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Development of a machine learning-based Parkinson's disease prediction system through *Ayurvedic dosha* analysis

Research Article

Vinayak Majhi[1], Bishnu Choudhury[2], Goutam Saha[3], Sudip Paul[1]*

1. Department of Biomedical Engineering, North-Eastern Hill University, Shillong, Meghalaya, India.
2. Department of Kayachikitsa, North Eastern Institute of Ayurveda and Homoeopathy, Shillong, Meghalaya, India.
3. Department of Information Technology, North-Eastern Hill University, Shillong, Meghalaya, India.

Abstract

The development of a machine learning (ML) based prediction model for Parkinson's disease (PD) using Ayurvedic literature is very rare in practice. In modern era of digitization and artificial intelligence this lack leads us for developing a significant and useful predictive model for PD in light of Ayurveda. As in contemporary Ayurvedic literature, PD has not been fully classified according to all of its motor and non-motor symptoms, with the exception of *Kampavata* or tremor, one of the cardinal motor symptoms of PD, we have taken the help of MDS-UPDRS-II and MDS-NMSQ scaling system as an initial input for this purpose. Based on the available literature, we determined our *tridosha* score using these scales, which become our main inputs to the ML algorithm, along with other general health attributes such as age, sex, and BMI. We applied various ML algorithms and ranked our best ML model based on their performance. For training and testing purposes, we used the Fox Insight dataset with n = 80,916 records including PD and control. Finally, we found that Kernel-SVM, SVM, Logistics Regression (LR), and XGBoost are our four most accurate algorithms, with an accuracy more than 92.5% with no dimensionality reduction applied. Here we chose the LR model as our best ML model, depending on the lower false positive rate of 0.045 with an accuracy of 92.6%. The designed LR model is statistically significant with $\chi^2(6) = 70703.137$, $p = 0.000$. The LR coefficient was also calculated for probability analysis and future implementation of digital Ayurveda-based PD prediction applications.

Key Words: *Tridosha;* Logistics Regression; Dimension Reduction; XGBoost; Kernel-SVM; UPDRS-II; NMSQ.

Introduction

Parkinson's disease (PD) is a neurodegenerative disease that occurs mainly in older people (1, 2). In modern medicinal practice the initial diagnosis of PD was made through the analysis of cardinal motor symptoms such as rigidity, bradykinesia, tremor and postural instability (3). In addition to these cardinal motor symptoms, there are several other types of motor and non-motor symptoms that can occur in and with PD (4, 5). But Ayurveda follows its own diagnostic process for identifying diseases through *dosha* analysis (6-8). In contemporary *Ayurvedic* literature PD cannot be justified completely; although various PD symptoms have been classified in Ayurvedic literature (9). The most common disease or symptom resembling PD is *Kampavata*, and many of the other PD symptoms, mainly motor symptoms, through which PD is diagnosed, fall under the category of *Vata dosha*, so PD is called *Vata dosha* disorder in *Ayurveda* (9, 10). If we want to consider all the different types of motor and non-motor symptoms that have emerged in PD over time, we can follow different standard scaling systems for assessing different motor and non-motor symptoms associated with PD (11, 12).

The Unified Parkinson's Disease Rating Scale (UPDRS), sponsored by the Movement Disorder Society (MDS), helps assess Parkinson's disease through non-motor and motor experiences of daily living and motor complications (13-15). The overall scaling system is divided into four categories, with the Daily Life motor experience questioners or UPDRS II questionnaires assisting in the identification of motor symptoms through patient or caregiver self-assessment (16). Similarly, the MDS Non-Motor Symptoms Questionnaire (NMSQ) follows the evolutionary technique of self-assessment for the estimation of non-motor symptoms (17, 18). The basic evolutionary technique of these two scaling systems is through the scoring method, in which a subject is scored depending on the occurrence of various motor and non-motor symptoms (13-15, 17, 18). This scoring system can be recalculated for the Ayurvedic *tridosha* system based on each motor and non-motor symptom. First of all, all motor symptoms govern the movement of the body, which can be correlated with the *Vata dosha* as in the Ayurvedic literature (9, 19). So we can easily assign the motor symptom score as a *Vata* score (19). Similarly, we can determine the non-motor symptom

*** Corresponding Author:**

Sudip Paul
Department of Biomedical Engineering,
North-Eastern Hill University,
Shillong 793022,
Meghalaya, India.
Email Id: sudip.paul.bhu@gmail.com

score as a *tridosha* score based on the available literature in *Ayurveda* as shown in table 1. The obtained *tridosha* score can be used to develop various predictive models for PD, which is a very rare practice in Ayurveda.

