the heart and blood vessels leads to Ischemic heart diseases, which is one of the major reasons of disabilities and death in any nation today. In 2010, the expenditure on direct healthcare due to cardiovascular diseases (CVDs) was US$863 billion which is expected to reach to US$20 trillion by 2030 [1]. Also in India, the CVD is a major threat for morality and disability. According to Registrar General of India and the Centre for Global Health Research, report (2000-2013) cardiac related diseases are the top most cause of death in India.

The severity of the disease can be reduced only with the early accurate diagnosis and immediate treatment [2]. CVD causes cardiac death or myocardial infraction due to the presence of plaques in arteries. The plaque grows to the point of blocking the arterial lumen, causing several clinical manifestation and reducing blood flow [3]. The plaque consists of cholesteryl esters; cholesterol; monocyte-derived macrophages; T lymphocytes; varying amounts of muscle cells; extracellular connective tissue and phospholipids. Extracellular matrix is created with the collection of the above stated particles that includes pericellular matrix, phospholipids, elastic fibers and proteoglycans [4-5].

The vessel wall of a normal artery has three layers, namely intima (inner layer), that consists of endothelial cells, media (middle layer), contains muscle cells and finally, adventitia (outer layer), majorly comprises of collagen fibers. The arteriosclerosis instigates with circulating inflammatory white blood cells (WBCs), hemodynamic forces and cholesterol. The vascular wall, which have high viscosity and turbulent flow, is penetrated and attached with leukocytes and low-density lipoprotein (LDL) [6].

The disease can be diagnosed using both invasive and non-invasive techniques. One of the invasive technique considered as a Gold standard is angiography, which is a painful and costly method. It also requires extensive clinical setup and technical expertise. On the other hand, there are number of noninvasive methods of diagnosis such as exercise stress testing, echocardiogram, magnetic resonance imaging, but the outcome of these methods are unconvincing and not promising as angiography [7-8]. Such limitations of diagnostic modalities inspires researchers to explore more accurate and less expensive techniques for disease diagnosis.

II. BACKGROUND

Machine learning techniques are getting popular in medical domain nowadays as it provides a number of tools by which large quantities of data can be automatically analyzed and assist the medical practitioners for early and accurate diagnosis of disease [9].

Zeinab Arabasadi et al (2017) proposed a hybrid method that uses genetic algorithm as a blend with neural network for the initial analysis of CAD, where initial weights were determined by using genetic algorithm. Author used Z-alizadeh Sani data set with 303 instances, to reduce the data dimensionality; information gain, principal component analysis are investigated. The hybrid method improved the accuracy of prediction of diagnosis of neural network. The model achieves the diagnostic accuracy of 93.85 % and sensitivity of 97% and specificity of 92% [10]. Babis et al (2017) performed analysis on three different data sets: South African Heart Disease, Heart Disease Database and dataset from Z-Alizadeh Sani. They performed predictive analysis that was based on Support Vector Machine, Decision Trees, Neural Networks and Naive Bayes. Further, the author performed descriptive analysis grounded on association and decision rules. The models proposed by authors are comparable with existing studies and in some cases comparable or better [11]. Verma et al. (2016) proposed hybrid method for coronary disease diagnostic using non-invasive clinical parameters.

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***** Correspondence Author (s)
Varun Sapra*, Dept. of Computer Science, Jagannath University, Jaipur, India.
Dr. Madan Lal Saini, Dept. of Computer Science, Jagannath University, Jaipur, India.

Author reduced the feature space using CFS based feature selection method with PSO search. Proposed method improved the prediction accuracy of diagnostic models [12]. Melillo et al. (2015) illustrated the significance of various DM techniques to predict major risk factors for cardiovascular diseases. They used Support Vector Machine (SVM), ANN, Random Forest techniques on heart rate variability. Higher predicted values were shown by data mining classifiers as compared to echo graphic parameters. The study proved that the performance of Random Forest is better than other classifiers [13]. Dai et al (2015) implemented different supervised learning techniques for the prediction of heart related hospitalization. They have used techniques, such as SVM, Naïve Bayes, AdaBoost logistic regression and a variation of a Likelihood Ratio [14]. Wu et al. (2013) proposed the method of magnetocardiography as a tool for detecting CAD non-invasively. They extracted two dominant parameters curvature of magnetic field zero line and the area ratio of the extrema circle. They used data of 97 subjects that were collected by four sensors. The data was arranged in a 2X2 array at 9 different positions. The result shows the sensitivity of 71.4% and specificity of 72% [15].

