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Research Article

The Impact of Clinical Parameters on LSTM-based Blood Glucose Estimate in Type 1 Diabetes

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Abstract:

Accurate forecasting of blood sugar levels is essential for managing diabetes, especially Type-1 reducing incidences, and diminishing care, costs in patients. In this study, a Long Short-Term Memory Recurrent Neural Network (LSTM) model has been employed to predict blood glucose levels using clinical data. The research focuses on identifying and analyzing several key parameters that play a significant role in determining future blood glucose levels, ensuring a robust and reliable prediction framework. We have considered patient-specific features: Insulin-Sensitivity-Factor (ISF), total daily dose (TDD) of insulin, HbA1C levels, height and weight of a patient, and age and gender while analyzing the prediction performance for Blood Glucose. We thought training LSTM models on a large dataset and studying the most important predictors with their predictive power would be beneficial. The results indicate that including these clinical parameters improves the accuracy of blood glucose prediction and provides valuable information for individuals to control diabetes. This analysis highlights the efficiency of LSTM networks in making use of patient data to improve prediction models, eventually aiding more effective and individualized treatment strategies for Type 1 diabetic patients (T1D). This work also examines the extent to which each parameter influences the prediction of future blood glucose levels, providing deeper insights into their relative impact and significance in the predictive model.

1. Introduction

Type 1 diabetes is a chronic disorder that usually appears at an early age, where the ability of the human body to produce insulin and continuously monitor and manage blood glucose is lost. It puts patients at severe health risks if not controlled. Thus, in such cases, accurate blood glucose level prediction is very important to avoid both of these conditions. Traditional models of blood glucose management mostly rely on manual adjustments based on historical data and empirical rules. Advanced machine learning techniques, however, hold open the possibility of going further in predictive accuracy by exploiting large datasets and sophisticated models.

LSTM networks as well as a variety of RNNs, have gained convincing results in time series predictions due to their capability to reflect on long-term dependencies and other patterns on sequential data. In the case of diabetes management, LSTM has been applied to answer questions of temporal patterns in blood glucose readings to predict future values with increased accuracy than conventional methods. This work is focused on foreseeing blood sugar levels in T1D patients using LSTM networks, in consideration of the specific clinical parameters at play that make prediction accuracy possible.

Clinical parameters such as ISF), TDD of insulin, HbA1C levels, height, weight, age, and gender are considered in this study. The features were selected given their predominance regarding diabetes management and a possible impact on blood glucose levels. These parameters will be fed into the LSTM network to find their independent and collective contribution toward predictive performance. Knowing how these features contribute in a potentially important way can be very helpful in tailoring more personalized strategies for diabetes management.

Knowing how important and related the input parameters chosen are to the patients is critical for a variety of reasons. First, the clinical parameters bearing the most significant influence on blood glucose levels should be recognized so that health professionals can individualize treatment plans. For example, knowing HbA1C levels and Total Daily Dose of insulin being strong predictors may guide changes in medication and lifestyle recommendations leading up to good glycemic control. Thus, several key parameters can be harnessed to establish personalized treatment plans that substantially improve the patient's outcome and reduce the risk of complications, raising the quality of life for those at life's edge with type 1 diabetes.

In this regard, the relationships between various patient features and blood glucose could be modeled to get further insights into the underlying mechanisms of diabetes management. Understanding these dependencies enables the uncovering of potential interactions between the variables of variables, for example, age and ISF in their relation to blood glucose. This is useful not just to clinicians but also in building advanced predictive models to better forecast blood glucose variation. Using such in-depth knowledge, one can further optimize predictive models to include the most relevant features and hence be more reliable and better tools for diabetes management.

In this research, the data were collected from fifteen Type 1 diabetic patients treated at Jeevan's Diabetic and Endocrinology Centre in Kerala, India. The dataset comprises detailed records of each patient's clinical parameters and blood glucose readings. Our approach involves training LSTM models on this comprehensive dataset, followed by analysing the performance of the model and the significance of each clinical parameter. The outcomes of this research are, therefore, anticipated to illuminate the significance of patient-specific features in the prediction of future blood sugar and further firmly establish the efficacy of LSTM networks for making better predictions in blood glucose. This study will, therefore, take a more detailed step toward obtaining an optimal and personalized treatment plan for patients with T1DM to improve their lifestyle.

