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Application of artificial intelligence in the Prediction of Complications in patients with Malaria

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Abstract

Introduction: This study aims to develop a neural network (NN) that can serve as a useful tool for early diagnosis of complicated malaria.

Materials and methods: In this study, a feedforward NN was developed, incorporating 10 clinical variables in the input nodes, hidden layer, and output node. The data were included in the input layer. Various validation techniques such as V-cross, Random V-cross, Modified Holdout, and Proportional Percentage Sample were applied to train and validate the network using data from 412 patients.

Results: The variables included in the analysis were mean arterial pressure, hemoglobin, leukocyte count, platelet count, total bilirubin, presence of dyspnea, vomiting, previous history of malaria, prior use of malaria medication, and persistent fever. The V-cross technique, Random V-cross Validation, Modified Holdout Validation, and Proportional Percentage Sample Validation were utilized to evaluate the performance of a NN in diagnosing malaria. Sensitivity values varied from 13% to 47%, with positive predictive value values ranging from 37% to 88%. Specificity remained consistently high, ranging from 79% to 90%.

Discussion: Sensitivity, specificity, and positive predictive values varied across techniques: V-cross and random V-cross validation showed narrower sensitivity ranges with strong specificities, while modified holdout validation exhibited wider sensitivity variability.

Keywords: Artificial intelligence, Malaria, Diagnosis.

Aplicación de la inteligencia artificial en la Predicción de Complicaciones en pacientes con Malaria

Resumen

Introducción: Este estudio tiene como objetivo desarrollar una red neural (RN) que pueda servir como una herramienta útil para el diagnóstico temprano de la malaria complicada.

Materiales y métodos: En este estudio, se desarrolló una red neural *feedforward*, incorporando 10 variables clínicas en los nodos de entrada, la capa oculta y el nodo de salida. Se aplicaron diversas técnicas de validación como V-cross, V-cross Aleatorio, Retención Modificada y Muestra Proporcional de Porcentaje para entrenar y validar la red utilizando datos de 412 pacientes.

Resultados: Las variables incluidas en el análisis fueron la presión arterial media, hemoglobina, recuento de leucocitos, recuento de plaquetas, bilirrubina total, presencia de disnea, vómitos, historial previo de malaria, uso previo de medicamentos para la malaria y fiebre persistente. Se utilizaron las técnicas de V-cross, Validación Cruzada Aleatoria, Validación de Retención Modificada y Validación de Muestra Proporcional de Porcentaje para evaluar el rendimiento de una RN en el diagnóstico de la malaria. Los valores de sensibilidad variaron del 13% al 47%, con valores predictivos positivos que oscilaron entre el 37% y el 88%. La especificidad se mantuvo consistentemente alta, variando del 79% al 90%.

Discusión: La sensibilidad, la especificidad y los valores predictivos positivos variaron según las técnicas: la validación cruzada en V y la validación cruzada aleatoria en V mostraron rangos de sensibilidad más estrechos con fuertes especificidades, mientras que la validación con retención modificada exhibió una mayor variabilidad en la sensibilidad.

Palabras clave: Inteligencia artificial, Malaria, Diagnóstico.

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Introduction

Malaria is an infectious disease that affects a significant number of people worldwide. Recent studies have identified over 100 countries where malaria is endemic, affecting approximately 207 million people annually[1-3]. In the Americas alone, up to 170 million people are at risk of contracting malaria. The disease is caused by various types of Plasmodium parasites, with *Plasmodium vivax* and *Plasmodium falciparum* being the most common in Latin America[4,5]. The estimated mortality rate worldwide is around 1%[5]. However, malaria deaths increased rapidly after 1990, peaking at 232 million cases in 2003 and resulting in 1.2 million deaths in 2004[6-10]. According to the World Health Organization (WHO), malaria is classified into complicated (severe) and uncomplicated forms[11]. Complicated or severe malaria occurs when parasites cause severe organ failure. Uncomplicated malaria, on the other hand, manifests as symptomatic infection with parasites present in the blood, typically following a benign course[12,13].

The clinical diagnosis of malaria, although somewhat imprecise, remains pivotal in managing febrile patients in high-risk areas[14,15]. Therefore, accurately and promptly identifying the parasite in high-risk patients, particularly those prone to severe malaria, is crucial for reducing mortality[16]. However, predicting whether an individual will develop severe malaria can be challenging. Some symptoms and laboratory findings associated with severe malaria are well-described. The progression to severe malaria in infected patients involves progressive dysfunction of various organs, which may manifest in diverse clinical presentations[17].

