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Role Of Zinc Transporter And SLC 30a8 Gene Polymorphisms In Type 2 Diabetes Mellitus

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Abstract:
This research seeks to understand the function of zinc transporter and SLC30A8 gene alleles polymorphisms in type 2 diabetes mellitus (T2DM) by using a large database containing 100,000 people genotypes. In order to assess the complexity of genetics and its implication in the development of T2DM, age, BMI, blood glucose levels as well as genetic predisposition were taken into consideration during examination. The SLC30A8 gene mutations was the association, revealed by the data analysis, with T2DM; this means that personalized risk assessment can be based on the patient's genetic profile. Besides that, the questionnaire also dealt with clinical aspects, possible therapeutic interventions as well as the economic factors relating to T2DM treatment. However, the conclusion of the multimodal learning pipeline model demonstrated the superiority of the Multilayer Perceptron (MLP) Classifier in predicting the diabetic characteristics, reaching an accuracy of 97.245%. Consequentially budget impact assessments demonstrated not only the clinical benefits of introducing such systems in diabetes care but also provided the decision makers with economic implications of patient benefits. In summary, our research would fill in the cognition, deregulation, therapeutics, economics and management gap, eventually strengthening personalized medicine and improved healthcare strategy.

Keywords: *type 2 diabetes mellitus, zinc transporter, SLC30A8 gene polymorphisms, machine learning, economic analysis*

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I. Introduction

For a huge burden to human health, T2DM is considered as a chronic health problem, characterized by insulin resistance and abnormal insulin production. With T2DM's pathogenesis being multifactorial, genetic factors have gained further spotlight as significant contributors to the increase in disease susceptibility and the disease's downward progression. A plethora of genes with a diverse array of mutations has been established as a chief factor in type 2 diabetes mellitus pathophysiology exploration. However, a particularly promising genetic segment for further study is the gene encoding zinc transporters, mainly the SLC30A8 gene. Zinc is a vitally important dietary micronutrient for multiple metabolism processes including pancreatic β-cell, insulin production and regulation of glucose homeostasis. On the inside of pancreatic β-cells, zinc is intimately implicated in storing and releasing insulin granules from the secretory organelles while also regulating the enzymes that degrade insulin and other hormones produced by these cells. SLCA30A8 is the gene that produces zinc transporter 8 (ZnT8) which is majorly expressed in the pancreatic β-cells and regulates zinc transport into the insulin secretory vesicles. For instance, gene previously called solute carrier family 30 (zinc transporter), member 8 (SLC30A8, renamed as ZnT8), carries different polymorphisms that affect its function in terms of zinc homeostasis in pancreatic β-cells and may also influence secretion of insulin. Gene polymorphisms of SLC30A8 and link to T2DM risk have produced some interesting studies concerning the possibility for genetic variations to reinforce the T2DM probability. Additionally they may demonstrates its importance in manifestation of T2DM related features like tolerance of blood sugar and hyper insulin reminiscence. To what extent SLC30A8 genes polymorphism affects the predisposition of T2DM and the relevant phenotypes is a pivotal issue to delve into, as it may reveal some insights into the molecular basis and advancement of the disease. The secondly, getting to know the play of genes and environment in diabetes type 2Etaiology can guide on personalized risk assessment and therapies which are adjusted to individual genetic profiles. In this framework, the research will fundamentally investigate the function of DMT1 and SLC30A8 gene variants in T2DM, enlightening about their implied relation to the origins of disease and its public health implications. Using a multidisciplinary approach incorporating genetic epidemiology, molecular biology, and clinical research strategies, this study intends to fill the gap in our knowledge of the hereditary predispositions to T2DM and consequently explore emerging strategies of tailored medicine for specific genetic subgroups.