2. Related works

This session represents an in-depth study specifically on blood glucose prediction, featuring numerous deep learning architectures as well as different data resources and durations when making the predictions. This collection provides a deep investigation of seminal works and identifies important trends and challenges for the constantly developing field. The overview is meaningful as it offers a relative view of what progress has been supported for adding valuable information on the outlook to follow in blood glucose forecasting by illustrating the significant impact of deep learning. As a result, it underscores the importance of literature reviews in creating a more thorough context and understanding of work.

The paper “Predicting Blood Glucose Using an LSTM Neural Network” by El Idrissi, Touria & Idri et al. [1] presents a deep-learning-based architecture for blood glucose prediction in people with diabetes. The proposed model uses an LSTM layer and two dense layers. Trials conducted on data from 10 diabetic patients demonstrated that this LSTM-based model outperforms existing LSTM and autoregressive (AR) models regarding prediction accuracy, as measured by root mean square error (RMSE). The study highlights the significance of deep learning approaches in improving blood glucose prediction and aiding diabetes management [1].

In their 2020 paper, “Blood Glucose Prediction with Variance Estimation Using Recurrent Neural Networks” [2], John Martinsson Alexander Schliep, Bjorn Eliasson, and Olof Morgen present a novel methodology for blood sugar forecasting in type 1 diabetics. Utilizing RNNs, their model predicts sugar levels up to one hour through the future based on continuous glucose monitoring (CGM) data. The model not only forecasts glucose levels but also estimates prediction certainty, aiding in managing diabetes by quantifying the reliability of predictions. Their approach demonstrates advanced performance, emphasizing the importance of machine learning in enhancing diabetes care [2].

In the paper "Multi-objective Genetic Programming for Blood Glucose Prediction" by Alberto Fernández-Rodríguez, David Camacho, and Agapito Ledezma (2022), the authors investigate the use of a multi-objective implementation of Genetic Programming (GP) for forecasting blood sugar levels in diabetes patients. The study compares traditional single-objective GP with a multi-objective approach, incorporating medical criteria to improve prediction accuracy and safety. Experimental results from two scenarios, the What-if and Agnostic scenarios, demonstrate that the multi-objective method produces better models by effectively traversing the search space and reducing dangerous mispredictions, thereby aiding in daily diabetes management and treatment recommendations [3].

In their study, “Enhancing self-management in type 1 diabetes with wearables and deep learning” [4], Taiyu Zhu, Chukwuma Uduku Kezhi Li, Pau Herrero, Nick Oliver, and Pantelis Georgiou

explore the integration of continuous glucose monitoring (CGM) and wearable sensor data to improve glucose level predictions for individuals with type 1 diabetes (T1D). Through continuous observation over six weeks involving 12 adults with type 1 diabetes, they developed the ARISES platform, which combines a deep learning algorithm with the data from CGM, carbs and insulin intake, and wristband sensors. Their algorithm achieved an average RMSE of 35.28 mg/dL for 60-minute glucose level predictions and demonstrated significant improvements in detecting hypoglycemia and hyperglycemia. The inclusion of wristband data notably enhanced prediction accuracy, underscoring ARISES' potential to improve real-time decision support and mitigate severe complications in T1D management [4].

There are a number of works done on this subject [5-29]. The paper "Multi-parameter Blood Glucose Prediction Algorithm for Type 1 Diabetes based on Hybrid Neural Network Deep Learning Technique" [23] by Zixuan Chen et al presents a hybrid model combining CNN and Transformer networks to predict blood glucose levels. The model uses previous sugar levels, amount of carbs consumed, and insulin amounts, with CNN extracting local features and Transformer capturing global dependencies. Tested with the UVA/Padova simulator [5] on data from 10 adults, the model achieved only a few errors and high accuracy, with "average MAPE values of 2.41%, 2.89%, and 3.19% for 15, 30, and 60-minute predictions, and RMSE values of 6.75, 10.51, and 15.98" [23]. In their paper published in 2023, Francesco Prendin and colleagues highlighted the significance of understanding "machine-learning models for blood glucose prediction" in T1D management [6]. They demonstrate that models need to be both accurate and physiologically sound for patient safety. Using SHAP (SHapley Additive exPlanations), they compare two LSTM models (p-LSTM and np-LSTM) with comparable prediction accuracy. Only p-LSTM correctly learned physiological relationships, making it more suitable for integration into decision support systems for corrective insulin bolus (CIB) suggestions, and ultimately improving patients' glycaemic control [6]. The paper by Ömer Atılım Koca and Volkan Kılıç (2024) introduces a multi-layer LSTM model for predicting glucose levels in diabetes management. Unlike traditional tools that use single-layer models and limited parameters, this approach incorporates multiple factors to improve accuracy. Tested on the OhioT1DM dataset, the model achieved an RMSE of 14.364 mg/dL over a 30-minute prediction horizon, demonstrating its effectiveness in managing glucose fluctuations and advancing diabetes care [7].

