








## NARRATIVE REVIEW

# The effect of machine learning algorithms in the prediction, and diagnosis of meningitis: A systematic review

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## Abstract

**Background and Aims:** This systematic review aimed to evaluating the effectiveness of machine learning (ML) algorithms for the prediction and diagnosis of meningitis.

**Methods:** On November 12, 2022, a systematic review was carried out using a keyword search in the reliable scientific databases PubMed, EMBASE, Scopus, and Web of Science. The recommendations of Preferred Reporting for Systematic Reviews and Meta-Analyses (PRISMA) were adhered to. Studies conducted in English that employed ML to predict and identify meningitis were deemed to match the inclusion criteria. The eligibility requirements were used to independently review the titles and abstracts. The whole text was then obtained and independently reviewed in accordance with the eligibility requirements.

**Results:** After all the research matched the inclusion criteria, a total of 16 studies were added to the systematic review. Studies on the application of ML algorithms in the three categories of disease diagnosis ability (8.16) and disease prediction ability (8.16) (including cases related to identifying patients (50%), risk of death in patients (25%), the consequences of the disease in childhood (12.5%), and its etiology [12.5%]) were placed. Among the ML algorithms used in this study, logistic regression (LR) (4.16, 25%) and multiple logistic regression (MLR) (4.16, 25%) were the most used. All the included studies indicated improvements in the processes of diagnosis, prediction, and disease outbreak with the help of ML algorithms.

**Conclusion:** The results of the study showed that in all included studies, ML algorithms were an effective approach to facilitate diagnosis, predict consequences for risk classification, and improve resource utilization by predicting the volume of patients or services as well as discovering risk factors. The role of ML algorithms in improving disease diagnosis was more significant than disease prediction and prevalence. Meanwhile, the use of combined methods can optimize differential diagnoses and facilitate the decision-making process for healthcare providers.

## KEYWORDS

algorithms, artificial intelligence, machine learning, meningitis

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## 1 | INTRODUCTION

Meninges are the membranes that surround the brain and spinal cord. Meningitis is an inflammatory disease that affects these membranes. It can be brought on by bacteria, mycobacteria, viruses, fungus, parasites, autoimmune, neoplastic, or drug-related reactions, as well as by a variety of infectious agents.<sup>1</sup> Meningitis is mostly brought on by bacterial, viral, and fungal diseases, according to earlier research.<sup>2,3</sup> However, it's primarily brought on by bacterial and viral illnesses that spread to the cerebrospinal fluid from other regions of the body. Even in areas with plenty of resources, meningitis reduction represents a worldwide health issue, and a clinical emergency.<sup>4</sup> Asian meningococcal disease outbreaks have been widespread over the past 30 years, according to studies from the World Health Organization.<sup>5,6</sup> A common and pandemic illness, meningococcal infection poses a serious threat to the entire world. 2.51 million new cases of meningitis were anticipated to have occurred globally in 2019 due to all causes, with an incidence rate of 32.4 cases per 100,000 people worldwide.<sup>7</sup> It is critical to diagnose the condition as soon as possible, particularly to distinguish between the two primary types of meningitis—bacterial and viral—in particular.<sup>8</sup> Failure to provide appropriate antibiotic treatment for bacterial meningitis can lead to severe and permanent consequences, invasive disease, and even death.<sup>9</sup> Overtreating viral meningitis instances or prescribing antibiotics without a warrant can result in alterations to the human microbiome, antimicrobial resistance, higher healthcare expenditures, and a great deal of stress for the patients.<sup>10</sup> Furthermore, the most severe type of tuberculosis that results in meningeal inflammation is called tuberculous meningitis (TBM). Nonetheless, TBM diagnosis is quite difficult. The biochemical and pathological features of cerebrospinal fluid (CSF) and clinical manifestations of TBM are generally comparable to those of numerous other CNS infections, particularly partially treated purulent meningitis (PM) and noninfectious inflammatory diseases of the central nervous system (CNS).<sup>11,12</sup> Due to their comparable clinical symptoms, TBM and viral meningitis (VM) may be challenging to distinguish from one another. Because of their deadly nature, prompt, accurate diagnosis, and appropriate treatment are imperative. If the patient has acute bacterial meningitis, delaying the start of proper treatment increases the risk of morbidity and fatality.<sup>13</sup> In this case, polymerase chain reaction (PCR) analysis can be used as a diagnostic tool, although it is time-consuming because it requires a direct CSF culture. It should be highlighted that not every clinic, particularly in less developed nations, has the necessary tools and competencies to conduct PCR analysis in CSF.<sup>14</sup>

Consequently, to facilitate decision-making and reduce avoidable hospital admissions and extended antibiotic usage, highly accurate clinical decision support systems (CDSS) are required. The use of digital technologies is not a new issue in the management of diseases today.<sup>15–23</sup> Over the past six decades, artificial intelligence (AI) has been widely used in many areas of medical research and clinical practice.<sup>24,25</sup> These days, AI methods like artificial neural networks (ANN) are being used by healthcare organizations to enhance data analysis, clinical diagnosis, cancer and other illness prediction, image analysis and interpretation, medication creation, and patient care.