In the last few years deep learning gained a lot of attraction of researchers especially in medical domain such as Clinical imaging, Electronic Health records, Genomics. Wang et al. in their paper emphasized on breast arterial calcifications (BACs), which is one of the prominent cause of CAD in women. For the accurate and automated detection of BACs, they developed 12 layer convolutional neural network. Their model implemented a pixel wise patch based procedure for the detection of BACs. They evaluated the performance of the model with 840 full-field mammograms which has been collected from 210 cases. The author used both the methods of analysis that includes free-response receiver operating characteristic (FROC) as well as calcium mass quantification. The FROC analysis yields the results which are almost similar to human experts and the linear regression analysis between the FROC and calcium mass produces a coefficient of determination of 96.24% [16]. Chowdhuryy *et al* proposed a machine-learning framework for an ultraportable ECG module that incorporates convolutional neural network with bio sensors. They used a dataset of 40 patients and achieved an accuracy of 92.3% [17]. Chunxue et al. proposed a novel approach of deep learning for mobile multimedia using greedy deep weighted dictionary learning technique. The proposed framework reduced the risk of over fitting and made convergent layers for increasing the accuracy. The model performed better and the values of performance parameters are comparable [18]. Liu et al. 2014, proposed the deep learning based framework for early identification of Alzheimer's disease, which contains stacked auto-encoders and a soft-max output layer, For experiment purpose author used neuro-imaging data of 311 subjects collected from Alzheimer's disease Neuro-imaging Initiative database. Proposed method achieves the prediction accuracy of 87.76 % for binary classification [19]. Farzi et al applied deep learning based network to diagnose attention deficit hyperactivity disorder. They proposed a method Boltzmann Machine, which converts a large number of problem features to compound features known as restricted using greedy algorithm to construct and train the structure of network. The proposed method improves the prediction accuracy of diagnosis [20].

Researchers are also facing another major challenge of dimensionality reduction in large datasets. The main aim is to find most significant features that can contribute maximum to the output. Manikandan *et al* (2017) proposed a wrapper based method for finding the optimal threshold value by passing the feature subsets iteratively to the classifier until highest accuracy is achieved. The author used symmetrical uncertainty method to weight the features [21]. Another novel technique binary coordinate ascent based on the coordinate descent algorithm was proposed by Amin et al. (2018). It is an iterative implementation for finding local optimization and can be used with both wrapper and filter methods. The evaluation of the algorithm is carried out on the basis of the area under receiver-operating-characteristic curve. The proposed algorithm showed a substantial improvement in terms of efficiency [22].

III. DATASET DESCRIPTION

The study was carried out to collect the data of symptomatic patients who were consecutive referrals for coronary angiography at Medical College, Shimla, India. Lab tests were performed by medical specialists under a controlled environment using standard protocols at hospital laboratory. The prominent biomarkers that were recorded for the patients included Age, Gender, Diabetes Mellitus, Chest pain type, Smoking habit, Triglyceride , Dyslipidemia, Low Density lipoprotein, Total Cholesterol , High Density lipoprotein, Body weight, Obesity, Height, Duke treadmill score, Duration recovery and the result of Coronary Angiography as target class are shown in Table 1.