II. Related Works

It has been the focus of many recent studies to investigate all possible factors, which have to do with both T1DM and T2DM on clinical level, inheritance, therapies, and the influence of T2DM on the various organ systems. The following studies contribute significantly to the understanding of diabetes management and its complications: Juan Pablo Pérez Bedoya alongside other researchers (2022) carried out a systematic literature review to scrutinize into the clinical outcomes of COVID-19 disease in patients favoring T1DM and T2DM. That protocol covers the evaluation objects and ways of completely scrutinizing the influence of COVID-19 over those people with diabetes. It highlights the nooks and crannies of the difficulties experienced by people with diabetes in coping with the disease. [12] Kazmierczak et al. (2023) revealed the outcomes of practical and structural health states, as well as adverse effects of vitreous body removal done on patients having moderate to severe proliferative diabetic retinopathy. Their research gave much-needed ideas to the whole field of management of diabetic retinopathy, a complication which diabetes of the 1st and second kinds, both, can cause while observing the importance of surgical interventions in the maintenance of vision and prevention of blindness. [12] The research pinpointed the genetic link between the rs7903146 polymorphism of the TCF7L2 transcription factor and T2DM through Kumar and colleagues in 2024. Through their research, these scientists reveal the connection between genetic variations and the development of obesity, which for in turn are the characteristics targets in the development of personalised therapeutics and preventive solutions. [13] In 2023, Li et al. explored the therapeutic potential of Pueraria thomsonii water extract in diabetic mice with a db/db special mouse and found that it has the ability to combat this condition. The research provides the evidence of the capabilities of herbal medicines to control T2DM at the levels of comprehensive metabolic regulation and gut microbiota illustrating innovative clinical practices. [14] Mabena et al in 2024 evaluated the effect of nutraceuticals on micro and macro vasculodies in diabetes induced by both type 1 and type 2. Alongside their study, which considers the effectiveness of nutraceutical treatments in relieving vascular complications diabetes patients may encounter, highlighting the significance of developing holistic approaches in diabetes management. [15] Palacios et al. (2023) budget impact analysis of FreeStyle Libre Flash CGMS® in T1DM and T2DM were performed in patients with the both conditions, being conducted in Argentina. In their study, the authors review the economic situation when employing continus glucose monitoring technology for diabetes mangement making it of high significance for the health sectors [16].

III. Methodology

Data Collection and Preprocessing:

The Kaggle dataset that we have analyzed includes parameters such as gender, ageing, Body Mass Index (BMI), Blood Glucose level, Hypertension, Heart Disease, smoking habits, HbA1c levels, and the diagnosis status of diabetes. Problematic cases of unavailable values and anomalies are dealt with through adoption of strategies like mean imputation or elimination, making data sound.

Feature Selection:

The critical factors to consider for exploring the genetic components and the underlying physiological elements that might be leading to type 2 diabetes (T2DM) are identified [1]. Selected values like age, BMI, blood glucose level, hypertension, and heart disease history are the demographics that are tied with T2DM.

Exploratory Data Analysis (EDA):

Data Analysis Methods such as EDA enables researchers to comprehend the distribution of facts, display details and also explore connecting patterns with these facts. We can generate various visualizations like histograms, box plots, and correlation matrices in order to study the datasets and get vital insights [17].

Model Development:

Machine learning models are trained to forecast diabetes statuses through selecting features that relate to the group of variables such as age, BMI, blood glucose level, and mutations in a particular genetic file like an SLC30A8 file. Five popular classification algorithms are utilized: SVM Classifier, Random Forest, Logistic Regression, Gradient Boosting Classifier, and MLP Classifier [18].

Model Evaluation:

The evaluation of the accuracy is used in the assessment of accuracy and other metrics including precision, recall, F1-score, and Receiver Operating Curve (ROC) with area under the curve (AUC). In creating a confusion matrix, rate of the model in predicting diabetic status is represented [2].

Comparison of Models:

One of the important factors considered in the evaluation is the comparison of the models in terms of their performance metrics in order to select the most accurate algorithm to predict diabetes status on the available dataset [9].

Logistic Regression:

P(Y=1|X) = 1 / (1 + exp(-(b0 + b1*X1 + b2*X2 + ... + bn*Xn)))

Logistic Regression models the probability of a binary outcome (Y=1 or Y=0) based on one or more predictor variables (X1, X2, ..., Xn). It estimates the coefficients (b0, b1, ..., bn) to fit the logistic function.

```
Initialize weights b0, b1, ..., bn
Iterate until convergence:
Compute predicted probabilities using the logistic function
Compute loss using the log-loss function
Update weights using gradient descent
```

Random Forest

Random Forest is a machine learning approach which builds decission trees during the training and emits the mode of the classes (Classification) or average prediction (regression) of the individual trees [3].

```
For each tree in the forest:
Randomly select features to split on
Construct decision tree
```

Support Vector Machine (SVM)