They consume less energy.<sup>26,27</sup> AI methods have been applied in the healthcare industry on a variety of levels, from creating diagnostic and prognostic models to forecasting the course of disease transmission.<sup>28–30</sup> A branch of artificial intelligence called machine learning (ML) is concerned with developing algorithms that let computers create complicated connection or pattern models from empirical data without the need for explicit programming.<sup>31</sup> ML is being studied and used in a variety of health informatics applications as a way to help clinical care providers improve the efficiency and quality of medical care.<sup>32–34</sup> ML can serve multiple purposes, including facilitating diagnosis in fields such as pathology<sup>35,36</sup> and radiology<sup>37</sup> to predict outcomes, risk stratification, and improving the use of resources by predicting the volume of patients or services.<sup>38</sup> Clinical infection research has seen a surge in the use of new supervised ML algorithms in recent years.<sup>39</sup> Large and complicated data sets can be analyzed by ML algorithms, which can then be used to spot patterns and trends that might be hard for people to see. In big data sets, algorithms can efficiently and accurately construct complicated nonlinear models that relate independent traits to their dependent counterparts.<sup>40</sup> Supervised and unsupervised learning approaches include the two main categories into which most ML algorithms fall.<sup>41</sup> The subsequent parts serve as an introduction to both. Techniques known as “supervised ML” include training a model using a variety of inputs (or features) that are connected to a predetermined result. When applied to fresh data, the algorithm will be able to predict outcomes when it has been properly trained. Models trained by supervised learning can produce discrete predictions (like positive or negative, benign, or cancerous) or continuous predictions (like a score ranging from 0 to 100). Unsupervised learning differs from supervised learning in that there is no predetermined result. Algorithms search for patterns in unsupervised learning without any user input. Therefore, unsupervised approaches are exploratory and are used to identify patterns or clusters that are not well defined inside data sets. Dimension reduction approaches<sup>42</sup> are another term for these techniques, which include principal component analysis, latent Dirichlet analysis, and t-Distributed Stochastic Neighbour Embedding (t-SNE). Numerous research have employed ML approaches to forecast infectious outbreaks in recent years, with encouraging outcomes. Previous research findings have demonstrated that ML algorithms may predict infectious illness onset and spread with an accuracy that is on par with or better than that of classic statistical methods.<sup>43</sup> A thorough summary of meningitis diagnosis methods must be given due to the multitude of new procedures that are being developed. To the best of our knowledge, this is the first review that looks at the body of research on meningitis diagnosis and prognosis. In addition, early and accurate diagnosis of meningitis plays an important role in preventing possible future outbreaks. Many previous works showed that ML approaches have been adopted by many researchers, but there has been no review to examine them in depth. Therefore, the purpose of this systematic review was to investigate ML algorithms for predicting and diagnosing different types of meningitis diseases.

## 2 | METHODS

### 2.1 | Study design

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 criteria<sup>44,45</sup> were followed in conducting this systematic review to report the evidence from the studies that were included in it. On November 12, 2022, a search of the PubMed, Embase, Scopus, and Web of Science databases was done for literature. The databases were searched using MeSH and Emtree terms and phrases.

### 2.2 | Eligibility criteria

Studies that satisfied the following inclusion criteria were added to the systematic review: (1) The inclusion criteria for this study were English-language research that employed ML to predict and diagnose meningitis illnesses. However, the following exclusion criteria applied: (1) the study's full text was not available in English; (2) publications other than journal articles (books, reviews, and letters); and (3) there was no connection between the study's goal and the title, abstract, or full text of the articles.

### 2.3 | Data extraction and synthesis

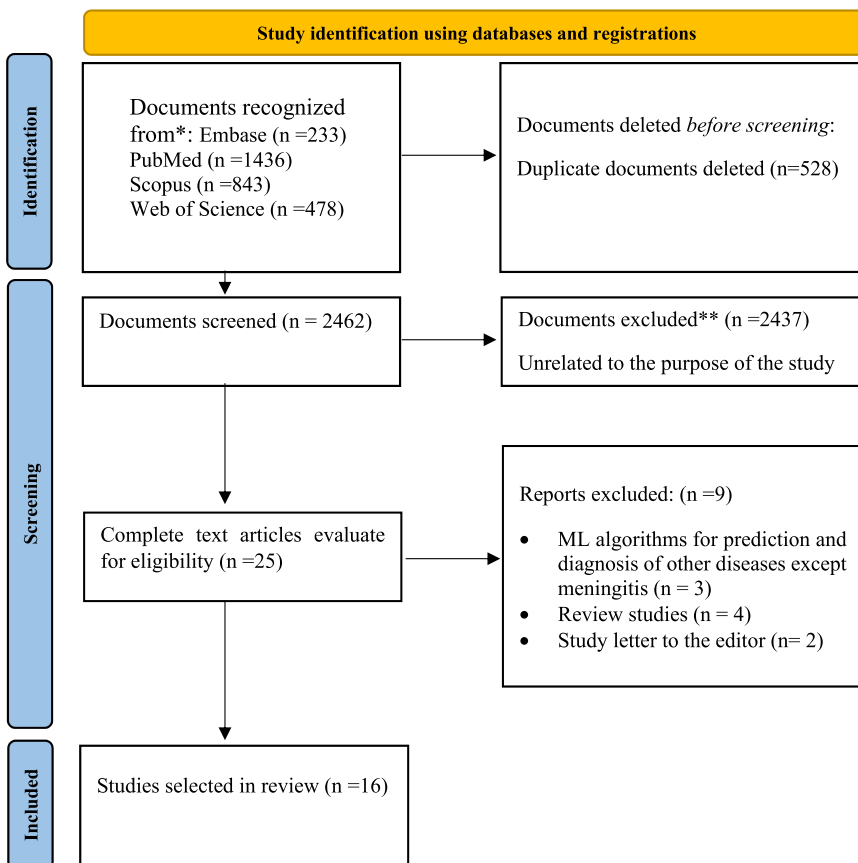
For this review, every article from the literature search was obtained, and duplicate articles were excluded. Titles and abstracts were