In the age of digitization and artificial intelligence, machine learning (ML) is proving to be a very powerful tool for diagnosing and predicting diseases (20, 21). In *Ayurveda*, ML is also used for disease diagnosis, *Prakriti* determination, *dosha* analysis and much more (22-25). But very limited research has been done on diagnosing PD in light of *Ayurveda*, particularly through *dosha* analysis with ML. In this research, we will try to design a significant ML algorithm for PD detection. To achieve this goal, we used UPDRS II (16) and the NMSQ (18) diagnostic scaling system with various other health attributes such as age, sex, height and weight. For this purpose, different ML algorithms were applied and the best model was chosen according to the performance evaluation of each model. Since our main goal is to design the ML model based on Ayurvedic *dosha* responses, we determined the *dosha* behavior for all motor and non-motor symptoms listed in UPDRS II and NMSQ. Finally, we developed our own Ayurvedic *dosha* based scaling system derived from the UPDRS II and NMSQ scaling system. The obtained *dosha* score is finally used to train and test the model. Finally, we have reached our best model that can predict PD with high accuracy. In addition, we have also determined the *dosha* behavior for PD, which may help in understanding the symptoms and the *dosha* relationship in future research.

Methods

Study design and participants

In this research, we selected our study participants with appropriate biomarker data from the Fox Insight (FI) dataset sponsored by the Michael J. Fox Foundation (26). In FI dataset there are different categorical data related to PD, through which we have taken the data tagged by "Your Movement Experiences" and "Your Non-Movement Experiences", self-assessment data relate to movement and non-movement experience of PD. The movement experience data is actually following the MDS-UPDRS II rating scale and the non-movement experience data is following the MDS-NMSQ rating scale format (16, 18). Besides these we have considered the other general informative data like age, sex, height (in centimeter) and weight (in kilogram) of the subject from the FI dataset with their respective motor and non-motor experienced data. We have derived BMI of the subject from the height and weight information by using formula-

$$BMI = \frac{Weight\ in\ kilogram}{\left(\frac{Height\ in\ centimeter}{100}\right)^2} \quad (27).$$

Here we have got total n=80,916 records of data including PD and Control subjects in which we have n=14,853 records of Male PD subjects, n=11,538 records of Female PD subjects, n=13,571 records of Male Control subjects, and n=40,954 records of Female Control subjects. All these records are consisting of the collection of 13 UPDRS-II questionnaires data, 30 NMSQ questionnaires data, including the information of age, sex, height and weight and derived BMI.

Data preprocessing

The data obtained were pre-processed and analyzed with IBM SPSS Version 28 (28). First, the imported data was processed for the missing value analysis (29). The incomplete data records were discarded or transformed according to the missing value types. The missing values for sex, height and weight of the subjects were discarded to avoid computational anomalies. The missing values related to symptoms were set to zero or no symptoms depending on the existence of records. Here we also considered the multiple entries of a single subject at different ages to better understand the combination of appearance and disappearance of symptoms over time. In addition, cumulative *dosha* score and BMI were calculated by SPSS. Also, multiple statistical analysis like mean with standard deviation (30), Pearson correlation (31) for each variable like gender, age and *Vata*, *Pitta*, *Kapha* *dosha* score were calculated by SPSS. Finally, the pre-processed data for machine learning model design was exported.

Dosha score determination

As UPDRS-II scale are consisting of questionnaires related to motor symptoms and we know that the motor problem are related to *Vata dosha* (19), so we have marked each questionnaires score as *Vata* score based on the symptoms severity. In UPDRS-II scale each symptoms is scored from 0 to 4 depending upon the symptoms severity, where 0 is stating the normal condition or the symptom is not present and 1 to 4 is marked as 1-slight, 2-mild, 3-moderate, and 4-severe (14). Here we have assign the *Vata* score from 0 to 4 as on the UPDRS-II score. The MDS-NMSQ questionnaires data have been scored by their respective involved *dosha* by 1 based on their presence in the subject as shown in the table 1. Finally, we have calculated the cumulative *dosha* score by adding up the each *dosha* score appeared in UPDRS-II and NMSQ responses and we get cumulative *Vata*, *Pitta*, and *Kapha* score. These three cumulative *dosha* scores, age, sex, and BMI are finally used to design the PD prediction model.

