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APPLICATION OF ARTIFICIAL INTELLIGENCE IN MONITORING AND PROGNOSIS OF HAND, FOOT, AND MOUTH DISEASE IN CHILDREN AT CAN THO CHILDREN'S HOSPITAL

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ABSTRACT

Background: *Hand, Foot, and Mouth Disease is a common pediatric infectious disease that can lead to serious neurological, cardiovascular, and respiratory complications if not detected early; however, early identification of severe progression remains challenging, and predictive models such as logistic regression and artificial intelligence may help support more objective risk assessment and monitoring.* ***Objectives:*** *1. To develop an artificial intelligence model for monitoring the status of Hand, Foot, and Mouth Disease in children; 2. To apply the artificial intelligence model for early prediction of the likelihood of severe disease progression, assisting physicians with timely treatment.* ***Materials and methods:*** *A cross-sectional descriptive study was conducted on 302 pediatric patients diagnosed with Hand, Foot, and Mouth Disease treated as inpatients at Can Tho Children's Hospital from October 2024 to October 2025, who met the criteria set by the Ministry of Health in 2024. Data were processed using R 4.3.1 and Python 3.11 software; a logistic regression model was used to construct a Nomogram, and the Random Forest model was used to predict severe progression.* ***Results:*** *Statistically significant independent prognostic factors included CRP, glucose, white blood cell count, convulsions, and pulmonary crackles ($p < 0.05$). The Nomogram model achieved an AUC of 0.833, a sensitivity of 82.1%, and a specificity of 78.3%. The artificial intelligence - Random Forest model achieved an Accuracy of 70.9%, Precision of 0.69, Recall of 0.71, and an F1-score of 0.69. The most important features in the model included number of treatment days (0.345), severity upon admission (0.157), and duration of fever (0.130).* ***Conclusion:*** *The combination of logistic regression and an artificial intelligence model shows high efficacy in predicting and monitoring the progression of Hand, Foot, and Mouth Disease, contributing to supporting physicians in early identification of high-risk pediatric patients, thereby improving the quality of treatment and clinical prognosis.*

Keywords: *Hand foot mouth disease, artificial intelligence, nomogram, Random Forest.*

I. INTRODUCTION

Hand, Foot, and Mouth Disease (HFMD) is a common infectious disease in children, especially in Southeast Asia, including Vietnam, caused by Coxsackie A6, A10, A16 viruses and Enterovirus 71 [1]. Most cases have a mild course; however, a significant proportion can rapidly progress to severe stages with neurological, cardiovascular, and respiratory complications, potentially leading to death if not detected early [2], [3]. Although the Ministry of Health has issued guidelines for clinical staging, the early identification of pediatric patients at risk of severe progression remains a challenge in clinical practice [1]. In this context, the development of Artificial Intelligence (AI) opens a new approach to leveraging clinical data for more objective and accurate prediction of severe disease risk [10]. Therefore, this study

was conducted to: 1) Develop an Artificial Intelligence (AI) model for monitoring the status of Hand, Foot, and Mouth Disease in children; 2) Apply the AI model for early prediction of the likelihood of severe disease progression, assisting physicians with timely treatment.

II. MATERIALS AND METHODS

2.1. Participants

Children diagnosed with Hand, Foot, and Mouth Disease (HFMD) treated as inpatients at Can Tho Children's Hospital during the period from October 2024 to October 2025, who met the diagnostic and disease staging criteria according to the Ministry of Health guidelines in 2024 [1].

- Inclusion criteria: Children under 15 years old with a confirmed diagnosis of HFMD and complete medical records, ensuring sufficient and reliable data for analysis throughout the study.

- Exclusion criteria: Children concurrently suffering from another severe acute illness or chronic diseases that may affect treatment outcomes, in order to minimize potential confounding factors and ensure the accuracy of the results.

2.2. Research methods

- Research design: Cross-sectional descriptive study.

- Sample size: The formula used to calculate sample size was:

$$n = \frac{Z^2_{1-\alpha/2} \times p(1-p)}{d^2}$$

Where: $Z^2_{1-\alpha/2}$ =1.96 (95% confidence level), d=0.04 (acceptable error), p= 0.153 according to the study by Liu *et al.* (2023) on the proportion of severe HFMD cases [7]. Substituting the values into the formula yields $n \approx 312$. In practice, 302 eligible pediatric patients were recruited.

- Sampling method: Convenience sampling was applied, with continuous recruitment of all eligible cases throughout the study period, ensuring that participants who met the inclusion criteria were systematically included as they became available.