independently screened in accordance with qualifying requirements. There were no articles in the review that didn't fit the requirements to be included. After that, the entire text was obtained and assessed by two distinct researchers in compliance with the qualifying requirements. Disagreements were resolved by discussions amongst researchers. The same checklist was utilized for data extraction. The data elements on this checklist were the study's title, publication year, nation, number of participants, kind of ML algorithms employed, effectiveness and performance of ML algorithms, type of meningitis the study was targeting, study objectives, and major conclusions.

## 3 | RESULTS

### 3.1 | Study selection

Figure 1 illustrates the procedure for finding and choosing research based on the PRISMA chart. Two thousand nine hundred and ninety relevant documents in all were chosen for examination. Two thousand four hundred and sixty-two papers were collected after the articles were reviewed and 528 duplicate studies were removed. The publications were then screened using their titles and abstracts. Upon completion of the review, 2437 articles that had no bearing on the goal of the investigation were eliminated. Following the full text evaluation of 25 publications, 9 of the original articles were eliminated, leaving 16 original articles for the study. Follow the results of search strategy in Table 1.



**FIGURE 1** Flowchart of screening and selection of studies.

### 3.2 | Study characteristics

Tables 2 and 3 provide information on the features of every study that was included. Out of the 16 studies that were included, 5 studies (31%) in China,<sup>46–50</sup> 3 studies in Greece (19%),<sup>51–53</sup> 2 studies in the Republic of Korea (12%),<sup>54,55</sup> and other studies in Kazakhstan (6%),<sup>56</sup> Iran (6%),<sup>57</sup> Russia (6%),<sup>58</sup> Ireland (6%),<sup>59</sup> Bosnia and Herzegovina (6%),<sup>60</sup> and Morocco (%)<sup>61</sup> have been done. Overall, the included studies included 39,462 participants.

The ML algorithms used in the studies include logistic regression (LR) (25%),<sup>46,48,51,54</sup> multiple logistic regression (MLR) (25%),<sup>50,52,53,61</sup> support vector machine (SVM) (19%),<sup>48,54,56</sup> artificial neural network (ANN) (19%),<sup>47,54,60</sup> random forest (RF) (19%),<sup>52,54,56</sup> decision tree (DT) (12%),<sup>57,58</sup> naive-Bayes (NB) (12%),<sup>52,54</sup> fast-and-frugal trees (FFTs) algorithm (6%),<sup>56</sup> and unsupervised ML approach (6%).<sup>59</sup>

The target meningitis diseases in the studies included bacterial meningitis (BM) (37%)<sup>51–53,56,57,61</sup> or enteroviral meningitis (EVM) (6%),<sup>56</sup> tuberculous meningitis (TBM) (25%),<sup>48,54,55,61</sup> viral meningitis (VM) (19%),<sup>52,54,55</sup> Neisseria meningitidis (6%),<sup>59</sup> lumbar drainage-related meningitis (LDRM) (6%),<sup>47</sup> healthcare-associated ventriculitis and meningitis (HAVM) (6%),<sup>58</sup> cryptococcal meningitis (CM) (6%),<sup>50</sup> PM (6%),<sup>46</sup> and pediatric purulent meningitis (PPM) (6%).<sup>49</sup>

### 3.3 | The effects of using ML algorithms in the diagnosis of meningitis

According to Table 3, half of the included studies examined the impact of using ML algorithms on the diagnosis of meningitis diseases.<sup>48,49,52,54–56,60,61</sup>

In their study, Eho and colleagues chose a feedforward ANN to develop an expert system. Two ML algorithms were used to develop this ANN. A Levenberg–Marquardt training algorithm for pattern recognition and a particle swarm optimization (PSO) algorithm he reported that the constructed artificial neural network (ANN) demonstrated the ability to accurately identify and distribute samples from the sick people's class with a sensitivity of 13.98%, and the class of healthy people's samples could be correctly identified and distributed with a specificity of 85.0%. The ANN's total accuracy was 96.67%.<sup>60</sup> In his research, Mentis also employed three ML algorithms (MLR, RF, and NB) to distinguish between bacterial and viral meningitis. ML algorithm performance was assessed using the cross-validation approach. For VM and 78% for BM, the ideal meningitis-type prediction was over 95%.<sup>52</sup> In a different study, Jeong employed ML modules to differentiate between TBM and VM. The ANN receiver operating characteristics for matrix completion have the largest area under the curve (AUC) of any ML method (0.85; 95% CI 0.79–0.89). In comparison to all residents (AUC range 0.67–0.72,  $p = 0.001$ ) and infectious disease experts (AUC 0.76;  $p = 0.03$ ), the ANN model's AUC was significantly higher.<sup>54</sup> Ma and colleagues also noted in their study that radiomics, as a quantitative analysis method, can use automatic data description algorithms to transform region of interest (ROI) image data into high-resolution and