Designing of mean score based PD predictive model

The working principle of UPDRS-II, and NMSQ scale based PD detection model is based upon the mean value of the overall score (58-60). We have obtained the mean with standard deviation value for PD subjects for both Male and Female category. The subject with PD having predicted positive if the total score obtained from UPDRS-II, and NMSQ is greater than the mean score subtracted by standard deviation of the particular sex Male or Female category.

$Total\ Score_{(UPDRS\ II\ +\ NMSQ)} \geq (Mean - Standard\ deviation)$..... for positive PD

$Total\ Score_{(UPDRS\ II\ +\ NMSQ)} < (Mean - Standard\ deviation)$..... for negative PD

The designed model was verified with our obtained dataset and the respective confusion matrix and accuracy score were obtained for model comparison.

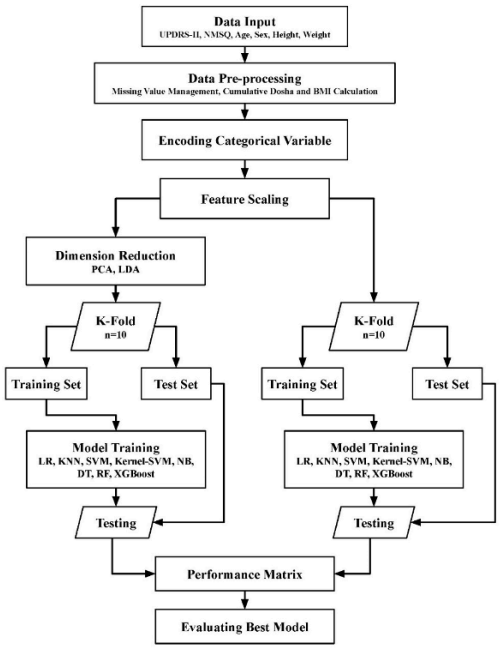
Table 1. List of MDS-NMSQ non-motor symptoms and their involved dosha score.

Non-Motor Symptoms	*Vata*	*Pitta*	*Kapha*
Dribbling of saliva during the daytime (19)	1	0	0
Loss or change in your ability to taste or smell (32-34)	1	0	1
Difficulty swallowing food or drink or problems with choking(19)	1	0	0
Vomiting or feelings of sickness (nausea) (35)	1	0	0
Constipation (less than three bowel movements a week) or having to strain to pass a stool (36-38)	1	1	0
Bowel (fecal) incontinence (37, 39)	1	0	0
Feeling that your bowel emptying is incomplete after having been to the toilet (37)	1	0	0
A sense of urgency to pass urine that makes you rush to the toilet (40)	1	0	0
Getting up regularly at night to pass urine (40)	1	0	0
Unexplained pains (not due to known conditions such as arthritis) (41, 42)	1	1	0
Unexplained change in weight (not due to change in diet) (43)	1	0	0
Problems remembering things that have happened recently or forgetting to do things (44)	1	0	0
Loss of interest in what is happening around you or in doing things (43)	1	0	0
Seeing or hearing things that you know or are told are not there in (44)	0	1	0
Difficulty concentrating or staying focused (44)	1	0	0
Feeling sad, 'low' or 'blue' (43)	1	0	0
Feeling anxious, frightened or panicky (43)	1	0	0
Feeling less interested in sex or more interested in sex (43, 45, 46)	1	0	1
Finding it difficult to have sex when you try (47)	1	0	0
Feeling light-headed, dizzy or weak standing from sitting or lying (44)	0	0	1
Falling (19)	1	0	0
Finding it difficult to stay awake during activities such as working, driving or eating (44)	0	0	1
Difficulty getting to sleep at night or staying asleep at night (43, 44)	1	0	0
Intense, vivid or frightening dreams(48-50)	1	0	0
Talking or moving about in your sleep, as if you are 'acting out' a dream(48-51)	0	1	0
Unpleasant sensations in your legs at night or while resting, and a feeling that you need to move (52, 53)	1	0	0
Swelling of the legs (54, 55)	1	0	0
Excessive sweating (56)	1	1	0
Double vision (57)	1	0	0
Believing things are happening to you that other people say are not (44)	0	1	0

Designing of Machine Learning based Ayurvedic PD predictive model.