- Research content

+ Surveying clinical and subclinical characteristics in children with HFMD.

+ Identifying factors linked to disease severity via multivariate logistic regression.

+ Developing a nomogram model based on logistic regression.

+ Applying the Artificial Intelligence model (AI - Random Forest) for early prediction of the likelihood of severe progression. For the development of the Artificial Intelligence model, the total dataset of 302 patients was randomly divided into a training set (80%, n = 242) and a testing set (20%, n = 60). The training set was used to build and optimize the Random Forest model, while the testing set was used as an independent internal validation set to evaluate predictive performance and reduce overfitting.

- Data processing method: Data were processed using R 4.3.1 and Python 3.11 software; quantitative variables are presented as mean ± standard deviation, and qualitative variables are presented as frequency and percentage. The performance of the AI model was evaluated using AUC, Accuracy, Precision, and Recall, ensuring a comprehensive assessment of model performance.

- Ethical Approval: The study was approved by the Institutional Ethics Committee under approval number 24.155.SV/PCT-HDDD, dated March 3, 2025. All patient

information was kept confidential and used solely for research purposes, in compliance with relevant ethical standards and data protection regulations, and all data were anonymized to ensure the privacy and rights of participants were fully protected throughout the study.

III. RESULTS

3.1. General Characteristics of the Study Subjects

Table 1. Characteristics regarding gender and age group (n= 302)

Characteristic		Frequency (n)	Percentage (%)
Gender	Male	171	56.6
	Female	131	43.4
Age Group	Under 12 months	22	7
	From 12 to under 24 months	110	37
	From 24 to under 36 months	76	25
	From 36 months and over	94	31

The proportion of male pediatric patients with HFMD was 56.6%, higher than females at 43.4%. The majority of pediatric patients with HFMD were under 36 months old. Patients aged 12 to under 24 months accounted for the highest percentage of HFMD cases at 37%. Patients under 12 months accounted for the lowest percentage at 7%.

3.2. Clinical and Subclinical Characteristics

Clinical Characteristics

Table 2. Clinical characteristics from onset to hospital admission (n= 302)

Characteristic	Frequency (n)	Percentage (%)
Skin lesions	258	85.4
Mouth ulcers	246	81.5
Startling	140	46.4
Fever $\geq 39^0$C	135	44.7
Irritability	59	19.5
Vomiting	48	15.9
Tachypnea	13	4.3
Diarrhea	11	3.6
Convulsions	10	3.3

Mouth ulcers and skin lesions were the two most common symptoms, accounting for 85.4% and 81.5%, respectively. The next two most common symptoms were startling accounting for 46.4%, and fever $\geq 39^0$C accounting for 44.7%.

Table 3. HFMD severity upon admission (n= 302)

HFMD Grade	Frequency (n)	Percentage (%)
2a	279	92.4
2b group 1	17	5.6
2b group 2	5	1.7
3	1	0.3

Upon admission, 92.4% of pediatric patients were classified as HFMD grade 2a, and 5.6% were diagnosed as grade 2b. Only 1 patient had HFMD grade 3.

Table 4. HFMD severity level based on disease progression (n= 302)

	Mild Severity	Severe Severity
Upon Admission	92.7	7.3
Progression	79.1	21.9

Upon admission, the majority of pediatric patients with HFMD were categorized as mild severity. Following the monitoring and treatment process, a number of pediatric patients with mild HFMD progressed to severe stages, causing the total number of severe cases to increase to 21.9%.

Subclinical Characteristics

Table 5. Characteristics of white blood cell count, platelet count, blood glucose, and CRP

Characteristic		Frequency (n)	Percentage (%)
White Blood Cell	≥16.000/mm^3	60	19.9
	<16.000/mm^3	242	80.1
Platelet Count	≥400.000/mm^3	72	23.8
	<400.000/mm^3	230	76.2
Blood Glucose	≥8.9 mmol/L	3	2.3
	<8.9 mmol/L	130	97.7
CRP	≥10mg/L	60	56.1
	<10mg/L	47	43.9
EV71	Positive	95	31
	Negative	207	69

19.9% of pediatric HFMD patients had a white blood cell count ≥16.000/mm^3. The proportion of pediatric HFMD patients with a platelet count ≥400.000/mm^3 accounted for 23.8%. In our study, only 3 out of 133 pediatric patients who had their blood glucose measured had a result ≥8.9 mmol/L. Among 107 children who underwent quantitative CRP testing, 60 children had a blood CRP level ≥10 mg/L. The percentage of children with a positive IgM EV71 test result accounted for 31%.