SVM is a supervised learning algorithm that constructs a set of hyperplanes in a high-dimensional space to classify the given dataset to various classes [19].

```
Choose a kernel function and kernel parameters
Formulate the optimization problem
Solve the optimization problem using quadratic programming
```

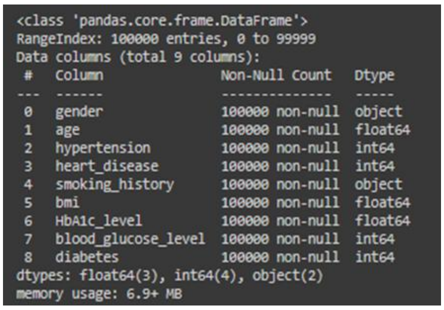
IV. Result And Analysis

Dataset Link: https://www.kaggle.com/code/willribeiro/diabetes-analysis-and-prediction/input

```
   gender   age  hypertension  heart_disease  smoking_history    bmi  HbA1c_level  blood_glucose_level  diabetes
0  Female  80.0             0              1            never  25.19          6.6                  140         0
1  Female  54.0             0              0          No Info  27.32          6.6                   80         0
2    Male  28.0             0              0            never  27.32          5.7                  158         0
3  Female  36.0             0              0          current  23.45          5.0                  155         0
4    Male  76.0             1              1          current  20.14          4.8                  155         0
```

Figure 1: Importing the dataset

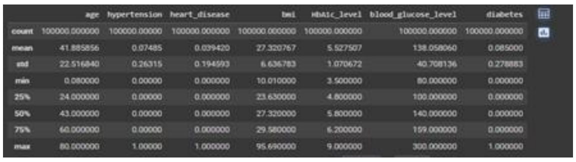
There are 100,000 items in the 9 columns of the given data. The data in these columns refers to specific people which includes their gender, age, blood glucose level, body mass index (BMI), blood pressure, heart disease history, presence of hypertension, presence of heart disease, smoking history, HbA1c level (a measurement of blood sugar control over time), and whether or not they have been diagnosed with diabetes (1 if yes, 0 if no).



```
<class 'pandas.core.frame.DataFrame'>
RangeIndex: 100000 entries, 0 to 99999
Data columns (total 9 columns):
 #   Column               Non-Null Count   Dtype
---  ------               --------------   -----
 0   gender               100000 non-null  object
 1   age                  100000 non-null  float64
 2   hypertension         100000 non-null  int64
 3   heart_disease        100000 non-null  int64
 4   smoking_history      100000 non-null  object
 5   bmi                  100000 non-null  float64
 6   HbA1c_level          100000 non-null  float64
 7   blood_glucose_level  100000 non-null  int64
 8   diabetes             100000 non-null  int64
dtypes: float64(3), int64(4), object(2)
memory usage: 6.9+ MB
```

Figure 2: Checking the columns

Type 2 diabetes mellitus is influenced in its development or progression by genes linked to the zinc transporter such as SLC30A8. In this particular context, the dataset can be utilised to investigate plausible correlations between genetic variables such as mutations in the SLC30A8 gene and the incidence of diabetes considering age, body mass index and blood glucose levels.



	age	hypertension	heart_disease	bmi	HbA1c_level	blood_glucose_level	diabetes
count	100000.000000	100000.00000	100000.000000	100000.000000	100000.000000	100000.000000	100000.000000
mean	41.885856	0.07485	0.039420	27.320767	5.527507	138.058060	0.085000
std	22.516840	0.26315	0.194593	6.636783	1.070672	40.708136	0.278883
min	0.080000	0.00000	0.000000	10.010000	3.500000	80.000000	0.000000
25%	24.000000	0.00000	0.000000	23.630000	4.800000	100.000000	0.000000
50%	43.000000	0.00000	0.000000	27.320000	5.800000	140.000000	0.000000
75%	60.000000	0.00000	0.000000	29.580000	6.200000	159.000000	0.000000
max	80.000000	1.00000	1.000000	95.690000	9.000000	300.000000	1.000000

Figure 3: Dataset Description

The dataset provides important indicators of health related to the impact of SLC30A8 gene polymorphisms and zinc transporters in type 2 diabetes mellitus. The mean age of the 100,000 entries is 41.89 years and the incidence of hypertension is 7.49%. Further, the diagnosis of heart disease is 3.94%. Although the average HbA1c level is 5.53 is accountable for showing consistent blood sugar management with an average BMI of 27.32. The average blood glucose level is 138.06 mg/dL, and 8.5% of people have diabetes. These results emphasise the significance of the dataset for investigating the hereditary and physiological components of type 2 diabetes mellitus.