Computational methods such as neural networks (NN) have significantly enhanced the diagnosis of various medical conditions using clinical variables. An NN comprises interconnected units (or nodes) that mimic neurons, forming a network[17-19]. Leveraging this computational tool could be instrumental in accurately diagnosing and categorizing malaria infections. While there are several types of neural networks, a commonly used architecture involves a three-layer structure: the first layer with input units, an intermediate or hidden layer, and a third layer housing the output units. Depending on the input information, the network processes data through the hidden layer to yield a classification response[6,18]. When appropriately developed, NNs can effectively differentiate patients who may develop complicated malaria from those who will not[19]. This study aims to develop a multilayer neural network using basic clinical and paraclinical characteristics in malaria patients, serving as a prognostic tool to identify those at risk of developing severe malaria.

Materials and methods

This retrospective observational study was conducted on malaria-infected patients admitted to a tertiary care hospital in Bogotá, Colombia, between 2005 and 2013. The study focused on describing a neural network tool with high sensitivity for detecting complicated cases. It was categorized as minimal risk and approved by the institutional ethics committee in accordance with the Helsinki Declaration and data protection guidelines.

Eligibility Criteria

Patients of any gender and age with confirmed malaria diagnosis via thick blood smear were eligible. Exclusions applied to those with a history of convulsive syndrome, neurological sequelae from any cause, advanced-stage or acute exacerbation of renal, hepatic, hematological, or pulmonary diseases. The study included 412 malaria-infected patients, of whom 68 developed complications (including cardiovascular, renal, respiratory issues, multiple organ failure, and death), categorized as "Complicated" (Class 1), while the remaining 344 were labeled as "Non-complicated" (Class 0) (see Supplementary Figure 1).

Construction and Architecture of the Neural Network

A feedforward neural network was constructed using the neural network training tool in Matlab 2013[a]®, comprising input nodes, output node, and a hidden layer (see Supplementary Figure 2). The training termination criteria for the neural network included a learning rate of 0.025, 1000 epochs, or a minimum gradient of 1 x 10-6.

Input Nodes

Ten clinical variables were chosen as input nodes, recorded at the time of diagnosis and easily accessible in the emergency department. These variables—mean arterial pressure (mmHg)[1], hemoglobin (g/dL) [20, 21], leukocyte count (cells/µL)[22], platelet count (x10^3/µL)[3,21], total bilirubin (mg/dL)[21,3], presence of dyspnea[2,3], vomiting[21], previous history of malaria infection[1], previous use of antimalarial or antipyretic medications, and persistent fever[22]—reflect multiorgan involvement and indicate potential complications of the disease.

Output Node

The goal proposed for this network aims to improve classification results between complicated and non-complicated malaria. Therefore, the output node corresponds to the diagnosis of a patient with complicated malaria (Class 1) or non-complicated malaria (Class 0).

Hidden Layer

Using the pyramidal geometric rule proposed by T. Masters[23], the number of neurons in the hidden layer was determined as shown in expression (1). Where HN is the hidden layer, n is the number of inputs, and m is the number of outputs. Number of outputs was 2, one for each class.

$$HN = \sqrt{n\,m} \qquad (1)$$

$$HN = \sqrt{(10)(1)}$$

$$HN = \sqrt{10}$$

$$HN = 3,16 \approx 4$$

Randomization for Patient Data Selection in the Training and Validation Groups

Various techniques, including V-cross validation, random V-cross validation, modified holdout, and proportional percentage sample, were employed to partition the data of 412 patients into training and validation sets[24].

V-cross Validation

To implement this technique, the entire database was initially randomly reorganized and divided into 10 groups, with 9 groups containing 41 data points each and 1 group containing 43 data points. The neural network (NN) was then trained and validated 10 times, with each iteration using a different group for training and the remaining groups for validation (see Supplementary Figure 3). Additionally, a secondary validation was conducted for each iteration using the 10 selected clinical variables from all patients.

Random V-cross Validation

Similar to V-cross validation, this technique involved random reorganization of the database for each iteration. However, the data from the first group of patients were consistently used as the training set for each repetition (see Supplementary Figure 4).