3.3. Developing an Artificial Intelligence (AI) Model to Monitor the Status of Hand-Foot-Mouth Disease in Children

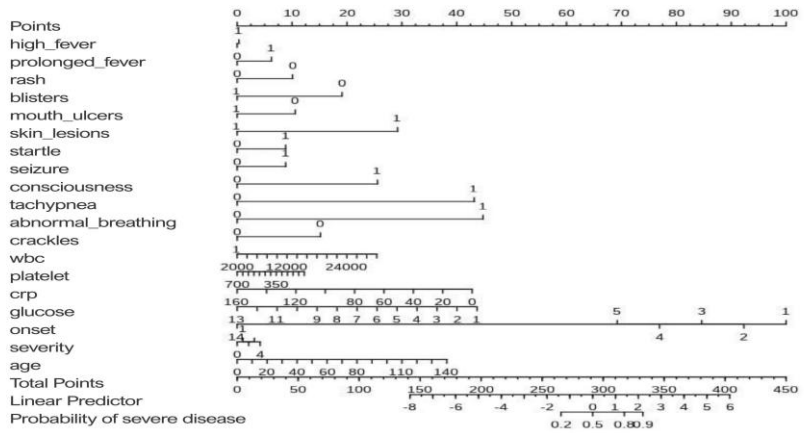

Figure 1. Nomogram for predicting the severe progression of HFMD

The variables contributing the highest points include CRP (≥10 mg/L), elevated blood glucose, white blood cell count ≥16.000/mm^3, convulsions, and pulmonary crackles (rales), reflecting the prominent role of inflammatory response and metabolic disturbance

in disease progression. The model achieved an AUC = 0.833, a sensitivity of 82.1%, and a specificity of 78.3%, demonstrating good discriminative ability between the severe and non-severe disease groups. As the total Nomogram score increases, the probability of severe progression increases correspondingly, supporting physicians in early assessment and timely intervention for high-risk cases.

3.4. Applying AI models to predict early disease progression

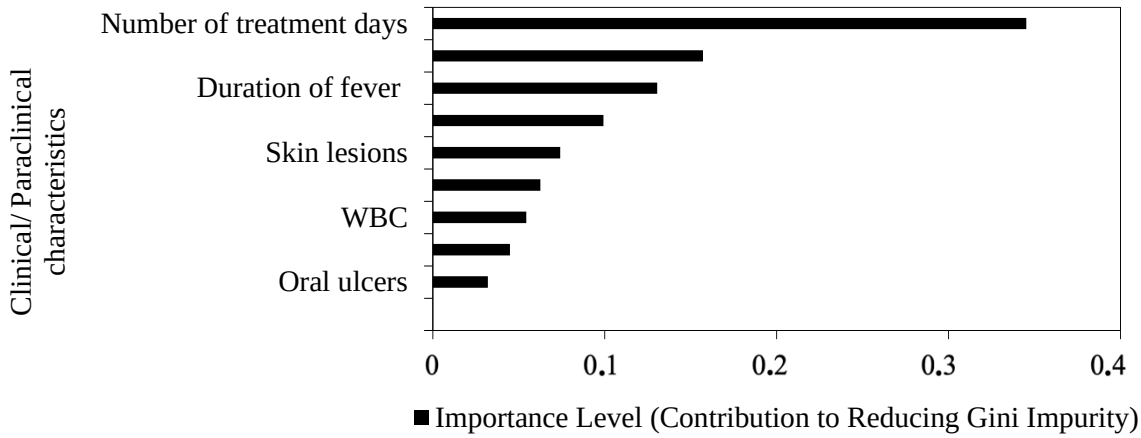

Figure 2. Feature Importance in Predicting Disease Severity

The important features includ ed number of treatment days (0.345), severity upon admission (0.157), and duration of fever (0.130), indicating that initial clinical presentations have high value in predicting severe progression. Other factors such as startling, white blood cell count, and platelet count also contributed to a certain extent, while convulsions appeared only in the later stage, resulting in a lower importance score.

Table 6. Performance of the AI Model in Predicting Disease Severity

Parameter	Value
Accuracy	0.7097
Average Precision	0.69
Average Recall	0.71
Average F1-score	0.69

The model achieved an Accuracy of 70.9%, indicating a relatively good predictive ability across the mild, moderate, and severe disease groups. The severe disease group (grade 3) had a Recall of 0.62, reflecting an acceptable ability to correctly identify severe cases, which is suitable for real-world medical data. The Precision and F1-score were relatively consistent, proving the model's stability and suggesting it can be used to support early identification of high-risk patients.