Our work focuses on improving glucose level predictions in diabetes management using a multi-layer LSTM model, distinct from previous single-layer approaches. By incorporating multiple input parameters and employing a more sophisticated neural network architecture. This research prioritizes evaluating how different clinical parameters, when combined, influence glucose prediction accuracy and their overall correlation with blood sugar levels. Additionally, our study aims to determine the importance of various clinical parameters and understand the relationships between them, providing deeper insights into their impact on glucose levels.

3. Material and Methods

The model uses LSTM networks to foresee blood sugar levels concerning various clinical parameters. This procedure began with data preprocessing and reshaping. After that, the reshaping of the input features took place by the LSTM network. The LSTM model was then created, structured with multiple layers, and trained on the Adam optimizer. The model efficiency is assessed using the MSE loss function. MAE, RMSE, and R^2. The importance of each clinical parameter was obtained by calculating weights and contributions associated with each feature in the input space of the trained model. An integrated method allows for examining the importance and influence of some patient-related features toward blood glucose prediction.

A. Dataset

The data used in this study was obtained from fifteen Type 1 diabetic patients from Jeevan's Diabetic and Endocrinology Centre located in Kerala, India. The number of continuous glucose monitoring days is from 4 to 14 days of data in each record. Clinical parameters captured in the records are continuous glucose monitor readings, age, HbA1C values, TDD, height, weight, insulin dose, and gender. The age group ranges from 25 to 76 years for the patients. For our study, we reformatted the original time-series data from Continuous Glucose Monitoring (CGM) recordings, which were stored in separate files for each patient. We consolidated this data into a new format with columns including CGM, Age, Gender, HbA1C, TDD of insulin, ISF, Height, Weight, Insulin dosage, and glucose readings at specific percentiles (PH60, PH120, PH180, PH210). This re-organization allowed us to pair each CGM reading with corresponding values at different percentiles, facilitating a more structured approach to analysis. To maintain patient confidentiality, every subject in

this dataset was assigned a unique number, which varied from 1001 to 1008. The final dataset contains 5000 records, out of which 4000 are used for training the model and the lasting 1000 records kept for testing. This setup provided the opportunity for high coverage in evaluating model performance and the influence of clinical parameters on blood glucose predictions.

B. Data Preprocessing

The data preprocessing is done for arranging the data suitable for training and testing. First, all the features, including their CGM readings, age, HbA1C, and other clinical parameters, were normalized to ensure a comparable scale. This step was very critical to enhance the convergence and performance of the LSTM network. Categorical variables, in this case, only gender, were numerically encoded to be able to fit in the model. Additionally, the data were reshaped to fit the input requirements of the LSTM network, with each feature set being organized into a 3D array representing samples, time steps, and features. This preprocessing ensured that the LSTM model could effectually learn patterns from the sequential data and improve the accuracy of blood glucose predictions. Figure 1 is a graphical representation of the original dataset, and Figure 2 represents the data after preprocessing.

C. Model Construction

This model uses an LSTM Network to predict future blood glucose levels, an example of a continuous variable indicating a measurement. The LSTM network will be most appropriate for time series data when it captures dependencies and patterns over time. LSTM has inherent capabilities in managing and retaining long-term dependencies in sequential data. LSTMs are specialized with memory cells and input, output, and forget gates; these provide it with the capacity to remember or forget information selectively over long sequences. This makes LSTMs quite effective in tasks related to time-series prediction, where the temporal trends and relationships in a dataset are very important. It may be also used to understand the influence of input features from the weights learned by the LSTM model, giving insights into the feature importance. Besides, the ability of the LSTM model to capture complex and nonlinear relationships between the features and target variables enhances predictive accuracy, hereby highlighting intrinsic correlations among input parameters. The prescribed model consists of several layers, each with specific mathematical operations. The input layer receives the input data which is already reshaped into a 3D tensor suitable for the LSTM layer.