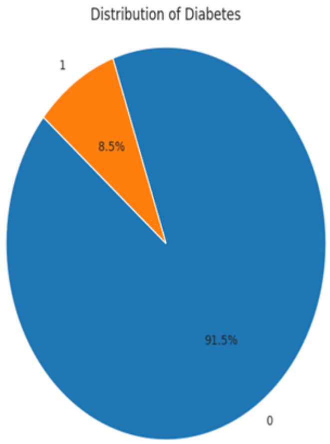


Figure 4: Diabetes Distribution in the dataset

The distribution of diabetes throughout the dataset is visually represented by the pie chart. Approximately 91.5% of people do not have diabetes with the remaining 8.5% having received a diagnosis.

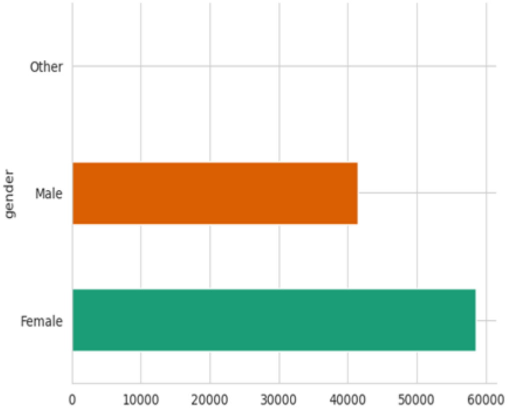


Figure 5: Gender distribution

The distribution of people according to gender is depicted in the horizontal bar plot. Of the total entries, 58,552 are made up of females, while 41,430 are made up of males. There are also other entries summing 18 are classified as "Other" gender.

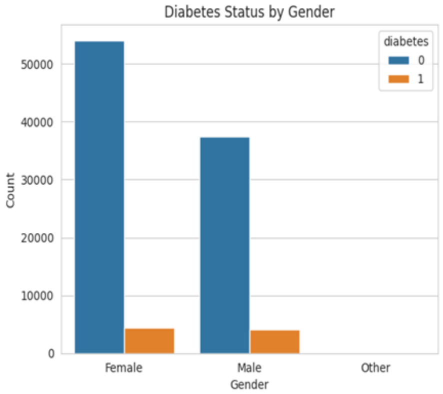


Figure 6: Diabetes distribution by gender

7.62% of females have been diagnosed with diabetes compared to around 92.38% of those who have not. According to the same statistics, 9.75% of males have diabetes and 90.25% do not. Only eighteen people fall into the "Other" gender group.

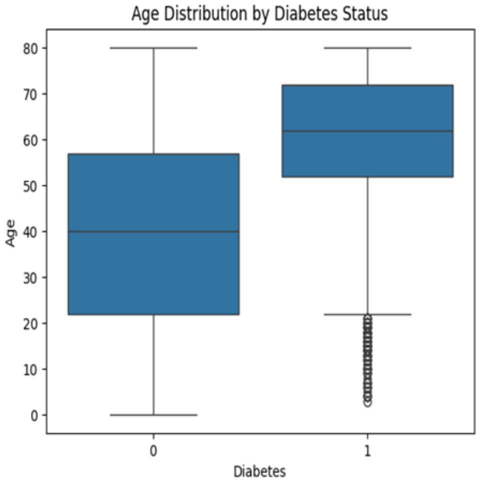


Figure 7: Age distribution based on Diabetes

The age distribution of those classified according to their diabetes condition is shown in the boxplot. The interquartile range (IQR) for non-diabetic persons (0) is 35.0 years, while their median age is 40.0 years. Those with diabetes (1) had a narrower IQR of 20.0 years and a higher median age of 62.0 years.