In the machine learning-based Ayurvedic predictive model, we used age, sex, BMI, and cumulative *Vata*, *Pitta*, and *Kapha* score as input to train the model. Here we used several machine learning classification algorithms like Logistics Regression (LR) (61), K-Nearest Neighbors (KNN) (62), Support Vector Machines (SVM) (63), Kernel Support Vector Machines (KSVM) (64), Naive Bayes (NB) (65), Decision Tree (DT) (66), Random Forest (RF) (67), and XGBoost (68) using scikit-learn (69) library of Python. We also applied the K-Fold cross-validation technique (70) to evaluate the best algorithm with the highest average accuracy. Before feeding the data for training and testing, we encoded (71) the categorical variable sex, followed by the feature scaling method for scaled variables such as *Vata* score, *Pitta* score, *Kapha* score, age, and BMI. After feature scaling (72), we used two different methods to develop our ML-based model. In the initial technique, we applied various dimension reduction algorithms (73) such as Principal Component Analysis (PCA) (74) and Linear Discriminant Analysis (LDA) (75) before applying the ML algorithm; and in another way we fed the data directly to train and test the ML algorithm without applying any dimension reduction algorithm. Finally, all these combinations of features and techniques were fed into the above ML algorithms and cross-validated with K-Fold of 10 iterations, and the best model and its relative features and techniques were chosen according to average accuracy (70). Figure 1 below shows the block diagram for evaluating the best model among different ML algorithms for predicting PD.

Figure 1. Block diagram for evaluating best ML algorithm.



For all models we generated the confusion matrix (76), receiver operating characteristic curve (ROC curve), and area under curve (AUC) (77, 78). Besides these we have also calculated the Sensitivity or True Positive Rate (TPR), Specificity or True Negative Rate (TNR), Precision or Positive Predictive Value (PPV), Negative Predictive Value (NPV), Fall-out or False Positive Rate (FPR), False Discovery Rate (FDR), Miss Rate or False Negative Rate (FNR), Accuracy (ACC), F1 Score (F1), and Matthews Correlation Coefficient (MCC) from the obtained confusion matrix for all our model (76). The confusion matrix is a very popular tool for evaluating the performance of the ML algorithm by comparing the actual value with the predicted value. The outputs of the confusion matrix for a binary classifier are True Positive (TP): where the output is predicted to be positive for an actual positive value, True Negative (TN): where the output is predicted to be negative for an actual negative value, False Positive (FP): where the output is predicted to be positive for an actual negative value, and False Negative (FN): where the output is predicted to be negative for an actual positive value (76). The other measurement scores from the obtained confusion matrix were calculated by the following formulas.

$$TPR = \frac{TP}{(TP + FN)} \quad (1)$$

$$SPC = \frac{TN}{(FP + TN)} \quad (2)$$

$$PPV = \frac{TP}{(TP + FP)} \quad (3)$$

$$NPV = \frac{TN}{(TN + FN)} \quad (4)$$

$$FPR = \frac{FP}{(FP + TN)} \quad (5)$$

$$FDR = \frac{FP}{(FP + TP)} \quad (6)$$

$$FNR = \frac{FN}{(FN + TP)} \quad (7)$$

$$ACC = \frac{(TP + TN)}{(TP+FP+TN+FN)} \quad (8)$$

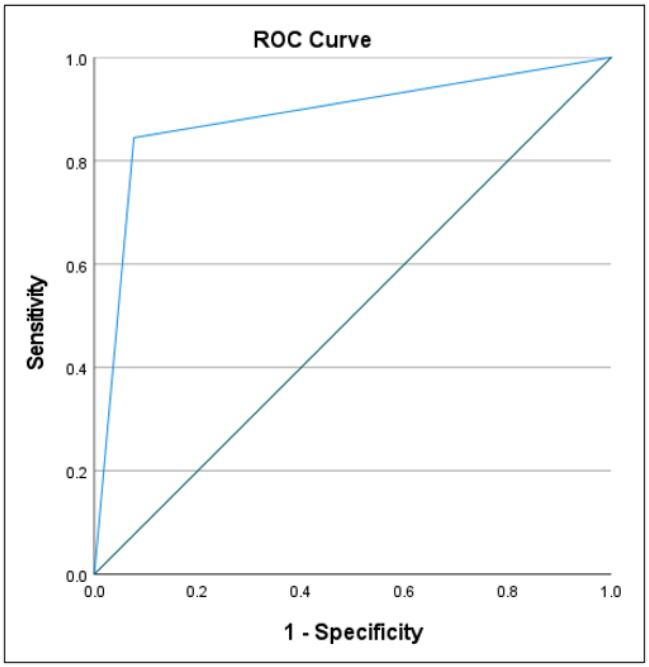
$$F1 = \frac{2TP}{(2TP + FP + FN)} \quad (9)$$

$$MCC = \frac{TP \times TN - FP \times FN}{\sqrt{(TP+FP) \times (TP+FN) \times (TN+FP) \times (TN+FN)}} \quad (10)$$