Table 1: Description of Coronary Artery Disease data features

S.No	Feature	Description	StDev	Mean
1	Age	Age	9.4	55.4
2	Gender	0=female, 1=male,	0.4	0.6
3	Dyslipidemia	0 = No and 1 = Yes	0.4	0.7
4	SH	Smoking Habit 0=Nosmoker, 1=past-smoker, 2= smoker	0.9	0.8
5	CPT	Patient having a particular type of Chest Pain 0 Non specific chest pain 1 =Atypical chest pain 2 = Typical angina chest pain	0.7	1.3
6	TG	Triglyceride	28.2	148.9
7	HTN	Hypertension or High Blood Pressure 0 = No and 1 =Yes	0.5	0.4
8	VO	Visceral Obesity 1=True 0= False	0.5	0.5

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9	TC	Total cholesterol	30.6	182.5
10	DM	Diabetes mellitus 0 = No and 1 = Yes	0.3	0.1
11	RBS	Random Blood Sugar	26.8	99.4
12	LDL	Low density lipoprotein	20.4	112.7
13	HDL	High density lipoprotein	0.6	1.6
14	ABI	Ankle-brachial index test	0.08	1.2
15	SBP	Systolic blood pressure	12.4	124.1
16	DBP	Diastolic blood pressure	7.09	77.9
17	WT	Weight	10.7	65.4
18	HT	Height	9.1	164.7
19	WC	Waist circumference	6.7	88
20	BMI	Body mass index	3.5	24
21	ED	Exercise Duration	1.7	7.8
22	DTH	Duke treadmill score	6.4	-4.8
23	METS	Metabolic exercise stress test	1.7	8.9
24	DR	Duration of recovery with persistent ST changes	1.5	1.5
25	RPP	Rate Pressure product	41.1	249.3

The dataset contains the data for 127 males with positive CAD and 103 male records were found with negative CAD attributes. Similarly the ratio for females was 37 for positive CAD and 68 with negative signs of the disease. The demographic markers are often considered as important for the prediction of cardiac risk of a patient. Figure 2. Shows that the majority of CAD subjects are males.

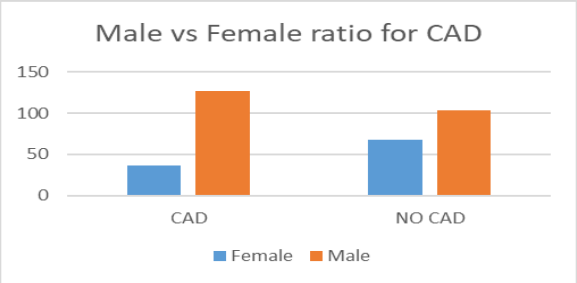

Figure 1: Ratio of Males and Females for Coronary Artery Disease

It is evident from the literature that smoking is one of the attribute which is considered as a prime fator for coronary artery disease, Figure 2 shows the number of males and females that are smokers or past smokers [23].

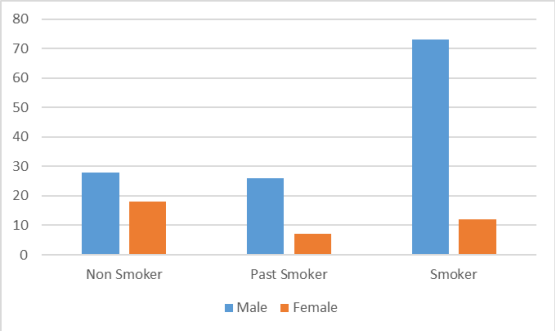

Figure 2: Ratio of Males and Females for positive CAD with smoking as a key attribute

IV. METHODOLOGY

A. *Feature Subset Selection Methods*

Feature selection is a essential to identify the most salient features from the data that have a significant effect on the output and discarding irrelevant (redundant) features with minimal effect with respect to the learning under consideration from the dataset. The main goals of feature selection are plummeting data dimensionality, scaling performance of prediction, and a better understanding of data for the better implementation of machine learning techniques [24].

Most of the feature selection algorithms follow a general architecture with four steps, generating a subset, doing evaluation, stopping criterion, and validation of result. Not only the reduction in feature space is important but the accuracy and relevancy of the subset is important [25]. The three common methods used for selecting relevant features are filter, wrapper and embedded. The filter method evaluates quality of selected features based on characteristics of data independent of any mining algorithm. Embedded methods are specific and identify features based on the learning procedure. The wrapper method evaluate best features based on application or accuracy from the classifier.

