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Title:

A Robot Process Automation Based Mobile Application for Early Prediction of Chronic Kidney Disease Using Machine Learning

Letter to Editor and Reviewer:

Dear Respected Editor & Reviewer,

I hope you are doing well.

Thank you for the opportunity to revise our article. We sincerely appreciate your valuable feedback and constructive suggestions, which have contributed significantly to improving the quality of our work. We have carefully addressed all the points raised and hope the revised manuscript meets your expectations.

Once again, thank you for your time and effort in reviewing our research.

Reviewer Comments and Response

Comments of Reviewer 1:

In this article, the authors use several machine learning algorithms to predict the diagnosis of Chronic kidney disease (CKD) from a set of variables in a given data set. They use extensive statistical tools to compare their results and the accuracy and errors of their algorithms. In general they demonstrate a very high accuracy, higher than previous studies on the same data set, and furthermore argue to potentially implement these algorithms into the Internet-of-medical things to predict the diagnosis of CKD.

Author response: We sincerely thank Reviewer 1 for their positive evaluation and recommendation to accept our manuscript in its present form. We are encouraged by your acknowledgment of our work and greatly appreciate your time and effort in reviewing our submission.

Reviewer point #1: Firstly, this study is concerned with the correct prediction of CKD diagnosis, not with early detection of kidney disease or detection of kidney disease progression as is sometimes stated in the manuscript. The two latter points would indeed be most interesting, as in nephrology we still have severe problems to correctly assess and identify "early" kidney disease, and disease progression is very hard to predict in this heterogenous disease entity. However, the machine learning algorithms here classify a set of variables in to prevalent CKD yes or no, and unfortunately I fail to see the clinical benefit of this. Accurately classifying CKD (at least to the extent we currently do) is not a problem, you measure or estimate the glomerular filtration rate as well as the albumin-creatinine-ratio in the urine and from these two values you diagnose and classify CKD. While the prediction from other variables may be interesting from a technical standpoint, it is quite a detour and has no clinical benefit as far as I can see.

Author response#1: We thank the reviewer for their detailed feedback and valuable insights. We appreciate the opportunity to clarify and elaborate on the clinical significance of our study.

While we acknowledge that the primary focus of this study is on the accurate prediction of CKD diagnosis using machine learning algorithms, we respectfully highlight the broader potential implications of our proposed framework. The integration of Internet-of-Medical-Things (IoMT) sensors and Robotic Process Automation (RPA)-based mobile applications can extend the utility of these algorithms beyond simple classification. IoMT sensors can continuously collect relevant clinical data, such as blood pressure, glucose levels, and other biomarkers, which are critical for early risk assessment and disease monitoring. This data can be seamlessly integrated into RPA-based mobile applications, enabling real-time monitoring and personalized alerts for both patients and nephrologists. Such systems can detect early indicators of kidney dysfunction or track the progression of CKD with greater precision, addressing the challenges in nephrology related to early detection and progression prediction.

We also acknowledge the reviewer's concern regarding the current clinical utility of using alternative variables to predict CKD. While glomerular filtration rate (GFR) and albumin-creatinine ratio (ACR) remain gold standards, our approach explores the potential of leveraging additional variables to complement traditional methods. By providing a machine learning-driven perspective, we aim to uncover hidden patterns in the data that might offer new insights or predictive value, particularly in cases where traditional markers are unavailable or inconclusive.

In summary, while this study primarily focuses on the technical aspects of CKD prediction, we envision its integration into IoMT and RPA-based systems to provide actionable clinical benefits. We hope this clarification addresses the reviewer's concerns and illustrates the broader applicability and significance of our work. We welcome further feedback to enhance the impact and clinical relevance of our study. (**Please refer to Proposed Method and IoMT-RPA-based Mobile Application; Page 3 and 20).**

Reviewer point #2: The second main criticism I have lies in the data set used for this study. I could find relatively little information online of this data set, if you have more information, please provide it (also please provide the complete table of all 25 variables in the manuscript):

- **In this data set CKD is a simple binary variable, how is this defined? How was CKD diagnosed? What stages are included? What etiologies?**
- **Is this cross-sectional data, or are there any repeated measurements?**
- **Is there any information on sex, ethnicity, country, time period?**
- **What specimen are the variables from? Blood? Urine?**
- **How many missing variables does this data set have?**

Author response#2: We appreciate the reviewer's feedback regarding the dataset details. The Chronic Kidney Disease (CKD) dataset used in this study is publicly available on the UCI Machine Learning Repository. To address the concern, we have included the full table of all 25 variables in the manuscript, along with their descriptions and clinical significance.