Results

By analyzing the mean of the UPDRS-II scores and the NMSQ score, we found that the overall mean (standard deviation) for PD is 22.622 (12.134). The mean (standard deviation) for male PD is 23.209 (12.294) and for female PD is 21.866 (11.882). According to the PD prediction model using the mean, we found that each subject is predicted as a PD if for male subjects and for female subjects. For our obtained dataset, these models have a true positive or true PD for n=22,591 or 85.6% of subjects, a true negative or true control for n=50,087 or 91.9% of subjects, for n=3,800 or 14, 4% of subjects predicted a false negative or false control and false positive or false PD for n=4,438 or 8.1% of subjects. The accuracy of this model is 89.82% considering the other factors like sensitivity 0.8560, specificity 0.9186, precision 0.8358, negative predictive value 0.9295, false positive rate 0.0814, false discovery rate 0.1642, false negative rate 0.1440, f1 score 0.8458, and Matthews correlation coefficient 0.7699. The following figure 2 is showing the ROC curve of the model.

Figure 2. ROC plot of the mean based PD predictive model with the AUC value 0.884



After calculating the cumulative *dosha* score for all our *tridosha* in relation to the UPDRS II and NMSQ scores, we calculated the Pearson's correlation for all our considered variables for ML models shown in Figure 3. This figure and its value show the linear relationship of all these variables.

Figure 3. Pearson's correlation matrix of all variable used in ML.

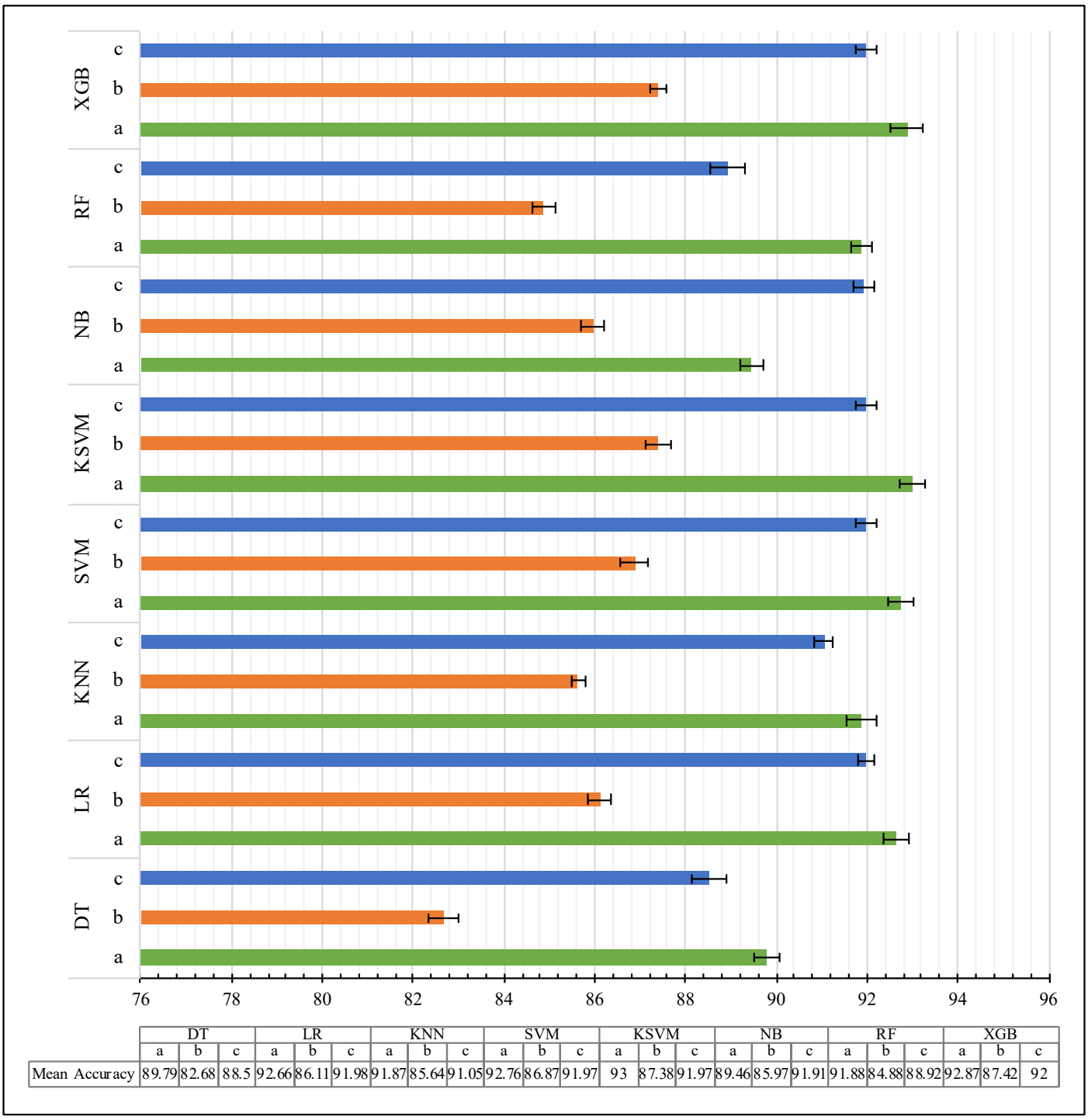
	Kapha Score	*Pitta* Score	*Vata* Score	Sex	BMI	Age
Kapha Score	1					
Pitta Score	0.665**	1				
Vata Score	0.73**	0.757**	1			
Sex	-0.207**	-0.157**	-0.257**	1		
BMI	0.005	0.012**	-0.001	-0.004	1	
Age	0.094**	0.116**	0.219**	-0.115**	0.014**	1