discoverable feature space data, enabling a more thorough review and utilization of the data. He concluded that the T2-weighted radiomic signature (T2WI) developed using the SVM classifier shows special diagnostic significance for TBM that may not be detected by an unaided eye in conventional MR images. Therefore, the automated segmentation of base reservoirs and the developed radiomic signature may provide complementary data to help diagnose TBM in a fully automated manner before the appearance of lesions with visible features.<sup>48</sup> Also, Babenk and his colleagues showed the ability to determine procalcitonin and C-reactive protein (CRP) with cut-off values for distinguishing between BM and EVM in children using the fast and cost-effective decision tree (FFTree) approach. Thus, if procalcitonin  $>0.16$  ng/mL defines BM and if CRP  $>31.2$  mg/L defines EVM, this study showed 100% sensitivity, 96% specificity, and 98% accuracy in differentiating all BM cases.<sup>56</sup> The Dendane study used a classification and regression tree (CART) and machine learning (MLR) to model the independent predictive aspects of TBM to generate a diagnostic rule. The regression tree's and the classification's sensitivity were 87% and 88%, respectively, for scores lower than 7. The corresponding specificities were 96% and 95%. The study's findings indicated that the clinical and laboratory characteristics found here could aid a doctor in making an exploratory diagnosis of TBM.<sup>61</sup> In addition, Sang-Ah Lee devised a new scoring system using the results of MLR analysis and recent research data. These points were given to each factor by considering the odds ratio scores and achieving the highest receiver operating characteristic (ROC) value for predicting TBM; he concluded that this new diagnostic system can be used for quick and easy differential diagnosis.<sup>55</sup> Also, in a study aimed at analyzing the diagnostic value of magnetic resonance imaging (MRI) based on ICA in children with purulent meningitis (PM), Dafei Wei and colleagues found that it is more accurate and clearer than traditional image processing and can provide a more accurate auxiliary basis for detecting the details of the lesion. Additionally, it demonstrated increased clinical utility in the formulation of a comprehensive PPM diagnosis and treatment strategy.<sup>49</sup>

### 3.4 | Effects of using ML algorithms in predicting meningitis disease

Of the 16 included studies, 8 studies of ML algorithms regarding the ability to predict disease (including cases related to the discovery of risk factors and identification of high-risk patients,<sup>46,47,57–59</sup> the risk of death in patients,<sup>50</sup> the consequences of disease in childhood,<sup>53</sup> and etiology<sup>51</sup>) were used. In a study conducted by Cheng and colleagues, the aim was to create a predictive model for purulent meningitis in preterm infants to help doctors develop new diagnostic and treatment strategies. The prediction model was developed using LR and regression analyses of the least absolute shrinkage and selection operator (LASSO). Premature babies' risk of meningitis might be predicted by his prediction model.<sup>46</sup> Wang and colleagues study also selected three supervised ML algorithms, SVM, RF, and