II. DISCUSSION

4.1. General Characteristics of the Study Subjects

Among the 302 children with HFMD, males accounted for 56.6%, which was higher than females (43.4%), consistent with recent epidemiological reports indicating a slightly higher incidence of HFMD in boys [3], [6]. Children under 36 months old accounted for

69%, particularly the 12-24 months group (37%), which aligns with recent studies showing that children under 3 years of age are at higher risk due to immature immune responses and increased exposure in community settings [3], [7].

4.2. Clinical and Subclinical Characteristics

The most common symptoms were skin lesions (85.4%), mouth ulcers (81.5%), and startling (46.4%). Fever $\geq 39^0$C accounted for 44.7%, indicating a clear inflammatory response. Regarding subclinical characteristics, white blood cell count $\geq 16.000/mm^3$ accounted for 19.9%, platelet count $\geq 400.000/mm^3$ accounted for 23.8%, CRP ≥ 10 mg/L accounted for 56.1%, and the portion of positive EV71 test results was 31%, reflecting the role of inflammatory reaction and immune dysfunction in the disease progression mechanism [5], [7].

Upon admission, 92.4% of pediatric patients were at grade 2a, with only 7.6% in the severe group (grade 2b-3). However, during treatment, the portion of severe cases increased to 21.9%, proving that the disease can progress rapidly, requiring close monitoring within the first 48-72 hours [6].

4.3. Efficacy of the Nomogram Model in Predicting Severe Progression

Specifically, elevated CRP and leukocytosis reflect systemic inflammatory response and have been reported as prognostic markers in Vietnamese pediatric populations [4], [8]. High blood glucose indicates metabolic stress during the acute phase and has been associated with severe progression in recent meta-analyses [4], [7]. Pulmonary crackles and convulsions represent cardiovascular and central nervous system involvement in advanced stages of the disease [2], [3].

The Nomogram estimates the probability of severe progression based on the total score of clinical and subclinical factors; the model achieved an AUC of 0.833, sensitivity of 82.1%, and specificity of 78.3%, demonstrating good discrimination between severe and non-severe cases. The risk increases proportionally with the total score, enabling visual risk quantification. Compared with the study by Pham Thanh Binh (2022) (AUC = 0.78) [9], the higher AUC in our study suggests that incorporating markers of inflammatory response and metabolic disturbance improves predictive accuracy. Therefore, the Nomogram serves as an effective tool for early risk stratification and supports improved monitoring and prognosis of HFMD in provincial pediatric hospitals.

4.4. Application of the Artificial Intelligence (AI) - Random Forest Model

The Random Forest model was developed on the same dataset (302 pediatric patients), divided into an 80% training set and a 20% testing set. The model yielded Accuracy = 70.9%, Precision = 0.69, Recall = 0.71, and F1-score = 0.69, reflecting stable predictive performance. Compared to the study by Chen L. *et al.* (2023), which achieved an Accuracy of 68.2% [10], the current model shows equivalent or superior efficacy, demonstrating the Random Forest model's ability to handle non-linear data and recognize characteristic patterns suitable for pediatric medical data.

The most important features were the number of treatment days (0.345), severity upon admission (0.157), and duration of fever (0.130), highlighting the impact of onset timing and initial clinical severity on predicting severe progression. Other variables such as startling (0.063), white blood cell count (0.054), and platelet count (0.045) also contributed to the model, whereas convulsions (0.000) showed low importance because they typically appear later in the disease course.

Thus, the artificial intelligence model supports early risk stratification from hospital admission and aligns with Nguyen M.H. (2024) on the application of machine learning in predicting infectious diseases in children [11], reinforcing the role of artificial intelligence in clinical decision-making and early warning for Hand, Foot, and Mouth Disease.

IV. CONCLUSION

The study identified CRP, glucose, white blood cell count, pulmonary crackles, and convulsions as independent prognostic factors for severe HFMD. The Nomogram demonstrated good predictive performance (AUC = 0.833), enabling early risk stratification, while the Artificial Intelligence - Random Forest model achieved an accuracy of 70.9%, supporting early detection of severe progression from admission. The integration of logistic regression and artificial intelligence offers an effective approach to improving monitoring, prognosis, and treatment of HFMD in pediatric settings.

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