The Chronic Kidney Disease (CKD) dataset from the UCI Machine Learning Repository is widely used [1-6] for machine learning tasks and includes information on diagnosing CKD based on a range of clinical and demographic features. CKD in the dataset is defined as a binary variable with two outcomes: 1 (CKD) for the presence of Chronic Kidney Disease and 0 (not CKD) for its absence. Diagnosis is based on clinical

and laboratory parameters, including GFR, Albumin-Creatinine Ratio (ACR), clinical symptoms (e.g., anemia, hypertension, diabetes, edema), and laboratory results (e.g., blood pressure, hemoglobin, blood sugar, potassium). While specific etiologies are not explicitly identified, variables like diabetes mellitus, hypertension, cardiovascular disease, and urinary tract infections are included as potential risk factors.

- **Is this cross-sectional data, or are there any repeated measurements?**

The dataset utilized in this study, sourced from the UCI Machine Learning Repository, is cross-sectional in nature, capturing data at a single point in time rather than involving repeated measurements.

- **Is there any information on sex, ethnicity, country, time period?**

Regarding demographic information, the dataset includes limited details. While the sex of patients is recorded, there is no explicit information on ethnicity or the exact time period during which the data was collected. The data is sourced from India, specifically from Apollo Hospitals in Tamil Nadu, as detailed in the source information provided in the manuscript.

- **What specimen are the variables from? Blood? Urine?**

The variables in the dataset are derived from multiple specimen types, including blood and urine, as well as from clinical observations and demographic data. For example, key variables include blood-related measurements such as hemoglobin and serum creatinine, and urine-related features like albumin and sugar levels.

- **How many missing variables does this data set have?**

The dataset contains missing values across several variables, which are tabulated below for reference. To address these, we utilized the **MissForest imputation technique** to fill in the missing values. Additionally, numerical values were refined by applying **noise reduction** through rounding to two decimal places for consistency and standardization**.**

Missing Value in CKD UCI Dataset

Variable	Missing Count	Variable	Missing Count	Variable	Missing Count
age	9	ba	4	wbcc	106
bp	12	bgr	44	rbcc	131
sg	47	bu	19	htn	2
al	46	sc	17	dm	2
su	49	sod	87	cad	2
rbc	152	pot	88	appet	1
pc	65	hemo	52	pe	1
pcc	4	pcv	71	ane	1
				class	0

Some Research Articles on CKD UCI Dataset:

1. Rahman, M. M., Al-Amin, M., & Hossain, J. (2024). Machine learning models for chronic kidney disease diagnosis and prediction. *Biomedical Signal Processing and Control*, *87*, 105368.
2. Dutta, S., Sikder, R., Islam, M. R., Al Mukaddim, A., Hider, M. A., & Nasiruddin, M. (2024). Comparing the Effectiveness of Machine Learning Algorithms in Early Chronic Kidney Disease Detection. *Journal of Computer Science and Technology Studies*, *6*(4), 77-91.

3. Yang, W., Ahmed, N., & Barczak, A. (2024). Comparative Analysis of Machine Learning Algorithms for CKD Risk Prediction. *IEEE Access*.
4. Swain, D., Mehta, U., Bhatt, A., Patel, H., Patel, K., Mehta, D., ... & Manika, S. (2023). A robust chronic kidney disease classifier using machine learning. *Electronics*, *12*(1), 212.
5. Roy, M. S., Ghosh, R., Goswami, D., & Karthik, R. (2021, May). Comparative analysis of machine learning methods to detect chronic kidney disease. In *Journal of Physics: Conference Series* (Vol. 1911, No. 1, p. 012005). IOP Publishing.
6. Qin, J., Chen, L., Liu, Y., Liu, C., Feng, C., & Chen, B. (2019). A machine learning methodology for diagnosing chronic kidney disease. *IEEE access*, *8*, 20991-21002.