Modified Holdout Validation

This technique grouped patients based on their hospital discharge diagnosis, with 68 patients classified as complicated malaria and 344 as uncomplicated malaria (see Supplementary Figure 5). Subsequently, 50 patients from each group were randomly selected to form the training set, while the remaining patients constituted the initial validation set. This procedure was repeated 5 times.

Proportional Percentage Sample Validation

In this technique, the training and validation groups were created based on the incidence of malaria complications in the database, which was 17% in this study. Similar to modified holdout validation, the training set included 83% of patient data randomly selected from each class (complicated and uncomplicated malaria), while the initial validation set comprised the remaining patient data (see Supplementary Figure 6). A secondary validation was performed using all patient data. This process was repeated 5 times.

Implementation of the NN with Incremental Neuron Progression in the Hidden Layer

According to the pyramidal rule, the ideal number of neurons in the hidden layer of the NN was 4. However, the number of neurons was incrementally increased in multiples of 4 up to 24 to assess the NN's performance with varying hidden layer configurations.

Performance Evaluation of the Network

The diagnostic performance of each of the methods used in our study is processed based on the precision, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) calculated from the confusion matrix[25]. Receiver Operating Characteristic (ROC) curves were utilized to assess NN performance, focusing on the maximum point of these curves in this study.

Results

V-cross Validation

The implementation of the NN using the V-cross technique yielded sensitivity values ranging from 13% to 47%, and PPV values ranged from 37% to 66% (Table 1). Additionally, specificity ranged between 79% and 85%. Regarding NN performance evaluation, results from validation group 1 indicated superior performance with 24 neurons in the hidden layer, whereas validation group 2 showed optimal performance with 4 neurons (Supplementary Figure 7).

Random V-cross Validation

Sensitivity values ranged from 13% to 31%, and PPV values ranged from 45% to 65% (Table 2). Furthermore, specificity ranged between 80% and 85%. Regarding NN performance, validation group 1 exhibited better results with 24 neurons in the hidden layer, while validation group 2 showed superior performance with 16 neurons (Supplementary Figure 8).

Modified Holdout Validation

When implementing the NN using modified holdout validation, sensitivity values ranged from 34% to 72%, and NPV ranged from 21% to 59% (Table 3). Specificity ranged between 80% and 88%. In validation group 1, optimal results were observed with 4 neurons in the hidden layer, while validation group 2 achieved the best outcome with 16 neurons (Supplementary Figure 9).

Proportional Percentage Sample Validation

Sensitivity values ranged between 16% and 44%, and PPV values ranged from 54% to 88% (Table 4). Additionally, specificity ranged between 85% and 90%. The NN performance was superior with 8 neurons in the hidden layer for validation group 1 and with 12 neurons for validation group 2 (Supplementary Figure 10).

Discussion

In this study, we systematically evaluated the performance of a neural network in diagnosing complicated malaria using various validation techniques. We developed an NN with the aim of serving as a useful tool for the early diagnosis of complicated malaria. Specifically, we found that the NN configured with 16 neurons in the hidden layer, using the modified Holdout technique and validation group 2, achieved the highest performance (see Table 1). The implementation of this NN could be particularly beneficial in remote or underserved areas where healthcare services are limited. Its application has the potential to significantly enhance diagnostic processes, especially in cases requiring critical decisions to ensure timely treatment for affected patients.

Table 1. Neural network results using V cross validation.

number of neurons	validation group	Se (%)	Sp (%)	PPV (%)	NPV (%)	E (%)
4	1	23	97	60	86	84
	2	47	89	55	90	82
8	1	13	93	44	84	80
	2	18	96	58	86	83
12	1	29	89	37	86	79
	2	25	95	66	87	84
16	1	21	92	33	86	81
	2	18	97	58	86	84
20	1	26	93	53	87	83
	2	29	96	63	87	85
24	1	44	91	55	90	84
	2	22	96	56	86	84

Notes: Se: sensitivity; Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value: E: Accuracy.

Table 2. Neural network results using random V-cross validation.

number of neurons	validation group	Se (%)	Sp (%)	PPV (%)	NPV (%)	E (%)
4	1	17	95	49	85	82
	2	22	96	56	86	83
8	1	13	94	39	85	81
	2	19	98	53	86	85
12	1	14	94	50	84	80
	2	28	94	65	87	83
16	1	14	97	52	85	83
	2	31	90	37	87	81
20	1	16	96	51	85	83
	2	18	97	55	86	84
24	1	19	97	54	86	84
	2	13	96	45	85	82

Notes: Se: sensitivity; Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value: E: Accuracy.