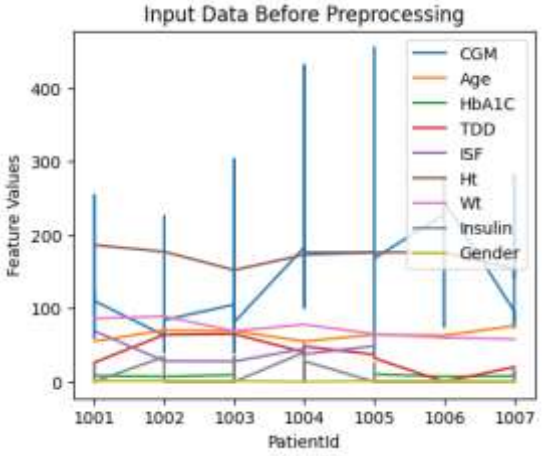

Figure1: *Original Dataset*

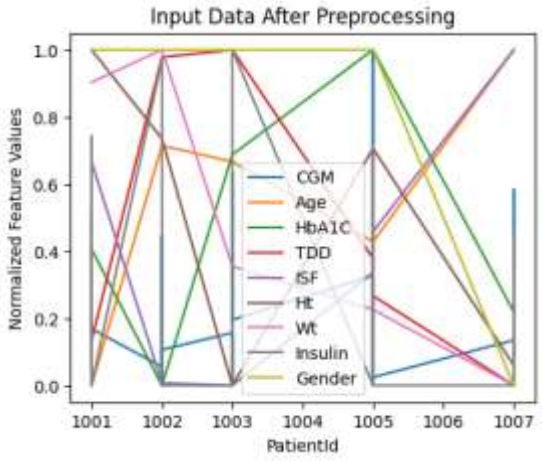

Figure 2: *Pre-processed Data*

The LSTM Layer is responsible for processing the serial input and outputs a 2D tensor with 50 neurons. The Dense Layers further transform the data through fully connected layers with ReLU activations, reducing the dimensions progressively. The output-layer is responsible for producing the final result.

Input Layer: A 3D tensor X with shape (samples, time steps, features)) is given as input. For this model, it is (n,1,10), where the number of samples is denoted as n, time step 1, and 10 is the number of features. This layer uses 'MinMaxScaler' to standardize the feature values within the range of 0 and 1. This enhances the functionality of the neural network model .

LSTM Layer: The first layer is an LSTM layer with 50 units and ReLU activation. The individual inputs are fed through the LSTM units, which maintain an internal cell state that retains information across time steps.

For a single LSTM unit at time step t:

$$input\_gate=\sigma(Wi\cdot[hprevious, xcurrent]+bi)$$

where, "σ represents the sigmoid function, Wi is the weight matrix for the input gate, hpreviousℎ is the hidden state from the previous time step, xcurrentx

is the input at the current time step, and bi is the bias term for the input gate".

forget_gate=σ(Wf·[hprevious,xcurrent]+bf)

Wf is the weight matrix for the forget gate, and bf is the corresponding bias

output_gate=σ(Wo·[hprevious,xcurrent]+bo)

where Wo is the weight matrix for the output gate, and bo is the related bias.

Cell candidate C′=tanh(WC·[hprevious,xcurrent]+bC)

Where hyperbolic tangent function (tanh) is used to compute the candidate cell state, influenced by the weight matrix WC and its associated bias bC.

Cell state: C=forget_gate⊙Cprevious +input_gate⊙C′

Where ⊙ denotes element-wise multiplication and Cprevious is the cell state from the previous time step.

Hidden state: h=output_gate⊙tanh(C) [21]

represents the combination of the output gate and the current cell state.