** Correlation is significant at the 0.01 level (2-tailed).

Through this matrix we can observe that all three *doshas* are positively correlated with age, implying that with age all three *doshas* are significantly get vitiated. While the negative correlation with gender shows that the male subjects suffer more from *dosha* disorders than the females. Likewise, increasing age increases the risk of developing PD.

In an ML-based PD prediction system, we found that KSVM without dimensionality reduction algorithm has the highest mean accuracy of 93% with a standard deviation of 0.28%. Figure 4 below shows a comparative bar chart of the mean accuracy with standard deviations for different ML algorithms with and without dimension reduction.

Figure 4. Comparative bar chart of mean accuracy values with standard deviation of all applied ML algorithms with or without dimension reduction. (a) Represents the ML algorithms without dimensionality reduction. (b) Represents ML algorithms with PCA dimension reduction. (c) Represents ML algorithm with LDA dimension reduction.



	DT			LR			KNN			SVM			KSVM			NB			RF			XGB		
	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c	a	b	c
Mean Accuracy	89.79	82.68	88.5	92.66	86.11	91.98	91.87	85.64	91.05	92.76	86.87	91.97	93	87.38	91.97	89.46	85.97	91.91	91.88	84.88	88.92	92.87	87.42	92

Here we found that except the NB algorithm, all the other algorithms have the higher average accuracy without the dimensionality reduction, and even the NB algorithm with LDA could not reach the highest accuracy among other algorithms. So, in this problem, dimensionality reduction like PCA or LDA may not play a significant role in achieving the accuracy, and we found that the ML algorithm without dimensionality reduction technique has the higher accuracy. The following table 2 shows the confusion matrix, figure 5 shows the ROC curves with AUC, and figure 6 shows the line chart of different measured characteristic values of all considered ML algorithms without dimensionality reduction.

Table 2. Confusion matrix of the all ML algorithm tested on 20% data of the entire dataset.

ML	True	True	False	False
Logistics	4421	10506	444	813
K-Nearest	4515	10351	599	719
Support	4446	10503	447	788
Kernel	4531	10466	484	703
Naive Bayes	4390	10075	875	844
Decision	4406	10148	802	828
Random	4466	10412	538	768
XGBoost	4562	10442	508	672

Figure 5. ROC curve and AUC of all considered ML algorithms generated from the test set obtained from the 20% of the whole dataset.