Feature selection techniques are used to achieve best results with minimal resource investment. Nowadays, researchers are moving from the classical techniques to a new species of bio inspired evolutionary optimization techniques that are based on principles of biological systems [26]. These techniques are widely accepted and implemented by researchers to eliminate or discard insignificant features to increase the accuracy measure of the prediction. Lin et al 2015 [27] proposed hybrid method for the selection of optimal features with endocrine based Particle Swarm Optimization (PSO) and Artificial Bee Colony algorithm (ABC). The author extracted the significant features to improve the performance the proposed model. Yang et al. worked with nature inspired Bat Algorithm for solving complex non-linear engineering optimization problems. They have successfully implemented the technique for eight constrained problems. The results obtained by the method are superior to many existing methods [28].

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Amin et al [22] used ANN for the prediction and classification of heart disease, further author used Genetic algorithm for the optimization of the network and were able to achieve the performance accuracy of 89 %.

B. *Multilayer Perceptron*

Multilayer Perceptrons (MLPs) are supervised feed forward networks that are widely used for identifying complex relationships among inputs and outputs by recognizing patterns in data and for the processing of information that contains a number of layered interconnected elements. These are layered networks and are trained with the backpropagation learning algorithm. MLP neural network contains a set of input nodes, a single output layer and in between one or number of hidden layers for computation and transfer of information to output layer by means of an activation function. Castro et al proposed a method for assessing the impact of three parameters on the sum of squared error (SSE). The parameters were neurons per hidden layer, activation function and no. of hidden layers. The results proved that neurons per hidden layers and no. of hidden layers have a substantial effect on SSE [29].

Activation function is used for bringing non-linearity in the output. Different activation functions can be implemented with MLP as:

Sigmoid: It is used to predict the probability between 0 and 1.

$$\sigma(x) = \frac{1}{(1+e^{-x})} \quad (1)$$

tanh: It is a hyperbolic tangent function that gives outputs in the range from -1 to 1.

$$\tanh(x) = 2\sigma(2x) - 1 \quad (2)$$

ReLU (Rectified Linear Unit): It is widely used activation function mostly used in convolutional neural networks.

$$f(x) = \max(0, x) \quad (3)$$

V. PROPOSED MODEL

In this paper, we propose a model that consists of preprocessing of the data by using the attribute mean for the samples belonging to the same class, reduction in feature subset space with cfs selection method along with Bat search technique. Finally, model is constructed using MLP with keras library. The model constructed was fed with entire dataset with all the features and performance measures were recorded and then the model is again implemented using reduced feature subset which was obtained after implementing correlation based feature subset and bat search algorithm and again the performance measures were recorded and compared with the earlier results.

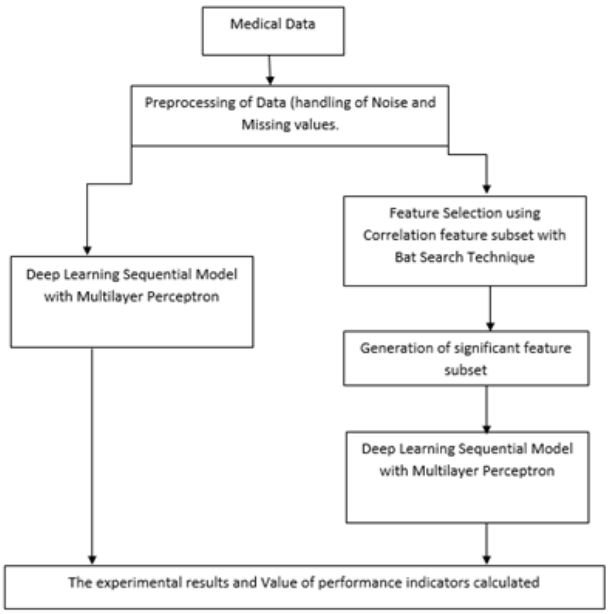

Figure2: Proposed Model

Correlation based feature subset

CFS (Correlation based Feature Subset Selection) method comes under the category of Filter methods that makes use of the evaluation formula integrated with an appropriate correlation measure and a heuristic search strategy. Although wrapper methods are faster than filter but when compared, in many cases CFS gave comparable or better results and outperformed the wrapper methods especially on small datasets. The objective of CFS is to evaluate significant features that sufficiently correlate themselves with class label. The assessment function used in CFS is as follows:

$$Merit_s = \frac{Y\overline{fcc}}{\sqrt{Y+Y(Y-1)\overline{ffc}}} \quad (4)$$

Where subset s contains Y features, mean feature class is shown as $\overline{fcc}$ and $\overline{ffc}$ calculates average feature inter correlation.

Bat Search algorithm was first discussed by Xin-She Yang in 2010. The method increases solution diversity by using a frequency tuning technique in the population. The algorithm use frequency signals for echolocation. Each bat is having a velocity v_i^t and a location z_i^t, at iteration t, in a y dimensional search or solution space. Among all the bats, there exists a current best solution $x*$. The experiments were conducted for dimensionality reduction of the feature space using Weikato Environment for Knowledge Analysis toolkit [30].

Artificial Neural Network with keras library

Deep learning was developed from artificial neural network, and now it is a prevalent field of machine learning. It is different from traditional artificial neural networks, by the number of hidden layers, the connections or associations between them and their learning capability for abstractions of inputs. The study focuses on the enhancement of prediction accuracy using Tensorflow and keras library for deep learning using non –invasive clinical risk factors for Coronary

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Artery Disease patients. The computational model consists of input, output and computational layers.

The model consists of five fully connected layers. The first layer is the input layer, then there are three hidden layers for performing internal computations and an output layer. The dataset is then divided into input and output variable. The input contains all the 24 attributes and the second category is output which holds the class that predicts the possibility of having a CAD or not. After identifying the input, the type of model is to be selected and compiled. To develop a binary classification model we have taken a sequential model from keras library.

The initial dimension of the input layer is set and uniform weight initialized method has been used to initialize the weights and ReLU activation function is added to the model. Model is further optimized with Adaptive moment estimation for weight balancing. Further model is compiled and error is calculated by using a loss function. Here in this model cross entropy is used for error calculation.

VI. RESULTS

The model was constructed using collected dataset and the performance was assessed for Mean Squared error, Mean absolute error, Accuracy, Precision, recall and f1 score. Train and test approach are used to construct and test the model on complete set of features and optimized features evaluated using bat search method. The model is tested, performance measures are calculated. Table 2 shows the mean squared and absolute errors and accuracy and Table 3 contains performance parameters like Precision, Recall and F1-score. The results have also been calculated for the entire dataset and the results are shown in Table 4 and Table 5.

Table 2: Accuracy/MSE/MAE of optimized network model

Model	Accuracy	MSE	MAE
Network model with optimized features	89.6	9.55	20.95

The higher values of the calculated parameters shown in Table 2 and Table 3 gives the effectiveness of the model. Table 2 shows the accuracy of the model with reduced feature set to 88.6% with mean squared error of 10.55% and mean absolute error of 21.95%. Figure 3a, 3b and 3c shows the behavior of some significant parameters for reduced feature subset. Figure 3(a) shows the accuracy of the model whereas figure 3(b) and figure 3(c) shows the MSE and MAE for the significant features. The proposed model achieves the prediction accuracy of 89.6% with optimized features and precision and recall for non-ischemia is 0.88% and 0.90% and for ischemia class is 0.89% and 0.87%.