Dense Layers: After the LSTM layer, we have three dense layers each containing 32, 16 and 1 units. The first two layers use the ReLU activation function, which is mathematically represented as ϕ(z)=max (0, z) [22]. The final dense layer has no activation function, suitable for regression tasks as it outputs a continuous value. Each layer applies a linear transformation followed by an activation function:

hidden_state_1=ReLU(W1·input+b1)

- W1 represents the weight matrix associated with the first layer,
- Input refers to the input to the layer, and
- b1 is the bias term for the first layer.

hidden_state_2=ReLU(W2·hidden_state_1+b2)

- W2 represents the weights connecting neurons in the first and second layers,
- hidden_state_1 is the output from the first hidden layer, and
- b2 is the bias term for the second layer.

output=W3·hidden_state_2+b3

- W3 denotes the weight matrix for the output layer,
- hidden_state_2 is the output from the second hidden layer, and
- b3 is the bias term for the output layer. [10].

Given the input X, the output prediction Y_{pred} of the LSTM-based model can be represented as:

$$Y_{pred}=W_{output}\cdot(W2\cdot ReLU(W1\cdot ht+b1)+b2)+b_{output}$$

The terms W1, W2, b1, b2, and b_{output} are the parameters of the dense layers in the neural network. Here's what each term represents:

- **W1**: The weight matrix for the first dense (fully connected) layer. This matrix transforms the input from the LSTM layer (ht) into the hidden representation in the first dense layer.
- **b1**: The bias vector for the first dense layer. This vector is added to the product of W1 and ht before applying the ReLU activation function.
- **W2**: The weight matrix for the second dense layer. This matrix transforms the output of the first dense layer (ReLU(W1·ht+b1)) into the hidden representation in the second dense layer.
- **b2**: The bias vector for the second dense layer. This vector is added to the product of weigh matrix of this layer and the output of previous layer before applying the activation function.
- **W_{output}**: Weight matrix for the final output layer. This matrix transforms the result from the second layer (ReLU(W2·ReLU(W1·ht+b1)+b2) into the final prediction.
- **b_{output}**: The bias vector for the final output layer. This vector is added to the product of W_{output}t and the result of the second dense layer to get the final prediction y_{pred}

Model Training: The model compilation is done using the Adam optimizer and MSE loss function. The optimizer adjusts the weights to minimize the loss:

$$Loss=\frac{1}{n}\sum_{i=1(}^{n} yi-y\hat{}i)^2$$

For the training purpose the number of epochs is selected as 64 with a batch size of 8. During training, the model undergoes 64 epochs of forward and backward propagation. In each epoch, the input data flows through the LSTM and dense layers to generate the output. The forward proliferation involves passing the input data through the LSTM layers, which capture sequential habits, and then through the dense layers, which refine the prediction. In backward propagation phase, gradients of the loss function concerning the model parameters are computed through Time (BPTT). These gradients indicate how much the loss would change with respect to changes in each parameter. The Adam optimizer then updates the weights based on these gradients, allowing the model to minimize the loss function effectively, Early stopping is included to prevent overfitting, which halts training after 40 epochs if the validation loss

does not improve. This technique ensures that the model maintains generalization capabilities. After training, predictions are done on the test data set, which involves performing a forward pass through the trained model to generate the predicted values (y^). Figure 3 shows the construction of the prescribed model

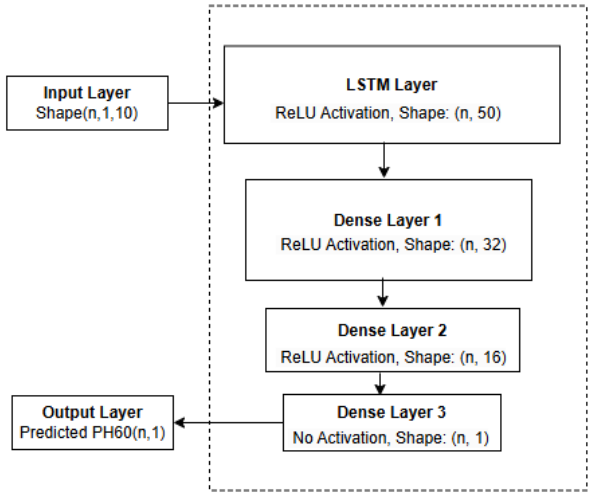

Figure 3: *The model architecture*

4. Results and Discussions

The study highlights several key results. First, the prediction capacity of the LSTM-based model would be demonstrated for the primary objective of the study by utilizing some performance metrics: MAE, RMSE, and R^2 score; second, investigating the importance of each clinically assessed parameter during the prediction process. Analyzing feature importance through model weights identifies which clinical parameters significantly contribute to blood glucose prediction. Finally, the study explores the relationships between the clinical parameters, illustrating how they interact and collectively contribute to the prediction. Figure 4 represents a line graph showing a subset of the predicted blood glucose values versus the actual values.