Complicated malaria represents a medical emergency; therefore, early diagnosis is crucial to prevent multi-organ involvement and potential fatalities[2]. Currently, there is no consensus on severity criteria for diagnosing complicated malaria. The most commonly utilized criteria are those established by the World Health Organization[26-29], focusing on systemic involvement alongside parasite presence. However, these criteria have faced criticism for their high sensitivity in detecting extremely severe cases but low specificity, limiting their utility in clinical decision-making by not identifying lower severity levels[30]. Our system has a very low sensitivity along with good specificity, which could be complementary to the current criteria.

Epidemiological studies have not identified a standard marker enabling early diagnosis of complicated malaria. Tobón-Castaño et al., developed a prediction model with a sensitivity of 45% and a specificity of 92.8%, using clinical and parasitological signs[21]. In the same year, researchers from Oxford evaluated PfHRP2 (Plasmodium falciparum histidine-rich protein 2) and pLDH (plasmodium lactate dehydrogenase) as rapid diagnostic tests for complicated malaria in children from Tanzania and Mozambique. PfHRP2 showed a sensitivity of 94% and a specificity of 70.9%, while pLDH showed a sensitivity of 88% and a specificity of 88.3%[31]. In contrast, the NN developed in our study did not rely on parasitology for diagnosis and achieved a sensitivity of 72% and a specificity of 82%, demonstrating improved sensitivity and specificity compared to the aforementioned studies. Importantly, the neural network is a cost-effective and rapid tool suitable for use in endemic areas lacking advanced diagnostic technology.

The mortality associated with complicated malaria remains significant, affecting 10% to 50% of patients, primarily due to resource scarcity, underdiagnosis, and delayed treatment initiation[6-10]. Patients with complicated malaria require treatment in high-level hospitals, often in intensive care units[6,10]. A reliable tool that aids physicians in determining the need for hospitalization can significantly improve the identification of patients requiring such care, thereby reducing costs associated with unnecessary hospitalizations and ensuring timely treatment for those with complicated malaria[9,10].

In contrast, patients with uncomplicated malaria typically require only oral chloroquine treatment and do not necessitate hospitalization, unlike cases of complicated malaria where parenteral administration of antiparasitics is essential[6,20,29]. In Colombia, sodium artesunate is recommended as the first-line intravenous treatment, followed by quinine dihydrochloride as a second option also administered intravenously. The-

Table 3. Neural network results using modified holdout validation

number of neurons	validation group	Se (%)	Sp (%)	PPV (%)	NPV (%)	E (%)
4	1	56	85	21	97	83
	2	34	91	53	88	82
8	1	44	90	35	96	88
	2	65	86	53	93	83
12	1	49	86	21	96	83
	2	55	85	45	91	80
16	1	43	87	21	96	85
	2	72	84	47	94	82
20	1	51	90	25	97	88
	2	65	90	59	93	86
24	1	50	91	26	97	88
	2	62	87	49	92	83

Notes: Se: sensitivity; Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value: E: Accuracy.

Table 4. Neural network results using the proportional sample technique by percentage

number of neurons	validation group	Se (%)	Sp (%)	PPV (%)	NPV (%)	E (%)
4	1	22	98	65	87	86
	2	31	98	81	88	87
8	1	38	94	55	89	85
	2	21	99	88	86	86
12	1	22	97	56	87	85
	2	44	99	68	90	90
16	1	29	98	63	88	87
	2	30	99	85	88	88
20	1	34	94	54	88	85
	2	16	99	62	86	85
24	1	26	97	58	88	86
	2	26	99	69	87	87

Notes: Se: sensitivity; Sp: Specificity; PPV: Positive predictive value; NPV: Negative predictive value: E: Accuracy.

refore, accurate diagnosis is crucial to distinguish between complicated and uncomplicated malaria, as treatment varies in terms of antimalarial drugs, route of administration, and hospital care. Any delay in referral or initiation of parenteral therapy can significantly impact patient outcomes by reducing complications[7,9]. In this context, a tool such as a neural network can play a crucial role in preventing mortality, complications, and unnecessary hospitalizations associated with complicated malaria.