Table 3: Performance parameters for optimized model

Class	Precision	Recall	F1 score
No ischemia	0.88	0.90	0.89
Ischemia	0.89	0.87	0.87

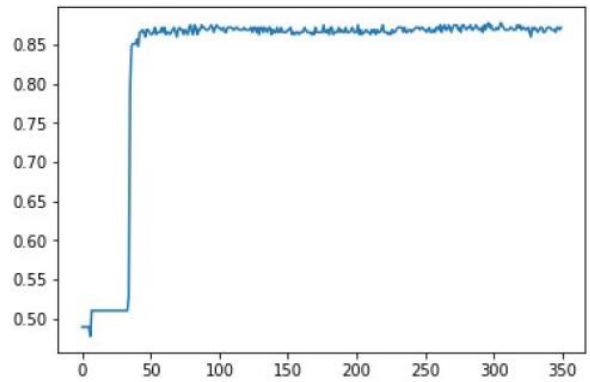

Figure 3 (a): Accuracy of model with optimized features

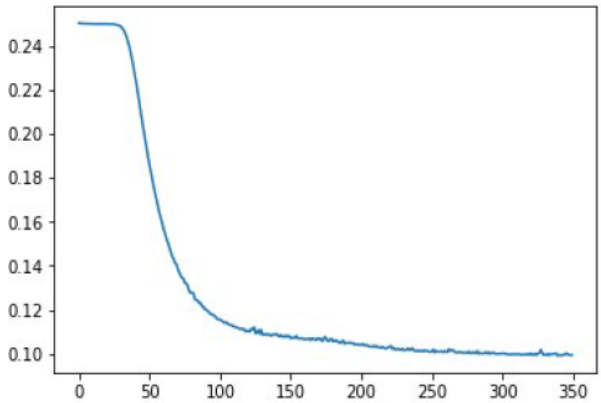

Figure 3 (b): Mean Squared error with optimized features

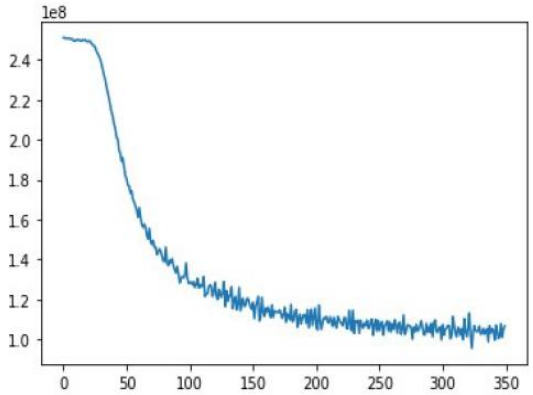

Figure 3 (c): Mean Absolute error with optimized features

The values are calculated for all the parameters and are shown in Table 4 and Table 5 and the behavior of the parameters is shown in Figure 4(a), Figure 4(b) and Figure 4(c). The results clearly shown that the performance of the model with all the features are not promising as compared to the results achieved using optimized feature subset.

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Table 4: Accuracy/MSE/MAE of network model considering all the features

Model	Accuracy	MSE	MAE
Deep learning model with considering all the features	87.76	10.4	23.29

Table 5: Precision/Recall and f1 score considering all the features

Class	Precision	Recall	F1 score
No ischemia	0.92	0.83	0.87
Ischemia	0.84	0.93	0.88