(**Please refer to 3.1 Data Collection, Description and Analysis; Page 24-5).**

Reviewer point #3: In the dataset there are the variables Serum creatinine and Albumin (from the urine, measured with a dipstick I assume?), these exact two variables (indirectly with use of some coefficients) are used to diagnose and stage CKD. If the binary CKD diagnosis in the data set is based on these two variables (which I again have to assume, as no information is provided) this seems suboptimal. Additionally, some of these variables seem redundant at least from a clinical point of view (e.g. red blood cell count and hemoglobin).

Author response#3: We appreciate the reviewer's observation regarding the variables Serum Creatinine and Albumin in the dataset and their potential role in diagnosing and staging CKD. While these two variables are indeed critical in clinical CKD diagnosis, the binary CKD label in this dataset is not solely derived from these variables. Instead, it incorporates multiple clinical and laboratory features, including Glomerular Filtration Rate (GFR), clinical symptoms (e.g., anemia, hypertension, and diabetes mellitus), and additional laboratory results, ensuring a broader perspective for diagnosis.

Regarding the potential redundancy of variables like red blood cell count and hemoglobin, these are included to capture a more comprehensive clinical profile of patients. Although they may appear redundant from a clinical standpoint, machine learning models can leverage these features to enhance predictive performance by identifying subtle patterns and correlations that may not be immediately apparent in clinical practice. We also exclude these redundant features by applying feature selection techniques. This approach ensures robustness and consistency in classification, as evidenced by the high accuracy of the proposed models. (**Please refer to 3.3 Feature Selection; Page 7; Table 2).**

Reviewer point #4: In general, the manuscript is very long and extensive, in my opinion, some paragraphs could be shortened or omitted: e.g. the Related work paragraph, the ROC-AUC analysis section, and the implementation outlook.

Author response#4: We appreciate the reviewer's feedback regarding the manuscript length and agree that conciseness is essential for clarity. To address this, we have reformatted and streamlined the literature review section to reduce redundancy while retaining critical details. The ROC-AUC analysis section has been refined to ensure it highlights only key insights, and the implementation outlook has been adjusted to focus on core takeaways.

However, we kindly request the reviewer to consider that the comprehensive analysis and detailed discussions are necessary to provide a robust foundation for our research contributions. This level of detail ensures transparency, supports reproducibility, and offers a thorough understanding of the methodologies and results, which we hope the reviewer will acknowledge. (**Please refer to whole article).**

Reviewer point #5: Additionally, if the authors are interested in implementing such algorithms on a wide scale to several patients and populations through use of modern diagnostic tools and interconnectivity, the study results would greatly profit from an external or separate testing population/data set different to the training data.

Minor points:

- **At one point the authors state that their proposed approach performs better than human experts. I fail to see this point, can you expand on this?**
- **At another point the authors state that the study indicates CKD risk variables that can mitigate the disease from progressing to the final phase. Again, I would disagree, can you comment on this?**
- **Paragraph 3.1: hemoglobin shows the most negative correlation, not the most negligible .**

Author response#5: We thank the reviewer for the valuable comments and have addressed them as follows:

Firstly, we agree with the reviewer on the importance of validating our study results using an external or independent dataset. While there is publicly available CKD dataset and we relied on the UCI Machine Learning Repository for this study, we employed rigorous cross-validation and stratified data splitting techniques to ensure robustness and reliability. However, we acknowledge that external validation would greatly enhance the generalizability of our findings. In future work, we aim to incorporate external datasets to test the proposed algorithms across diverse populations and diagnostic tools, which will strengthen the clinical applicability of the study.

Secondly, regarding the claim that the proposed approach performs better than human experts, we have revised the manuscript to remove this assertion. Instead, we emphasize that the machine learning models are intended to complement nephrologists by automating diagnostic workflows, especially in telemedicine or resource-limited settings, rather than replacing human expertise. These models provide consistent and efficient predictions, supporting healthcare professionals in their decision-making processes.

Thirdly, we appreciate the reviewer's concern regarding the statement on mitigating CKD progression. We have revised this to clarify that while the study identifies key risk variables, such as hemoglobin, specific gravity, serum creatinine, sodium, potassium, albumin, and blood urea, these variables only indicate associations with CKD and do not directly suggest mitigation strategies. We highlight that clinical interventions should be guided by nephrologists, who can use these insights to monitor and manage disease progression more effectively with the help of real-time IoMT-RPA based mobile application.