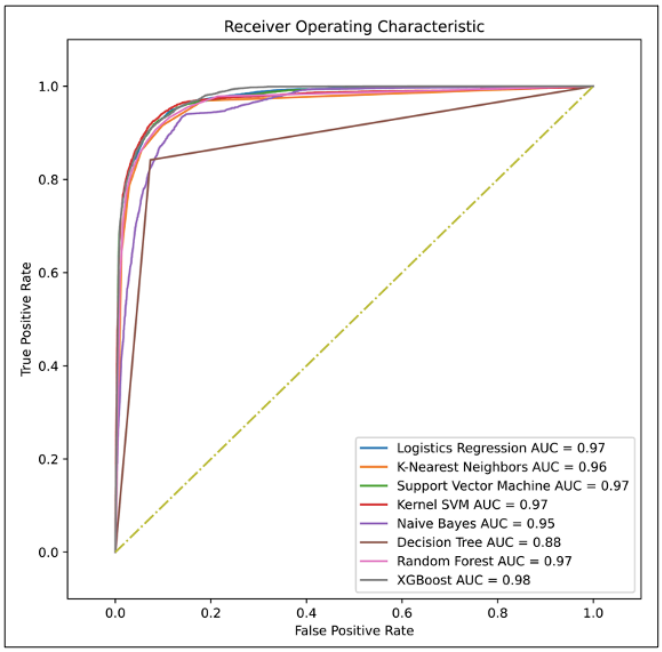
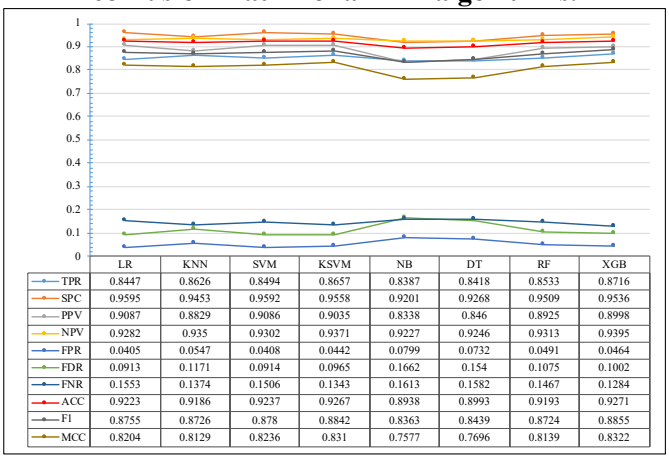


Figure 6. Line chart showing the variations of different measured values from the obtained confusion matrix of all ML algorithms.



	LR	KNN	SVM	KSVM	NB	DT	RF	XGB
TPR	0.8447	0.8626	0.8494	0.8657	0.8387	0.8418	0.8533	0.8716
SPC	0.9595	0.9453	0.9592	0.9558	0.9201	0.9268	0.9509	0.9536
PPV	0.9087	0.8829	0.9086	0.9035	0.8338	0.846	0.8925	0.8998
NPV	0.9282	0.935	0.9302	0.9371	0.9227	0.9246	0.9313	0.9395
FPR	0.0405	0.0547	0.0408	0.0442	0.0799	0.0732	0.0491	0.0464
FDR	0.0913	0.1171	0.0914	0.0965	0.1662	0.154	0.1075	0.1002
FNR	0.1553	0.1374	0.1506	0.1343	0.1613	0.1582	0.1467	0.1284
ACC	0.9223	0.9186	0.9237	0.9267	0.8938	0.8993	0.9193	0.9271
F1	0.8755	0.8726	0.878	0.8842	0.8363	0.8439	0.8724	0.8855
MCC	0.8204	0.8129	0.8236	0.831	0.7577	0.7696	0.8139	0.8322

Discussion

In this research, we attempted to develop a PD prediction model based on Ayurvedic biomarkers such as the *tridosha* variation. The initial goal of this design is to develop a self-assessment diagnostic tool that allows an ordinary person to check PD status by answering some simple questionnaires without any special medical knowledge and expertise through the Ayurvedic diagnostic method. To achieve this goal, we considered the UPDRS and NMSQ scaling system for PD assessment (59). In the UPDRS scaling system, UPDRS II questionnaires are essentially designed for self-assessment recording systems of motor symptoms (16), and NMSQ questionnaires are for non-motor symptoms (18). In the first method, we developed a model by which the UPDRS II score and the NMSQ score were calculated and added, and the PD prediction is made on the basis that the obtained score is equal to or higher than the subtracted value of the Mean and standard deviation values obtained from our dataset for a specific gender category. In this method we did not use Ayurvedic biomarkers, age and BMI information. We used this model as a reference model for comparing our ML-based Ayurvedic PD prediction model. In the second method, we derived *Vata*, *Pitta* and *Kapha* scores from each UPDRS II and NMSQ attribute and calculated the cumulative *dosha* score and applied the different ML algorithms with the age, gender and BMI information of the subjects. After comparing each ML algorithm with our reference mean based model we have found for each ML based model have the higher accuracy score than the reference mean based model except Naive Bayes ML algorithm. This comparison proves that the Ayurveda-based ML algorithm can also be used to predict PD and shows the higher accuracy than our general mean-based self-assessed PD prediction model. This is one of the new findings in this research on an Ayurveda-based self-assessment PD diagnostic system.