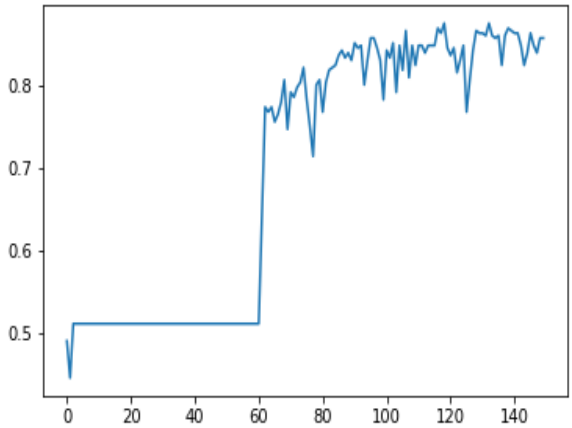

Figure 4 (a): Accuracy of model with all the features

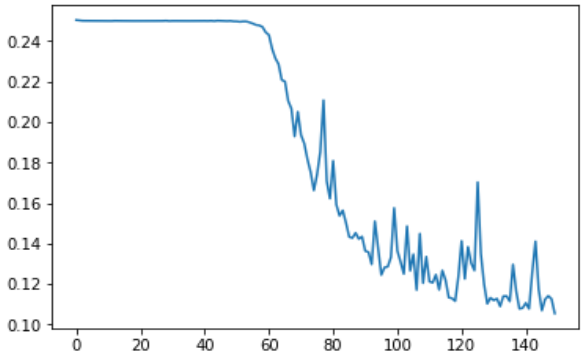

Figure 4 (b): Mean Squared error with all the features

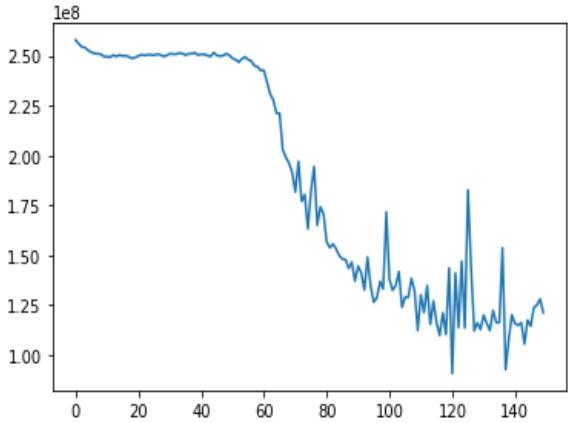

Figure 4 (c): Mean Absolute error with all the features

The proposed method is also compared with the work, carried out by Verma et al. [14] in 2016 on the similar data set. The author compared the performance of multilayer perceptron (MLP), Multinomial logistic regression model (MLR), Fuzzy Unordered rule induction algorithm (FURIA) and C4.5 on the dataset with all the features.

Table 6: Performance of FURIA, MLP, MLG and C4.5 using complete dataset

Algorithm	Percentage Accuracy	% of Instances wrongly classified
FURIA	77.9	22.8
MLR	83.5	16.4
C4.5	77.3	22.6
MLP	77.0	22.9

Further, the authors optimized their method by using Particle Swarm optimization (PSO) with classification techniques and achieved the following results.

Table 7: Computation of Performance indicators with PSO method & classification technique (5 predictors with 335 instances)

Algorithm	Accuracy	Wrongly Classified Instances	% improvement
FURIA	80.29	19.70	2.39
MLR	84.17	15.8	0.67
C4.5	77.9	22.08	0.6
MLP	79.7	20.2	2.7

Finally, they further implemented a hybrid method with feature subset method (correlation feature subset) with PSO and k-means clustering and achieved the following results

Table 8: Accuracy for hybrid method using PSO with k-means algorithm + classification)

Algorithm	Accuracy	Wrongly classified instances	% improvement
FURIA	82.8	17.13	2.51
MLR	88.4	11.5	4.23
C4.5	80.68	19.3	2.78
MLP	84.11	15.8	4.41

The comparison showed that the model under consideration achieved the accuracy of 89.6%, outperformed the results of the techniques used in the study.

VII. DISCUSSION & CONCLUSION

Classification performance of models depends on the type of problem, as it rely on the techniques used for data preprocessing, algorithm selection for constructing and validating the model and feature selection methods. The study implemented the deep learning method for predicting Coronary heart disease with correlation based method for subset selection method with Bat search. Dimensionality of the data set is reduced to identify the high risk factors for ischemia.

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Only few parameters are needed to construct the model. The most influential risk factors identified to predict the ischemia are age, smoking habits, Diabetes mellitus, High density lipoprotein, Body Mass Index, Duration recovery and duke treadmill score. We excluded chest pain type while constructing model because it is oriented towards one type of class. Deep learning based method achieved the prediction accuracy of 89.6%. By reducing the dimensionality of the feature space the accuracy of the deep learning method is increased by 0.84%. Results are promising and can be used as an adjunct tool in clinical practices.

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