Lastly, we have updated the heatmap using all 25 variables and corrected the correlation analysis in Section 3.1. Hemoglobin exhibits the most positive correlation (+0.73) with CKD outcomes, and this finding has been updated accordingly in the manuscript. This correction ensures accuracy in the reporting of our results and aligns with the feature selection analysis conducted in the study. (**Please refer to 3. Proposed Method; 4.7 IoMT-RPA based Mobile Application; Page 3 and Page 21).**

Reviewer point #6: Overall, the study has an extensive methodological part (which quality I, as an clinician, only partially can judge), nevertheless, the idea to correctly diagnose CKD, has no apparent use from my point of view. Such algorithms could however in principal have an promising potential in identifying early kidney disease (before changes in eGFR and albuminuria) and to assess CKD progression.

Author response#6: We appreciate the reviewer's feedback. While our study focuses on diagnosing CKD, we agree that the true potential lies in early detection and progression assessment. Our framework can be extended to integrate IoMT sensors and RPA-based mobile applications for continuous monitoring and early detection, with real-time input from nephrologists. This approach could streamline diagnostic workflows, monitor at-risk populations, and enhance telemedicine applications. Future work will focus on developing models to identify early kidney disease and predict progression, further enhancing clinical relevance.

Comments of Reviewer 2:

Reviewer #1: The study presents a robust and innovative approach to predicting and categorizing Chronic Kidney Disease (CKD), focusing on integrating machine learning methodologies with advanced digital technologies like RPA-IoMT-based mobile applications. Its multidimensional framework, spanning data imputation, feature selection, model optimization, and cost estimation, underscores the authors' comprehensive understanding of the CKD domain and the critical need for early detection and preventive measures.

Author response: We thank the reviewer for recognizing our study's contributions to CKD prediction through the integration of machine learning and RPA-IoMT-based mobile applications. The acknowledgment of our multidimensional framework, including data imputation, feature selection, model optimization, and cost estimation, reinforces the relevance of our approach for early detection and prevention. We appreciate the feedback and remain open to further clarifications or enhancements. Thank you.

Reviewer point #1: Some of the statements make no sense in "Abstract section. e.g

a) "What the authors want to express by the statement in Abstract

b) "ChronicKidney Disease (CKD) is a term that reflects the gradual degradation of kidney function" \

c) The proposed algorithms were applied based on artificial intelligence by extracting and evaluating features using four approaches from pre-processed and attended CKD datasets.

d) Algorithms including MKR Stacking, RF, and MKR Voting demonstrated high accuracy of 99.50%, 98.75%, and 98% on WRF data, respectively, and a substantial prediction percentage and decreased time while identifying CKD.

Author response#1: We sincerely thank the reviewer for highlighting ambiguities in the abstract. We have thoroughly revised the abstract to improve clarity and ensure that all statements convey precise and meaningful information. (**Please refer to Abstract; Page 1).**

Reviewer point #2: Has the author followed ethical guidelines before claiming the statements like: The study's most decisive outcome is fewer false-negative and false-positive values for identifying CKD, supporting the assertion that our proposed approach performs better than human experts.

Author response#2: We appreciate the reviewer's observation regarding the ethical implications of the stated contribution. In response, we have carefully rephrased the contribution to ensure that it accurately reflects the findings of our study while avoiding overgeneralized claims. The revised statement reads: "The

study's most significant outcome is the reduction in false-negative and false-positive rates for CKD identification, reinforcing the assertion that the proposed approach supports nephrologists in making well-informed and rational decisions." This revision eliminates any implicit comparison with human experts and instead emphasizes the role of the proposed method as a supportive tool for clinical decision-making. The updated statement aligns with ethical standards by presenting the contribution in a measured and responsible manner. (**Please refer to List of Contribution before the Section2; Page 1).**

Reviewer point #3: Motivation and research gap is not stated properly.

Author response#3: Thank you for your valuable feedback regarding the need to better articulate the motivation and research gap. In response, we have revised the introduction to emphasize the clinical importance of early CKD detection and the role of machine learning-based CAD systems in overcoming the limitations of current diagnostic methods. Additionally, we have added a dedicated paragraph at the end of the literature review to clearly highlight gaps in previous studies, such as limited use of ensemble methods, insufficient feature extraction techniques, and the lack of integration with real-time healthcare systems like IoMT and RPA. These updates provide a clear rationale for our study and address the identified gaps, strengthening the manuscript's contribution. (**Please refer to 1. Introduction and 2 Literature Review; Page 1 and page 2-3).**

Reviewer point #4: What is the "correlation analysis" used in this study, elaborate.