**TABLE 1** Outcomes of search strategies for every database.

#	PubMed database search approach	Results
1	"Meningitis"[MeSH Terms]	58,233
2	"Meningitis"[Title/Abstract] OR "Meningitides"[Title/Abstract] OR "Pachymeningitis"[Title/Abstract] OR "Pachymeningitides"[Title/Abstract]	60,083
3	"Machine learning"[MeSH Terms]	50,896
4	"Machine learning"[Title/Abstract] OR "deep learning"[Title/Abstract] OR ((supervised[Title/Abstract] OR unsupervised[Title/Abstract]) AND learning[Title/Abstract]) OR "feature selection"[Title/Abstract] OR ("support vector machine"[Title/Abstract] OR "SVM"[Title/Abstract]) OR ("classification method"[Title/Abstract] OR "pattern classification"[Title/Abstract] OR "classification pattern"[Title/Abstract] OR "classification algorithm"[Title/Abstract]) OR ((clustering[Title/Abstract] OR clusters[Title/Abstract]) AND (analysis[Title/Abstract] OR algorithm[Title/Abstract])) OR ("multiple kernel learning"[Title/Abstract] OR "MKL"[Title/Abstract]) OR ("relevance vector machine"[Title/Abstract] OR "relevance vector machines"[Title/Abstract] OR "RVM"[Title/Abstract]) OR "neural network"[Title/Abstract] OR ("iterative learning"[Title/Abstract] OR "learning classifier"[Title/Abstract] OR "learning classifier"[Title/Abstract]) OR ((Bayes[Title/Abstract] AND Bayesian[Title/Abstract]) OR (model[Title/Abstract] OR algorithm[Title/Abstract] OR network[Title/Abstract] OR classification[Title/Abstract] factor))	1,133,855
5	1 OR 2	81,844
6	3 OR 4	1,138,633
7	5 AND 6	1436
#	Embase database search approach	Results
1	"Meningitis":ti,ab,kw OR "meningitides":ti,ab,kw OR "pachymeningitis":ti,ab,kw OR "pachymeningitides":ti,ab,kw	74,564
2	"Machine learning":ti,ab,kw OR "deep learning":ti,ab,kw OR ((supervised:ti,ab,kw OR unsupervised:ti,ab,kw) AND learning:ti,ab,kw) OR "feature selection":ti,ab,kw OR ("support vector machine":ti,ab,kw OR "SVM":ti,ab,kw) OR ("classification method":ti,ab,kw OR "pattern classification":ti,ab,kw OR "classification pattern":ti,ab,kw OR "classification algorithm:ti,ab,kw") OR ((clustering:ti,ab,kw OR clusters:ti,ab,kw) AND (analysis:ti,ab,kw OR algorithm:ti,ab,kw)) OR ("multiple kernel learning":ti,ab,kw OR "MKL":ti,ab,kw) OR ("relevance vector machine":ti,ab,kw OR "relevance vector machines":ti,ab,kw OR "RVM":ti,ab,kw) OR "neural network":ti,ab,kw OR ("iterative learning":ti,ab,kw OR "learning classifier":ti,ab,kw) OR ((Bayes:ti,ab,kw OR Bayesian:ti,ab,kw) AND (model:ti,ab,kw OR algorithm:ti,ab,kw OR network:ti,ab,kw OR classification:ti,ab,kw OR factor:ti,ab,kw))	367,681
3	1 AND 2	233
#	Scopus database search approach	Results
1	TITLE-ABS-KEY ("Meningitis") OR ("Meningitides") OR TITLE-ABS-KEY ("Pachymeningitis") OR TITLE-ABS-KEY ("Pachymeningitides")	107,785
2	TITLE-ABS-KEY ("machine learning") OR TITLE-ABS-KEY ("deep learning") OR TITLE-ABS-KEY ((supervised OR unsupervised) AND learning) OR TITLE-ABS-KEY ("feature selection") OR TITLE-ABS-KEY ("support vector machine" OR "SVM") OR TITLE-ABS-KEY ("classification method" OR "pattern classification" OR "classification pattern" OR "classification algorithm") OR TITLE-ABS-KEY ((clustering OR clusters) AND (analysis OR algorithm)) OR TITLE-ABS-KEY ("multiple kernel learning" OR "MKL") OR TITLE-ABS-KEY ("relevance vector machine" OR "relevance vector machines" OR "RVM") OR TITLE-ABS-KEY ("neural network") OR TITLE-ABS-KEY ("iterative learning" OR "learning classifier") OR TITLE-ABS-KEY ((bayes OR bayesian) AND (model OR algorithm OR network OR classification OR factor))	2,235,412
3	1 AND 2	843
#	Web of science database search approach	Results
1	TS=("Meningitis") OR TS=("Meningitides") OR TS=("Pachymeningitis") OR TS=("Pachymeningitides")	52,150
2	TS=("machine learning") OR TS=("deep learning") OR TS=((supervised or unsupervised) and learning) OR TS=("feature selection") OR TS=("support vector machine" or "SVM") OR TS=("classification method" or "pattern classification" or "classification pattern" or "classification algorithm") OR TS=((clustering or clusters) and (analysis or algorithm)) OR TS=("multiple kernel learning" or "MKL") OR TS=("relevance vector machine" or "relevancevector machines" or "RVM") OR TS=("neural network") OR TS= ("iterative learning" or "learning classifier") OR TS=((Bayes or Bayesian) and (model or algorithm or network or classification or factor))	1,068,270
3	1 AND 2	478

TABLE 2 Summary of specifications of included studies.

References (Country)	Target meningitis disease	Data set size	Algorithms and/or techniques	Performance of ML algorithms
Cheng et al. <sup>46</sup> (China)	PM	168	LR	Brier score was 0.17, the calibration slope was 0.966, and the concordance index was 0.82018
Wang et al. <sup>47</sup> (China)	LDRM	273	ANN, RF, SVM	Training set: SVM: Sensitivity (0.880), specificity (0.665), accuracy (0.693) RF: Sensitivity (0.920), specificity (0.689), accuracy (0.719) ANN: Sensitivity (0.920), specificity (0.790), accuracy (0.807) Testing set: SVM: Sensitivity (0.750), specificity (0.783), accuracy (0.679) RF: Sensitivity (0.833), specificity (0.826), accuracy (0.691) ANN: Sensitivity (0.500), specificity (0.696), accuracy (0.667)
Ma et al. <sup>48</sup> (China)	TBM	371	(SVM)/(LR)	AUC 0.751
Wei et al. <sup>49</sup> (China)	PPM	235	ICA	Accuracy rate (95.5%), sensitivity (90.5%), specificity (85.5%)
Karanika et al. <sup>51</sup> (Greece)	BM	2477	Model for logistic regression with conditions	The following diagnostic variables have positive predictive values (PPVs) for the identification of meningitis-causing pathogens: Headache (73.8), vomiting (64.2), meningeal symptoms (63.7), hemorrhagic rash (93.4), seizures (42.3), and positive gram stain (57.5)
Šeho et al. <sup>60</sup> (Herzegovina)	Meningitis	1000 (200 healthy, 800 patients)	ANN	Accuracy (96.69%), sensitivity (98.13%), specificity (85.0%)
Zhao et al. <sup>50</sup> (China)	CM	555	MLR	Sensitivity (74.1%), specificity (83.8%), PPV (44.8%), negative predictive value (NPV) (94.8%)
Mentis et al. <sup>52</sup> (Greece)	BM\VM	4339	NB, RF, MLR	Meningitis detected: NB: Viral meningitis (96%), bacterial meningitis (83%) RF: Viral meningitis (89%), bacterial meningitis (88%) MLR: Viral meningitis (94%), bacterial meningitis (68%)
Jeong et al. <sup>54</sup> (Korea)	TBM	203	ML algorithms ANN, SVM, NB, LR, RF	ANN: IterativeImputer: Sensitivity (76.7), specificity (92.3), accuracy (87.7), SoftImputer: Sensitivity (68.3), specificity (86.0), accuracy (80.8) RF: IterativeImputer: Sensitivity (70.0), specificity (92.3), accuracy (85.7), SoftImputer: Sensitivity (63.3), specificity (93.7), accuracy (84.7) NB: IterativeImputer: Sensitivity (60.0), specificity (92.3), accuracy (82.8), SoftImputer: sensitivity (80.0), specificity (83.2), accuracy (82.3) LR: IterativeImputer: Sensitivity (73.3), specificity (93.7), accuracy (87.7), SoftImputer: Sensitivity (71.7), specificity (89.5), accuracy (84.2) SVM: IterativeImputer: Sensitivity (56.7), specificity (95.8), accuracy (84.2), SoftImputer: Sensitivity (75.0), specificity (88.1), accuracy (84.2)