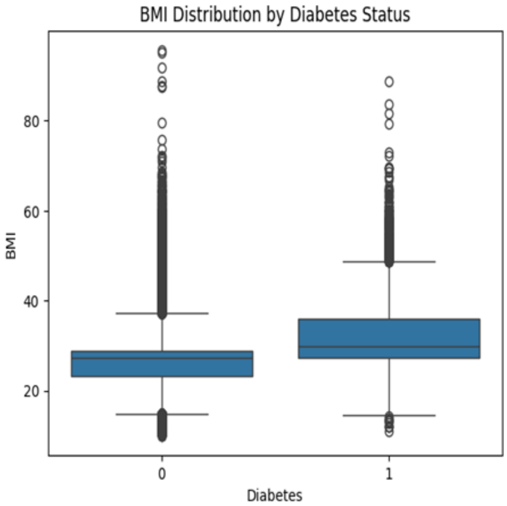


Figure 8: BMI distribution based on Diabetes

The interquartile range (IQR) for non-diabetic persons (0) is 5.63, while their median BMI is 27.32. The median BMI of diabetics (1), on the other hand, is higher at 29.97 with a broader IQR of 8.59. In general, those with diabetes have higher BMI values than those without diabetes, according to this comparison of BMI distributions.

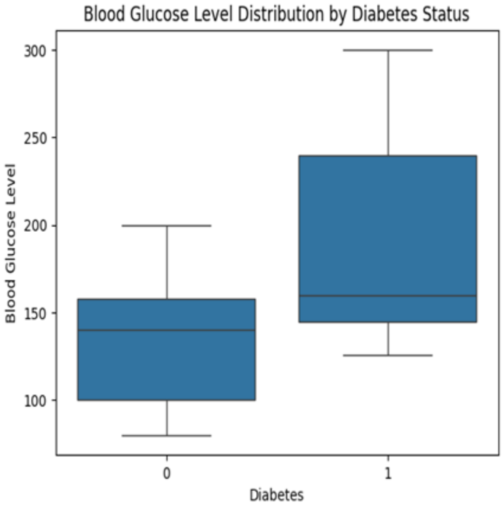


Figure 9: Blood Glucose level distribution based on Diabetes

The information offered shows that those with diabetes and those without diabetes have different blood glucose levels. The median blood glucose level in non-diabetic persons (0) is 140.0, with a smaller interquartile range (IQR) of 58.0. Those with diabetes, on the other hand, (1) had a wider IQR of 95.0 and a higher median blood glucose level of 160.0, suggesting more variability and perhaps worse blood sugar management.

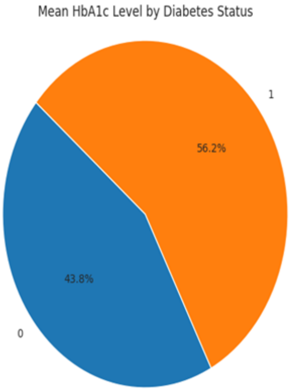
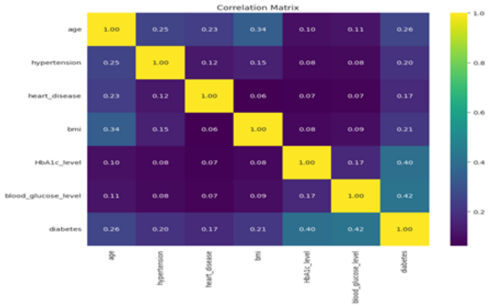


Figure 10: Mean HbA1c distribution based on Diabetes

The mean HbA1c level of 5.40 in non-diabetic persons indicates stable blood sugar management. On the other hand, those with diabetes had a much higher mean HbA1c level of 6.93, which denotes worse long-term blood sugar management.



	age	hypertension	heart_disease	bmi	HbA1c_level	blood_glucose_level	diabetes
age	1.00	0.25	0.23	0.34	0.10	0.11	0.26
hypertension	0.25	1.00	0.12	0.15	0.08	0.08	0.20
heart_disease	0.23	0.12	1.00	0.06	0.07	0.07	0.17
bmi	0.34	0.15	0.06	1.00	0.08	0.09	0.21
HbA1c_level	0.10	0.08	0.07	0.08	1.00	0.17	0.40
blood_glucose_level	0.11	0.08	0.07	0.09	0.17	1.00	0.42
diabetes	0.26	0.20	0.17	0.21	0.40	0.42	1.00

Figure 11: Confusion Matrix

Diabetes and age show a somewhat positive connection (0.258), suggesting that older people are more likely to get diabetes. Diabetes also shows positive connections with hypertension (0.198) and body mass index (0.214) is indicating that those with greater blood pressure and BMI are at a higher risk of developing the disease. Furthermore, there are higher positive connections between the HbA1c level (0.401) and blood glucose level (0.420) and diabetes.