Author response#4: Thank you for your valuable comment. In this study, we employed Pearson's correlation coefficient to perform the correlation analysis. This statistical method evaluates the linear relationship between different clinical variables and their association with CKD outcomes. Pearson's correlation values range from -1 to +1, where positive values indicate a direct relationship, negative values represent an inverse relationship, and values close to zero suggest no significant correlation. The analysis helped identify the most influential features, such as Albumin, Hemoglobin, and Specific Gravity, which are strongly correlated with CKD, providing crucial insights into the model's feature selection process. This explanation has been added to the revised manuscript for clarity. (**Please refer to 3.1 Data Collection, Description and Analysis; Figure 3; Page 4-5).**

Reviewer point #5: How MKR Stacking and MKR Voting is novel. Elaborate.

Author response#5: Thank you for your comment. The novelty of MKR Stacking and MKR Voting lies in their design to enhance performance through tailored ensemble modeling and hyperparameter tuning. MKR Stacking integrates three optimized base classifiers (MLP, KNN, RF) with Random Forest as a meta-classifier, leveraging cross-validation to prevent overfitting. MKR Voting combines probabilistic outputs using majority voting with hyperparameter-tuned models, such as KNN (K=16) and RF (100 iterations). These ensemble methods, developed by the authors, significantly improve prediction accuracy and robustness compared to traditional approaches, as validated by performance metrics in CKD detection. (**Please refer to 3.4.7 MKR Stacking and MKR Voting; Page 10-11).**

Reviewer point #7: Additionally, the article is missing some state of the art articles in this domain, which needs to be cited: https://doi.org/10.1007/s11042-024-20205-y, https://doi.org/10.1016/j.biosystemseng.2024.05.014, https://doi.org/10.1080/03007995.2024.2390046, https://doi.org/10.1080/10255842.2023.2181660

Author response#7: We thank the reviewer for highlighting the need to include additional state-of-the-art articles. Based on the relevance to our research, we have incorporated two of the suggested articles, which are now cited as references 58 and 59 in our revised manuscript. We believe these additions strengthen the

context and depth of our study. We hope the reviewer finds this update satisfactory. Thank you for the valuable suggestions. (**Please refer to References 58-59).**

Comments of Reviewer 3:

Reviewer point #1: Add a clear motivation for the research. Explain the importance of early detection of Chronic Kidney Disease (CKD) and how Robotic Process Automation (RPA) enhances traditional approaches.

Author response#1: Thank you for the valuable comment. We have revised the introduction to better clarify the motivation for this research. Early detection of Chronic Kidney Disease (CKD) is critical in improving patient outcomes, as it allows for timely intervention to prevent further kidney damage, reduce the risk of progression to end-stage renal disease (ESRD), and minimize associated complications such as cardiovascular diseases. Traditional methods of CKD detection often require time-consuming manual processes and can be prone to human error. This study proposes integrating Robotic Process Automation (RPA) with machine learning-based diagnostic systems to streamline and automate the detection process. RPA enhances traditional approaches by automating repetitive tasks such as data preprocessing, feature extraction, and model execution, ensuring faster, more accurate, and efficient CKD diagnosis. The integration of RPA with machine learning algorithms will improve clinical decision-making and provide more accessible and reliable tools for early CKD detection. (**Please refer to 1. Introduction and 2 Literature Review; Page 1 and page 2-3).**

Reviewer point #2: Highlight the specific contributions and novelty of the proposed mobile application.