TABLE 2 (Continued)

References (Country)	Target meningitis disease	Data set size	Algorithms and/or techniques	Performance of ML algorithms
Babenko et al. <sup>56</sup> (Kazakhstan)	BM\EYM	269	FFTs	Sensitivity (100%), specificity (96%), accuracy (98%)
Drew et al. <sup>59</sup> (Ireland)	Neisseria meningitidis	16258	ML method using unsupervised	The rate of MenW colonization was found in young Irish people (n = 171/1260, 13.5%) who had received the meningococcal C vaccine and in non-Irish adults (n = 5/81, 6%, $\chi^2 = 3.6$ , p = 0.05) who had received the MenC vaccine but were 20 years of age or older but were not Irish
Lee et al. <sup>55</sup> (Korea)	TBM, VM	98: TBM, <sup>47</sup> VM <sup>52</sup>	MLR and univariate analysis	The AUC (sensitivity, 80.4%; specificity, 89.4%; positive predictive value, 89.1; negative predictive value, 80.8%) was 0.901 (CI, 0.838–0.863; p < 0.001).
Mirkhani et al. <sup>57</sup> (Iran)	BM	7945	DT	Accuracy (78%), sensitivity (87%), specificity (70%), area under the curve (AUC) (84%)
Savin et al. <sup>58</sup> (Russia)	HAVM	2286	ML techniques based on trees	The area under the receiver-operating characteristic curve (ROC-AUC) is 0.75, and the F-1 score is 0.29
Dendane et al. <sup>61</sup> (Morocco)	BM\TBM	508	MLR	The specificity was 96% and 95%, respectively, while the sensitivity for CART was 87% and 88% for a score greater than 7
Vasilopoulou et al. <sup>53</sup> (Greece)	BM	2477	MLR	Multivariate investigation of the following predictive variables for pediatric bacterial meningitis sequelae: p Value (<0.001), hemorrhagic rash OR: (0.21), 95% CI: (0.06–0.69), p Value (0.011), seizures OR: (5.36), 95% CI: (2.63–10.90), p Value (0.004), CSF protein >100 mg/dL OR: (2.97), 95% CI: (1.06–8.29), p Value (0.038), positive blood culture OR: (2.66), 95% CI: (1.24–5.72), p Value (0.012)

Abbreviations: BM, bacterial meningitis; HAVM, healthcare-associated ventriculitis and meningitis; MLR, multiple logistic regression.