Model	Accuracy	Precision	Recall	F1-score	ROC-AUC
Logistic Regression	0.959	0.863934	0.617096	0.719945	0.804011
Random Forest	0.97015	0.948345	0.687939	0.797421	0.84222
Support Vector Machine	0.9607	0.97428	0.55445	0.706716	0.776541
Gradient Boosting Classifier	0.97235	0.987342	0.685012	0.808849	0.842096
MLP Classifier	0.97245	0.9841	0.688525	0.810196	0.843743
LSTM	0.96665	0.944492	0.647541	0.768322	0.821994

Table 1: Running the models

The accuracy, precision, recall, F1-score, ROC-AUC, and other performance parameters for several machine learning models in predicting diabetes status are shown in the table. These measures are used to show how well each model does in identifying people based on several health criteria as either diabetics or non-diabetics.

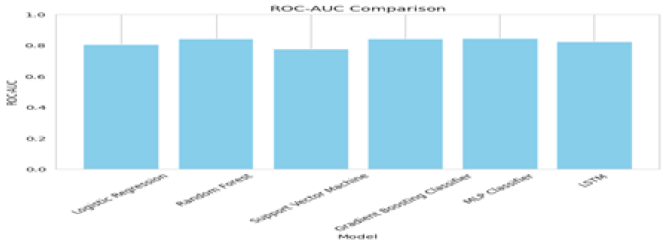


Figure 12: ROC-AUC Comparison

With an ROC-AUC of 84.37%, the MLP Classifier tops the field in diabetes status prediction, with Random Forest and Gradient Boosting Classifiers following closely behind.