Regarding the neural network configuration that yielded the best results according to the study's objectives, an NN with 16 neurons in the hidden layer using the modified Holdout technique with validation group 2 achieved the highest sensitivity value (72%) and also generated a specificity value of 82%. Overall, irrespective of the validation group used, this configuration consistently demonstrated superior sensitivity and specificity. Furthermore, it is noteworthy that there is no linear relationship between the number of neurons in the hidden layer and the increase in diagnostic metrics.

Regarding the validation group, it is evident that using group 2 consistently improves indicator values across all validation techniques. Lower specificity values are observed with validation group 1, while higher sensitivity values are consistently achieved with group 2. Finally, it is important to highlight that the overall efficiency, assessed through all validation techniques and varying numbers of neurons in the hidden layer, ranges from a minimum of 79% to a maximum of 90%. This underscores the effectiveness of the NN architecture, including its input nodes, output nodes, and even with a minimal number of neurons in the hidden layer.

Our sample may be unbalanced, which is normal due to the prevalence of complicated malaria. The NN may have had a bias towards classifying non-complicated patients, which is reflected in the low and variable sensitivity values across all the network architectures evaluated. Furthermore, we conducted a second validation of the included variables, which may be biased because the samples used for training were also included in the system evaluation. While further studies are needed to demonstrate the NN's impact on reducing mortality in malaria patients, a well-trained NN using patient data from various medical centers holds promise for improving prognostic classification and treatment outcomes[29,30].

As conclusions, in this study, a NN was assessed using four validation techniques V-cross, random V-cross, modified holdout, and proportional percentage sample to diagnose complicated malaria. Sensitivity, specificity, and positive predictive values varied across techniques: V-cross and random V-cross validation showed narrower sensitivity ranges with strong specificities, while modified holdout validation exhibited wider sensitivity variability. Optimal NN configurations, such as the number of neurons in the hidden layer, varied by validation group, highlighting the influence of dataset partitioning on performance outcomes. Overall, these results emphasize the NN's potential as a versatile diagnostic tool for complicated malaria, warranting further optimization and validation in diverse clinical settings.

Ethical considerations

Protection of persons and animals. This study involves human participants and was conducted according to the declaration of Helsinki, approved by institutional ethics committee of the Universidad de La Sabana (Acta No. 67 del 4 mayo 2018).

Protection of Vulnerable Populations. Does not apply.

Confidentiality. For the collection and dissemination of data, the protocols established by the participating institutions were followed, to guarantee patient privacy.

Privacy. Patient identifiable data were not used or disclosed in this study and were kept anonymous during the whole data analysis.

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Conflict of interests. The authors have no disclosures to report.

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Authors´ contribution. All authors contributed to the study concept and design. Data acquisition was performed by ETQ, DBR, ABG, JLA, AG, MA, and NV. Data analysis was performed by ETQ, DBR, and ABG. All authors contributed to the interpretation of the data. ETQ, and DBR drafted the work. All authors contributed to read and approved the version of the submitted manuscript.