**TABLE 3** Summary of purpose and results of included studies.

References (Country)	Purpose of study	The result of the study
Cheng et al. <sup>46</sup> (China)	creating a predictive model for the early PM to aid physicians in creating fresh diagnostic and treatment approaches	The risk of PM in premature newborns can be predicted using this predictive model. This prediction model may be used as a guide to establish whether a lumbar puncture is necessary and whether antibiotics need to be given as soon as possible.
Wang et al. <sup>47</sup> (China)	It was to use supervised ML techniques to build prediction models	The RF and SVM models performed satisfactorily. Site leakage: The most reliable and significant predictor is RF. Using predictions based on the ML algorithm in addition to their current methods for detecting high-risk patients may prove useful for future healthcare personnel.
Ma et al. <sup>22</sup> (China)	The creation and assessment of a radiomic signature based on magnetic resonance imaging (MRI) using a multicenter data set to detect hidden basal reservoir changes in TBM patients	Combining deep learning segmentation with T2WI-based radiomic signatures can produce a fully automated, noninvasive technique to identify subtle alterations in basal reservoirs, which may aid in the diagnosis of TBM
Wei et al. <sup>49</sup> (China)	Investigating the diagnostic usefulness of MRI based on the ICA in children with purulent meningitis	Compared to typical image processing, the result of using ICA to display children's purulent meningitis MRI pictures is more accurate and clear, and it can serve as a more accurate supplemental basis for diagnosing the specifics of the condition. For complex PPM, developing a diagnostic and treatment strategy has greater clinical significance.
Karanika et al. <sup>51</sup> (Greece)	A method to predict the precise bacterial etiology of childhood bacterial meningitis is provided by the analysis of clinical symptoms and swift laboratory data	It appears that the clinical management and targeted treatment of BM may benefit from the use of clinical and laboratory predictors to assess the bacterial pathogen responsible for the disease rather than just predicting the mortality outcome
Šeho et al. <sup>60</sup> (Herzegovina)	Using ANN to speed up meningitis diagnosis and minimize intrusive sample techniques	Meningitis can be accurately diagnosed using artificial neural networks, which can also be used to choose the best course of therapy and minimize the need for minor incisions
Zhao et al. <sup>50</sup> (China)	A novel scoring model has been developed and verified to forecast mortality risk in patients with CM who are HIV-positive	The first model for predicting outcomes in HIV/CM patients. The results of HIV/CM patients might be predicted using this approach.
Mentis et al. <sup>52</sup> (Greece)	Examination of three ML algorithms for bacterial and viral meningitis differential diagnosis	Whether a patient has viral or bacterial meningitis can be accurately diagnosed using machine learning (ML). The model that did the best job in forecasting bacterial meningitis was RF, whereas NB did the worst. The MLR model outperformed the other two models in predicting the percentage of viral meningitis in all age categories. As a result, by merging MLR and RF models, differential diagnosis can be strengthened.
Jeong et al. <sup>54</sup> (Korea)	Using ML methods, such as deep learning models, to differentiate between viral and tuberculous meningitis	The ability to discriminate between TBM and VM appears to be facilitated by ML approaches. Additionally, compared to a nonexpert doctor, the ANN model appears to perform better in terms of diagnosis.
Babenko et al. <sup>56</sup> (Kazakhstan)	Children's bacterial meningitis can be distinguished from viral meningitis by looking at the ML	The FFTree approach exhibited procalcitonin and CRP determination with cut-off levels to distinguish between bacterial and EVM in youngsters
Drew et al. <sup>59</sup> (Ireland)	Using ML, examine student risk variables for the meningococcal pharyngeal vector	Meningococcal vector risk factors can be found using unsupervised ML
Lee et al. <sup>55</sup> (Korea)	creating a grading system using tree analysis to address issues like the difficulty in identifying TBM and differentiating it from VM	The following situations call for the employment of this system:-VM and TBM differential diagnosis-rapid and simple TBM diagnosis
Mirkhani et al. <sup>57</sup> (Iran)	To stop bacterial meningitis epidemics in Iran, a predictive model is being developed to speed up the detection of individuals with acute bacterial and nonbacterial meningitis	This model can aid epidemiologists and health policymakers in locating bacterial meningitis epidemics and guiding their decisions on the dynamics of infection



TABLE 3 (Continued)

References (Country)	Purpose of study	The result of the study
Savin et al. <sup>58</sup> (Russia)	Employing tree-based ML techniques, to quantify the prevalence of HAVM in the neuro-ICU and to pinpoint HAVM risk variables	Because it makes it possible to identify nonlinear interactions between factors, tree-based ML is a useful method for researching risk factors
Dendane et al. <sup>61</sup> (Morocco)	Moroccan researchers have created a straightforward diagnostic method based on clinical and laboratory data to help identify TBM in adult patients	The clinical and laboratory indicators found in this study appear to be useful for the medical professional in making an empirical diagnosis of TBM and can be applied in situations where microbiological diagnostic support is not as robust
Vasilopoulou et al. <sup>53</sup> (Greece)	Using a multivariate analysis method, the objective is to describe the clinical and laboratory features of a sizable group of children with BM and to determine independent prognostic markers for outcomes	When it comes to choosing patients for more rigorous treatment and identifying potential candidates for novel treatment approaches, a combination of characteristics predicting outcomes in childhood BM may be helpful

Abbreviations: BM, bacterial meningitis; HAVM, healthcare-associated ventriculitis and meningitis; TBM, tuberculous meningitis.

ANN, to build binary LDRM prediction models following a four-step method of meta-parameter setting, model training, model evaluation, and model validation. The outcomes demonstrated the predictive ability of the RF and SVM models, with the RF model performing best for detecting high-risk patients.<sup>47</sup> Drew also stated in a study that unsupervised ML provides a useful technique for detecting meningococcal vector risk factors. Additionally, it can be a helpful tool for sifting through big data sets to find groups of people who share similar traits and could enhance comprehension of patterns found in data sets.<sup>59</sup> Savin conducted an observational cohort study in Russia that included high-risk neurological patients in the ICU. To determine the factors that contribute to the development of healthcare-associated ventriculitis and meningitis (HAVM), he used regression, ML, and relative risk analysis. He demonstrated that tree-based ML is a useful method for examining risk factors because it makes it possible to identify nonlinear interactions between factors.<sup>46</sup> According to Zhao, a scoring model that was developed using six easy-to-understand, practical, and accurate variables is appropriate for screening high-risk AIDS patients who have either HIV/CM or cryptococcal meningitis. It also serves as a helpful tool for clinicians to assess the prognosis of hospitalized HIV/CM patients. Due to the fact that the new scoring model could reliably identify AIDS patients at high risk of dying in hospital if they contracted HIV/CM cryptococcal meningitis (area under the curve 0.876;  $p < 0.001$ ).<sup>37</sup>

## 4 | DISCUSSION

### 4.1 | Principal findings

Meningitis is a serious infectious disease that can have a negative impact on society as a whole. This illness is linked to a high death rate and severe neurological side effects. As a result, while AI has been able to play a significant role in meningitis diagnosis, its fast diagnosis is extremely critical. At many stages, from forecasting the course of disease propagation to the construction of diagnostic and prognostic

models, AI approaches, have been taken into consideration.<sup>62</sup> In this environment, ML systems that integrate and interpret vast volumes of complicated data are gaining popularity. Since ML algorithms may be used to predict and diagnose the inflammatory condition of meningitis, the goal of this systematic review was to gather the best available research information in this area.