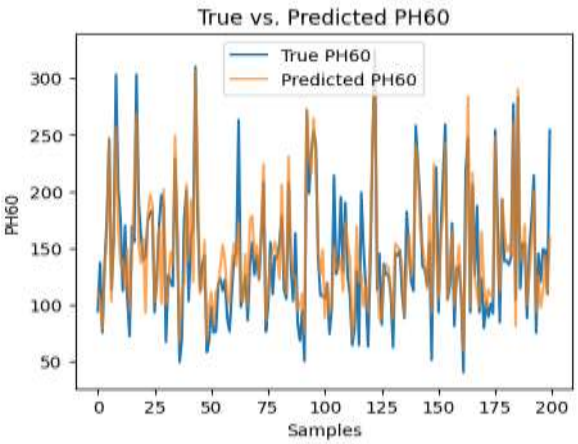

Figure 4: *Subset of actual PH60 vs Predicted PH60*

Figure 5 illustrates the training (TL) and validation loss (VL) across epochs, providing a visual representation of the model's learning progress. The x-axis represents the number of epochs. In the y-axis is the loss, which represents the performance of the model. The two lines on the graph are the TL and VL. The training loss measures how well a model performs on the data it used to learn. The validation loss shows the model's capacity to perform on new, unseen data. In the graph, we can see that as the model trains for longer, both the training and validation errors get smaller, suggesting that the model is improving its ability to learn and predict accurately. This suggests that the blood glucose prediction model effectively learns from the data and progressively improves its accuracy.

A. Model Analysis

The performance of the model is evaluated through MAE, RMSE, and R^2. MAE calculates the average absolute difference between the predicted value and

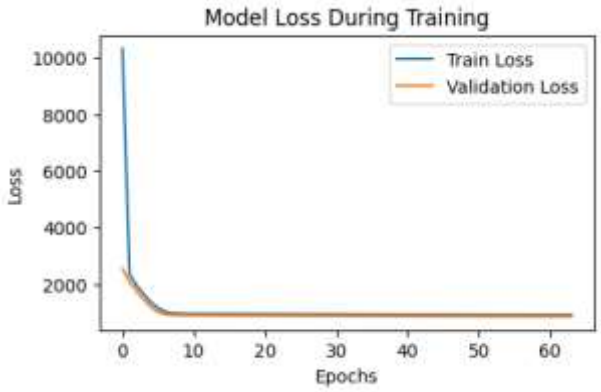

Figure 5: *Subset of actual PH60 vs Predicted PH60*

the actual values. RMSE squares the differences, averages them, and then takes the square root, making it more sensitive to large errors. R^2 indicates the proportion of variance in the dependent variable explained by the independent variable(s). A higher R^2 value suggests a better model fit, but it can be misleading if the data is not linear or if there are outliers. When the model was trained and executed for 60 minutes, it achieved the following results: an MAE of 22.143, an RMSE of 28.027, and an R^2 value of 0.756. This indicates the precision of the model and the extent to which it can explain the variability in the blood sugar values of type 1 diabetic patients. The results are summarised in table 1.

Table 1: *Performance Analysis of the model*

MAE	RMSE	R^2
22.143	28.027	0.756

The MAE of 22.143 shows that, on average, the model's predictions were off by about 22.143 blood glucose units. This gives a clear idea of how accurate the model's predictions were. The RMSE of 28.027 means that the model's errors were typically around 28.027 units. R^2 measures how well the model explains the changes in blood glucose levels. An R^2 of 0.756 indicates that the model accounted for about 75.6% of the variation in blood glucose. This shows a strong relationship between the model's predictions and the actual values, indicating that the model effectively captures the underlying patterns.

B. Feature Importance

The importance is derived from the mean absolute weights of the features in the LSTM layer. Higher importance indicates a greater influence of that parameter on the model's predictions. This helps in understanding which clinical parameters are most significant in predicting blood glucose levels. Figure 6 shows a bar plot that displays the significance of each clinical parameter used in the model.