As a result, we achieved the highest accuracy of 93%, which is almost 3% higher compared to our reference mean-based model using KSVM algorithm without applying dimensionality reduction. Apart from that, SVM, LR and XGB algorithm based models also have the higher accuracy near KSVM, and the accuracy difference is no more than 0.5%. Therefore, when choosing our best model among all these four models, we considered the FPR score as a reference. The FPR score actually expresses the false positive predictor score of any model. In the healthcare sector, false positive predictions generate unnecessary panic, increasing patient anxiety and also increasing unnecessary healthcare costs (79, 80). To account for this, we found that LR-based models had the lowest FPR value of 0.0405. In this context, the LR-based ML model turns out to be our best Ayurveda-based PD prediction model with an average accuracy of 92.66%.

The final equations of our ML-based PD prediction model based on Ayurvedic *Tridosha* scores, age, BMI and sex according to logistic regression (81, 82) is as follows.

$$z = -3.333 + (age \times 0.036) - (BMI \times 0.068) + (Vata \times 0.462) - (Pitta \times 0.605) - (Kapha \times 0.567) - 1.168_{(Female)} \quad (11)$$

$$Probability = \frac{1}{1+e^{-z}} \quad (12)$$

A person will be predicted as PD if $Probability \geq 0.5$.

The logistics regression model is statistically significant (82), $\chi^2(6) = 70703.137$, $p = 0.000$. The model explained 81.24 % (Nagelkerke R^2 (83)) of the variance in Parkinson's diseases and correctly classified

92.6 % of cases. Males are 3.216 times more likely to exhibit PD than females, OR (95% Confidence Interval) 3.216 (3.028 – 3.416), p=0.000. Increasing age is associated with an increased likelihood of exhibiting PD, OR 1.036 (1.034 – 1.039), p<0.001, but increasing BMI is associated with a reduction in the likelihood of exhibiting PD, OR 0.934 (0.929 – 0.94), p<0.001. Likewise, increasing *Vata* score is associated with an increased likelihood of exhibiting PD, OR 1.587 (1.574 – 1.601), p<0.001, but increasing *Pitta* score, OR 0.546 (0.526 – 0.567), p<0.001, and *Kapha* score OR 0.567 (0.544 – 0.591), p<0.001, are associated with a reduction in the likelihood of exhibiting PD.

Conclusion

In summary, we have successfully found and developed the most suitable ML algorithm, namely logistic regression, to predict PD through the comparative analysis between different ML algorithms and their performance. Also, we described the linear relationship of our considered attributes by Pearson's correlation and finally obtained the likelihood factor of different attributes with PD. This relationship and the predictor model demonstrate the significant scientific evidence of *dosha*-based analysis and modeling for Parkinson's disease in the light of *Ayurveda*. Although this research has several limitations, we did not apply the deep learning algorithms to develop this predictive model. Apart from that, besides UPDRS II motor symptoms and NMSQ non-motor symptoms, we did not consider other attributes such as previous medical history records, current health status, family history of neurological disorders, environmental exposure, lifestyle, etc. of PD available in the FI dataset. Each of these other symptoms can be correlated with the PD and with their respective *dosha* behavior, which can be done in future research. We have not included the *Prakriti* analysis due to unavailable data in the FI dataset. But the designed model guarantees the achieved accuracy of its excellence in the field of digital Ayurveda.

Declaration of interests

We declare no competing interests.

Ethical approval

FI study protocol and informed consent are reviewed by the New England IRB (IRB#: 120160179, Legacy IRB#: 14–236, Sponsor Protocol Number: 1, Study Title: Fox Insight).

Data availability

Data used in the preparation of this manuscript were obtained from the Fox Insight database (https://foxinsight-info.michaeljfox.org/insight/explore/insight.jsp) on 13/07/2022. For up-to-date information on the study, visit https://foxinsight-info.michaeljfox.org/insight/explore/insight.jsp

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