Author response#2: Thank you for your feedback. We have revised the manuscript to clearly highlight the contributions and novelty of the proposed mobile application. The application uses advanced ensemble machine learning models, such as MKR Stacking and MKR Voting, to deliver highly accurate CKD predictions by combining multiple classifiers. Additionally, it integrates Robotic Process Automation (RPA) to streamline data processing tasks, enhancing diagnostic efficiency. This combination of machine learning and RPA offers healthcare professionals a user-friendly tool for early CKD detection, enabling timely interventions and personalized treatment plans, thus advancing traditional diagnostic approaches. (**Please refer to List of Contribution before the Section2; Page 1, 5. Discussions; Page 21-22; Table 17)**

Reviewer point #3: Structure the section into distinct subsections for better readability:

2.1 Review Based on Machine Learning Methods: Discuss studies solely utilizing ML techniques for CKD prediction.

2.2 Review Based on Hybrid Methods: Summarize works that combine ML with RPA or other hybrid approaches.

Author response#3: Thank you for your valuable suggestion. As per your recommendation, we have restructured Section 2 into distinct subsections for improved readability. This restructuring improves the clarity and organization of the content, making it easier for readers to navigate and understand the different methodologies used in CKD prediction. (**Please refer to 2. Literature Review; Page 2-3).**

Reviewer point #4: Provide detailed steps of preprocessing, including techniques for handling missing values, normalization, and encoding.

Author response#4: Thank you for pointing out the need for detailed steps in the preprocessing phase. We have now included a comprehensive explanation of the preprocessing techniques in the revised manuscript. To address missing values in the dataset, we employed the MissForest algorithm, a robust imputation method based on Random Forests. We appreciate the feedback and remain open to further clarifications or enhancements. (**Please refer to 3.2 Data Preprocessing; Pages 5-6).**

Reviewer point #5: Clearly define symbols and terms in equations. For example, in Eq. 1.

Author response#5: Thank you for highlighting the importance of defining symbols and terms in the equations. We have addressed this by providing a clear and detailed explanation of all symbols and terms used in the equations throughout the manuscript. (**Please refer to all Equations).**

Reviewer point #6: Improve the quality of all figures to at least 300 dpi resolution.

Author response#6: Thank you for pointing out the need to enhance the quality of figures. These revisions aim to meet publication standards and enhance the overall presentation of the study. We hope the improved figures address the reviewer's concerns effectively.. (**Please refer to all Images).**

Reviewer point #7: Redesign Table 3 (Applied parameter grid) to ensure clarity and professional formatting.

Author response#7: We appreciate the reviewer's feedback regarding Table 3. The table has been redesigned to ensure clarity and professional formatting. The updated version features improved alignment, consistent font styles, and a clear presentation of the applied parameter grid for better readability and comprehension. We believe this revision adequately addresses the concern and enhances the overall quality of the manuscript. (**Please refer to Table 3; Page 11).**

Reviewer point #8: Perform ablation analysis to evaluate the impact of different features and model components.

Author response#8: We thank the reviewer for this suggestion. Ablation analysis has already been conducted and included in the manuscript to evaluate the impact of different features and model components. The analysis highlights the contribution of individual features and components to the overall model performance, demonstrating their significance in improving CKD prediction accuracy. The results of this analysis are presented in the corresponding section, further validating the robustness and reliability of the proposed approach. (**Please refer to Results part including performance on each feature selection technique; Pages 13-17).**

Reviewer point #9: Create a distinct section for discussing the results. Compare them with state-of-the-art methods and provide insights into the findings.

Author response#9: We appreciate the reviewer's comment. A distinct section titled "Discussion" has already been included in Section 5 of the manuscript, where the results are thoroughly analyzed. In this section, we compare the performance of our proposed approach with state-of-the-art methods, highlighting its superior prediction capabilities and discussing the underlying reasons for the observed improvements. The insights into the findings focus on the effectiveness of our ensemble models and the integration of Robotic Process Automation (RPA), providing a comprehensive understanding of the model's strengths and potential areas for future work. (**Please refer to 5. Discussions; Page 21).**

Reviewer point #11: Cite and benchmark the study against recent work such as:

ProteinCNN-BLSTM: An efficient deep neural network with amino acid embedding-based model of protein sequence classification and biological analysis.
Unveiling the prevalence and risk factors of early-stage postpartum depression: A hybrid deep learning approach.
Enhancing heart disease classification with M2MASC and CNN-BiLSTM integration for improved accuracy.

Author response#11: We appreciate the reviewer for suggesting relevant studies to benchmark against. Among the suggested works, two studies were found to be closely aligned with our research context and have been duly cited in the revised manuscript as references [54] and [64]. These citations provide a comparative perspective, strengthening our study's position by highlighting its novelty and relevance in relation to recent advancements in the field. (**Please refer to References; [54], [64]).**