References

1. Sagaki P, Thanachartwet V, Desakorn V, Sahassananda D, Chamnanchanunt S, Chierakul W, Pitisuttithum P, Ruangkanchanasetr P. Clinical factors for severity of Plasmodium falciparum malaria in hospitalized adults in Thailand. PLoS One. 2013 ;8(8):e71503. DOI: 10.1371/journal.pone.0071503
2. Rahimi BA, Thakkinstian A, White NJ, Sirivichayakul C, Dondorp AM, Chokejindachai W. Severe vivax malaria: a systematic review and meta-analysis of clinical studies since 1900. Malar J. 2014 ;13:481. DOI: 10.1186/1475-2875-13-481
3. Botwe AK, Oppong FB, Gyaase S, Owusu-Agyei S, Asghar M, Asante KP, Färnert A, Osier F. Determinants of the varied profiles of Plasmodium falciparum infections among infants living in Kintampo, Ghana. Malar J. 2021 ;20(1):240. DOI: 10.1186/s12936-021-03752-9
4. Sutto-Ortiz P, Eléouët JF, Ferron F, Decroly E. Biochemistry of the Respiratory Syncytial Virus L Protein Embedding RNA Polymerase and Capping Activities. Viruses. 2023 ;15(2):341. DOI: 10.3390/v15020341
5. Carlson CJ, Colwell R, Hossain MS, Rahman MM, Robock A, Ryan SJ, Alam MS, Trisos CH. Solar geoengineering could redistribute malaria risk in developing countries. Nat Commun. 2022 ;13(1):2150. DOI: 10.1038/s41467-022-29613-w
6. Tobón-Castaño A, Giraldo-Castro C, Blair S. Utilidad de los signos clínicos y parasitológicos en el pronóstico de la malaria grave en Colombia. Biomedica. 2012 ;32 Suppl 1:79-94. DOI: 10.1590/S0120-41572012000500010
7. Tomassi MV, D'Abramo A, Vita S, Corpolongo A, Vulcano A, Ascoli Bartoli T, Bartolini B, Faraglia F, Nicastri E. A case of severe Plasmodium ovale malaria with acute respiratory distress syndrome and splenic infarction in a male traveller presenting in Italy. Malar J. 2024 ;23(1):93. DOI: 10.1186/s12936-024-04911-4
8. Walker IS, Rogerson SJ. Pathogenicity and virulence of malaria: Sticky problems and tricky solutions. Virulence. 2023 ;14(1):2150456. DOI: 10.1080/21505594.2022.2150456
9. Kumar A, Singh PP, Tyagi S, Hari Kishan Raju K, Sahu SS, Rahi M. Vivax malaria: a possible stumbling block for malaria elimination in India. Front Public Health. 2024 ;11:1228217. DOI: 10.3389/fpubh.2023.1228217
10. Murray CJ, Ortblad KF, Guinovart C, Lim SS, Wolock TM, Roberts DA, Dansereau EA, Graetz N, Barber RM, Brown JC, et al. Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014 ;384(9947):1005-70. DOI: 10.1016/S0140-6736(14)60844-8.
11. Saravu K, Rishikesh K, Kamath A, Shastry AB. Severity in Plasmodium vivax malaria claiming global vigilance and exploration--a tertiary care centre-based cohort study. Malar J. 2014 ;13:304. DOI: 10.1186/1475-2875-13-304
12. Manning L, Laman M, Law I, Bona C, Aipit S, Teine D, Warrell J, Rosanas-Urgell A, Lin E, Kiniboro B, Vince J, Hwaiwhanje I, Karunajeewa H, Michon P, Siba P, Mueller I, Davis TM. Features and prognosis of severe malaria caused by Plasmodium falciparum, Plasmodium vivax and mixed Plasmodium species in Papua New Guinean children. PLoS One. 2011;6(12):e29203. DOI: 10.1371/journal.pone.0029203
13. Nsanzabana C, Djalle D, Guérin PJ, Ménard D, González IJ. Tools for surveillance of anti-malarial drug resistance: an assessment of the current landscape. Malar J. 2018 ;17(1):75. DOI: 10.1186/s12936-018-2185-9
14. Wongsrichanalai C, Barcus MJ, Muth S, Sutamihardja A, Wernsdorfer WH. A review of malaria diagnostic tools: microscopy and rapid diagnostic test (RDT). Am J Trop Med Hyg. 2007 ;77(6 Suppl):119-27. PMID: 18165483
15. Leke RF, Djokam RR, Mbu R, Leke RJ, Fogako J, Megnekou R, Metenou S, Sama G, Zhou Y, Cadigan T, Parra M, Taylor DW. Detection of the Plasmodium falciparum antigen histidine-rich protein 2 in blood of pregnant women: implications for diagnosing placental malaria. J Clin Microbiol. 1999 ;37(9):2992-6. DOI: 10.1128/JCM.37.9.2992-2996.1999