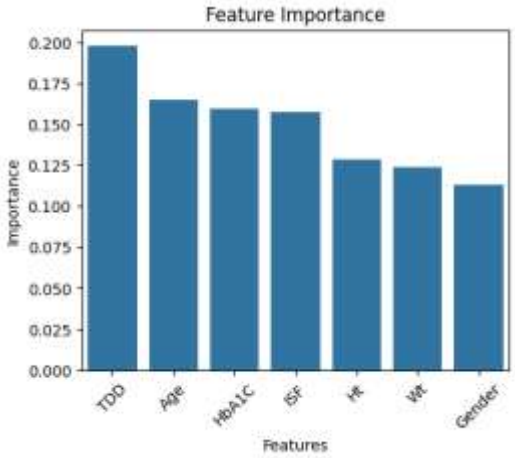

Figure 6: *Importance of each clinical parameter*

The y-axis represents the importance score, with higher values indicating a greater influence on blood sugar prediction. The x-axis lists the specific clinical features used in the model. The graph indicates that the TDD and ISF are the most influential factors in predicting blood glucose levels in this model. Age also holds significant importance, highlighting its relevance due to its impact on insulin sensitivity and metabolism. HbA1c, which measures average blood sugar control over the past few months, has a moderate importance score, suggesting its role in blood sugar prediction, though less critical for short-term forecasts compared to recent insulin intake. Conversely, Height, Weight, and Gender have relatively low importance scores, indicating their limited influence on blood sugar prediction in this specific model.

C. Correlation between Clinical Features

The relationship between the selected clinical parameters and the resultant variable is demonstrated using a correlation heatmap shown in Figure 7. The correlation values may fall within -1 and 1, where values nearer to 1 or -1 designate a solid correlation. The values close to zero represent a very weak correlation between the parameters. For example, ISF, and TDD appear to be highly correlated whereas, the correlation between PH60 and Height (Ht) is very weak. This helps to understand the relationships between different clinical parameters and their potential impact on the target variable.

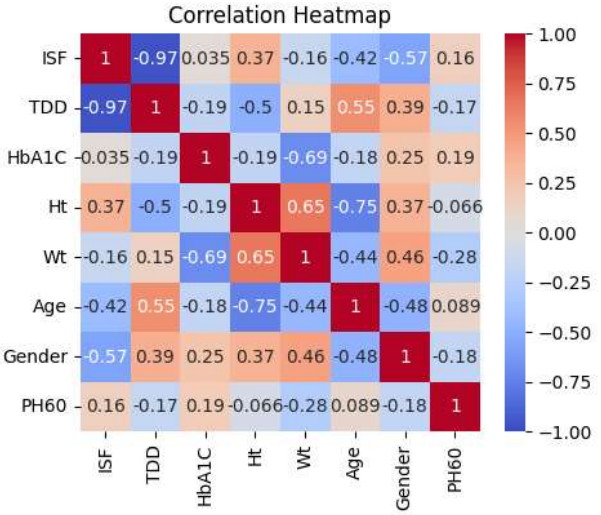

Figure 7: *correlation between the selected clinical parameters and the target variable*

5. Conclusion

The prescribed study aimed to construct a predictive model to forecast blood sugar level incorporating the features of the LSTM network. The model achieved a MAE of approximately 22.143 and a RMSE of around 28.027. Since the model has an R^2 score of 0.756, it exhibits a decent level of predictive accuracy, explaining about 75.6% of the variability in PH60. The study also depicted the importance of various clinical parameters in blood glucose prediction and the association between these features and the output variable. The developed LSTM model shows promise in predicting blood glucose levels in diabetic patients based on selected clinical parameters. Future work could explore incorporating additional features, fine-tuning the model architecture, and using larger, more diverse datasets to enhance predictive accuracy and generalizability. The findings highlight the critical role of insulin management in predicting blood

glucose levels, which could inform personalized diabetes treatment strategies.

Author Statements:

- **Ethical approval:** The conducted research is not related to either human or animal use.
- **Conflict of interest:** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper
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- **Author contributions:** The authors declare that they have equal right on this paper.
- **Funding information:** The authors declare that there is no funding to be acknowledged.
- **Data availability statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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