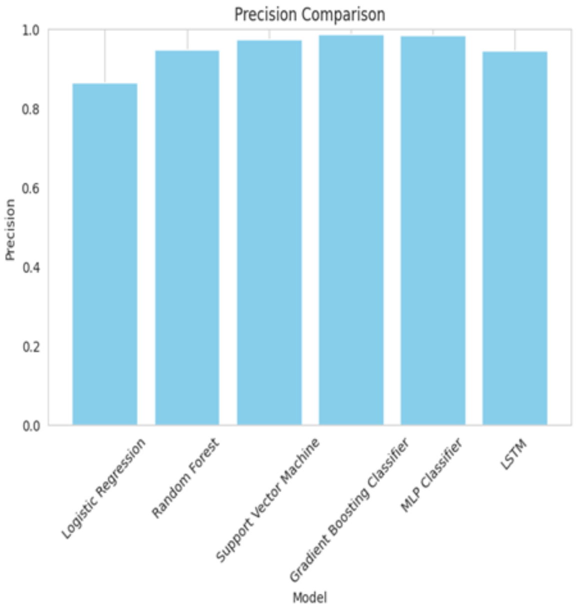


Figure 13: Precision Comparison

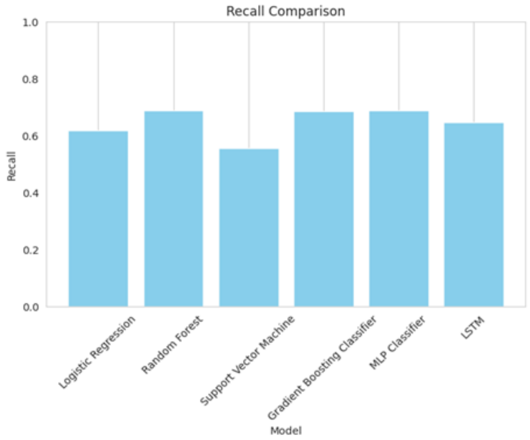


Figure 14: Recall Comparison

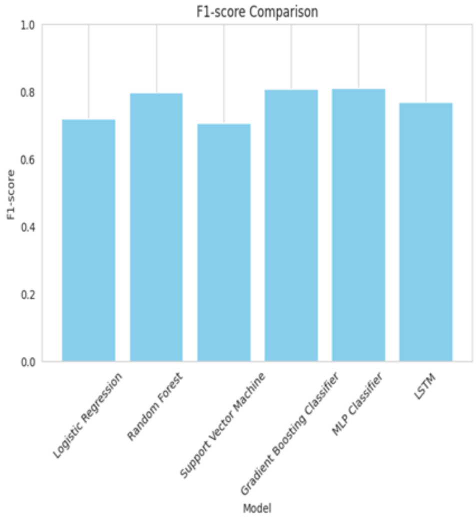


Figure 15: F1-Score Comparison

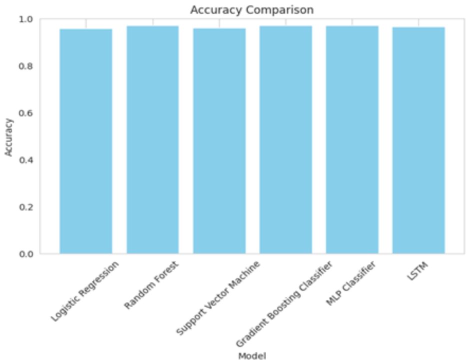
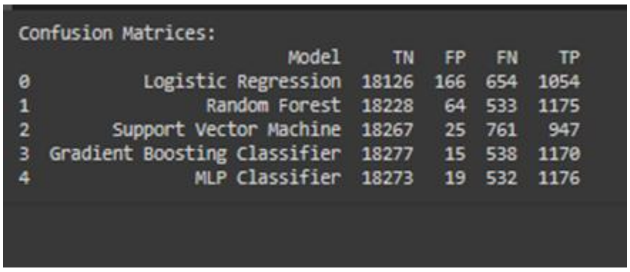


Figure 16: Accuracy Comparison



```
Confusion Matrices:
                         Model     TN   FP   FN    TP
0          Logistic Regression  18126  166  654  1054
1                Random Forest  18228   64  533  1175
2       Support Vector Machine  18267   25  761   947
3 Gradient Boosting Classifier  18277   15  538  1170
4               MLP Classifier  18273   19  532  1176
```

Figure 17: Accuracy Comparison

Considering all the matrixes that can be seen above, this can be said that MLP is nothing but the best-performing model that deals with the predictive analysis of the diabetes dataset as per the research requirement. In the precision, accuracy or the F1 value in all cases, MLP is performing better as compared to the other models.

V. Conclusion

The study explores various aspects interwoven into the loom of T2DM (type 2 diabetes mellitus), including the genes involved, clinical presentations cases, treatment venues and cost implications. An integrated analysis of the extracted data plus from the availability of literature could suggest interactions between the genetics, parameters used as biological measurements and diabetes type 2 that can be complex. The study of zinc transport and gene variation of SLC30A8 polymorphisms in relation to T2DM maps the importance of genetics in the risk factors of the condition. The dataset analysis helped to identify genetic associations, like mutations in the SLC30A8 gene, which were found to associate with T2DM incidence and may allow doctors to delineate who is at high risk for T2DM and which targeted interventions are applicable to different patients based on their genetic profile. However, the study of clinical outcomes and therapeutic interventions on T2DM gives room for in-depth understanding on the management of the condition and the different complications it can have. Studies that tried to tell us about severe effects of COVID-19 on people with diabetes have shown necessity to have specific strategies of healthcare for this vulnerable group of people. Also in relation to therapeutic interventions research, we have herbal medicine and nutraceuticals which are presenting with the most potent ways to improve diabetes management and provide novel modalities. The economic aspects of applying novel technological means for diabetic therapy, as for example application of Continuous Glucose Monitoring Systems are the illustration of the indispensability of the cost-effective health plans and the smart resource allocation strategies. Budget impact analyses is a great source of information for decision makers in the health care the option of informed policy decision and consequently the allocation of resources to manage diabetes is improved. In summary, it is the accumulation of a variety of knowledge levels, covering from the molecular genetics to the treatment and cost-effectiveness of the T2DM illness. With the use of the studies, healthcare professionals will begin to understand the underlying effects of T2DM complications, thus sharpening the way for personalised medicine approach, evidence-based healthcare practices, and better healthcare delivery systems among individuals with T2DM.

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[10] Juan Pablo Pérez Bedoya, Contributed Equally To This Work With: Juan Pablo Pérez Bedoya, Alejandro Mejía Muñoz, Alejandro Mejía Muñoz Noël,Christopher Barengo, ¶‡, N.C.B., Padv Also Contributed Equally To This Work. Paula Andrea Diaz Valencia ¶‡,N.C.B. And Padv Also Contributed Equally To This,Work, 2022. Type 1 And Type 2 Diabetes Mellitus: Clinical Outcomes Due To Covid-19. Protocol Of A Systematic Literature Review. Plos One, 17(9),.

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