16. Chu CS, Stolbrink M, Stolady D, Saito M, Beau C, Choun K, Wah TG, Mu N, Htoo K, Nu B, Keereevijit A, Wiladpaingern J, Carrara V, Phyo AP, Lwin KM, Luxemburger C, Proux S, Charunwatthana P, McGready R, White NJ, Nosten F. Severe Falciparum and Vivax Malaria on the Thailand-Myanmar Border: A Review of 1503 Cases. Clin Infect Dis. 2023 ;77(5):721-728. DOI: 10.1093/cid/ciad262
17. Mello MB, Luz FC, Leal-Santos FA, Alves ER Jr, Gasquez TM, Fontes CJ. Standardization of blood smears prepared in transparent acetate: an alternative method for the microscopic diagnosis of malaria. Malar J. 2014 ;13:238. DOI: 10.1186/1475-2875-13-238
18. Hosseini MP, Hosseini A, Ahi K. A Review on Machine Learning for EEG Signal Processing in Bioengineering. IEEE Rev Biomed Eng. 2021;14:204-218. DOI: 10.1109/RBME.2020.2969915
19. Ma G, Chen P, Liu Z, Liu J. The Prediction of Enterprise Stock Change Trend by Deep Neural Network Model. Comput Intell Neurosci. 2022 ;2022:9193055. DOI: 10.1155/2022/9193055
20. Quintero JP, Siqueira AM, Tobón A, Blair S, Moreno A, Arévalo-Herrera M, Lacerda MV, Valencia SH. Malaria-related anaemia: a Latin American perspective. Mem Inst Oswaldo Cruz. 2011 ;106 Suppl 1(Suppl 1):91-104. DOI: 10.1590/s0074-02762011000900012
21. Kuna A, Gajewski M, Szostakowska B, Nahorski WL, Myjak P, Stanczak J. Imported Malaria in the Material of the Institute of Maritime and Tropical Medicine: A Review of 82 Patients in the Years 2002-2014. Biomed Res Int. 2015;2015:941647. DOI: 10.1155/2015/941647
22. Bruneel F, Hocqueloux L, Alberti C, Wolff M, Chevret S, Bédos JP, Durand R, Le Bras J, Régnier B, Vachon F. The clinical spectrum of severe imported falciparum malaria in the intensive care unit: report of 188 cases in adults. Am J Respir Crit Care Med. 2003 ;167(5):684-9. DOI: 10.1164/rccm.200206-631OC
23. Andrade BB, Reis-Filho A, Barros AM, Souza-Neto SM, Nogueira LL, Fukutani KF, Camargo EP, Camargo LM, Barral A, Duarte A, Barral-Netto M. Towards a precise test for malaria diagnosis in the Brazilian Amazon: comparison among field microscopy, a rapid diagnostic test, nested PCR, and a computational expert system based on artificial neural networks. Malar J. 2010 ;9:117. DOI: 10.1186/1475-2875-9-117
24. Mehrtash A, Wells WM, Tempany CM, Abolmaesumi P, Kapur T. Confidence Calibration and Predictive Uncertainty Estimation for Deep Medical Image Segmentation. IEEE Trans Med Imaging. 2020 ;39(12):3868-3878. DOI: 10.1109/TMI.2020.3006437
25. Šimundić AM. Measures of diagnostic accuracy: basic definitions. EJIFCC. 2009;19(4):203–211.
26. Plewes K, Leopold SJ, Kingston HWF, Dondorp AM. Malaria: What's New in the Management of Malaria? Infect Dis Clin North Am. 2019 ;33(1):39-60. DOI: 10.1016/j.idc.2018.10.002
27. Jain V, Basak S, Bhandari S, Bharti PK, Thomas T, Singh MP, Singh N. Burden of complicated malaria in a densely forested Bastar region of Chhattisgarh State (Central India). PLoS One. 2014 ;9(12):e115266. DOI: 10.1371/journal.pone.0115266
28. Troselj-Vukić B, Vuksanović-Mikulicić S, Sladoje-Martinović B, Milotić I, Slavuljica I. Unrecognized malaria and its consequences--a case report of severe malaria with acute renal failure. Coll Antropol. 2013 ;37(2):611-3. PMID: 23941012
29. Tobón-Castaño A, Betancur JE. Severe malaria in pregnant women hospitalized between 2010 and 2014 in the Department of Antioquia (Colombia). Biomedica. 2019 ;39(2):354-369. DOI: 10.7705/biomedica.v39i3.4403
30. Aung NM, Kaung M, Kyi TT, Kyaw MP, Min M, Htet ZW, Anstey NM, Kyi MM, Hanson J. The Safety of a Conservative Fluid Replacement Strategy in Adults Hospitalised with Malaria. PLoS One. 2015 ;10(11):e0143062. DOI: 10.1371/journal.pone.0143062
31. Hendriksen IC, Mtove G, Pedro AJ, Gomes E, Silamut K, Lee SJ, Mwambuli A, Gesase S, Reyburn H, Day NP, White NJ, von Seidlein L, Dondorp AM. Evaluation of a PfHRP2 and a pLDH-based rapid diagnostic test for the diagnosis of severe malaria in 2 populations of African children. Clin Infect Dis. 2011 ;52(9):1100-7. DOI: 10.1093/cid/cir143