The evidence from this review shows that in all studies, ML techniques have been an effective and positive approach to facilitating disease diagnosis and prediction. According to the findings of our study, in eight cases of incoming studies, ML algorithms were used to diagnose the disease, and all studies indicated the high ability of ML algorithms to diagnose meningitis diseases.<sup>48,49,52,54–56,60,61</sup> So even in Jeong and colleagues study, it was stated that the ANN model can have better diagnostic performance than a nonspecialist doctor. The foundation of this approach was the validation of variables such demographics and standard and clinical diagnostic tests, which had the best power and sensitivity (100%) for separating BM from EVM. The FFTree model determined two parameters of procalcitonin and CRP in blood, which assisted the detection of BM from EVM.<sup>56</sup> Three ML algorithms (MLR, RF, and NB) were employed in a different study, and the results showed that using these algorithms in a multivariate manner as opposed to a univariate ROC curve treatment improved the accuracy in the differential diagnosis of meningitis. We applied these three algorithms to two age groups: younger than 14 and older than 14. When CSF neutrophils, CSF lymphocytes, NLR, albumin, glucose, gender, and CRP were used, MLR and RF often performed the best.<sup>52</sup> Another study of T2WI-based radiomic signatures developed using an SVM classifier showed a special diagnostic significance for TBM that could not be detected by an unaided eye in conventional MR images. Therefore, the automated segmentation of base reservoirs and the developed radiomic signature can provide complementary data to help diagnose TBM in a fully automated manner before the appearance of lesions with visible features.<sup>48</sup> In addition, another study in Morocco reported that using a simple diagnostic algorithm based on clinical and laboratory findings can help the physician in the experimental

diagnosis of TBM.<sup>61</sup> In this regard, the study of Jeong and colleagues reported that ML techniques have played a role in differentiating between TBM and VM.<sup>54</sup>

Among the ML algorithms used in the included studies, LR (25%)<sup>46,48,51,54</sup> and MLR (25%)<sup>50,52,53,61</sup> are the most used. However, among all the algorithms used, FFTs with accuracy (98%)<sup>56</sup> and ANN algorithms with accuracy (96.69%)<sup>54</sup> were more effective for diagnosis and differentiation in the type of meningitis, selection, and appropriate treatment. On the other hand, the NB algorithm with accuracy (83.5%) had the least effect in diagnosing the type of meningitis disease.<sup>54</sup> However, in the study of Jeong and colleagues, they found that the combination of RF and MLR algorithms is better than using one algorithm alone to optimize the diagnosis of meningitis.<sup>54</sup> In this regard, Yang and colleagues also found that the combination of ML algorithms and modern techniques such as CDSS has significantly facilitated clinical diagnosis and treatment. One of the challenges of traditional data analysis techniques is the rapid increase in multidimensional clinical data and the difficulty of integrating clinical information. Because clinical information from different fields is heterogeneous in terms of structure and meaning,<sup>63</sup> the combination and integration of ML algorithms seemed to be more effective for better diagnosis of diseases and differentiation between their types.

On the other hand, in eight cases of input studies from ML algorithms regarding the ability to predict meningitis disease (including cases related to the discovery of risk factors and identification of high-risk patients,<sup>46,47,57-59</sup> the risk of death in patients,<sup>50</sup> consequences of disease in childhood,<sup>53</sup> and etiology,<sup>51</sup> in this context, Zhao and colleagues reported that the use of a predictive model can assist clinicians in determining whether lumbar puncture and antibiotic use are appropriate in preterm infants with high-risk factors. This, in turn, lowers the incidence of unwarranted treatments and sequelae and decreases the chance of missed meningitis diagnoses.<sup>50</sup> In a different study, scientists presented and simulated a model that predicts meningococcal meningitis and its varieties using an AI technique known as the Bayesian Belief Network. This model was constructed with information gathered from the meningitis medical archive and a Bayesian server. The model demonstrated a sensitivity of 97.12% and a prediction accuracy of 99.99% for meningococcal meningitis.<sup>64</sup> Santangelo and colleagues concluded that it is feasible to anticipate the emergence and progress of some infectious illnesses in this respect after conducting a comprehensive study with the goal of demonstrating whether it is possible to predict the spread of infectious diseases early using ML. Additionally, they said that correct and respectable outcomes may be obtained by integrating a variety of methods and ML algorithms.<sup>43</sup> Therefore, it would seem that, with additional development, the ML algorithm-based prediction model might complement the present approaches for identifying high-risk patients and grow to be a valuable tool for clinical staff in the future.

Peiffer-Smadja and colleagues study, which sought to educate physicians on the application of ML in infectious illness diagnosis, classification, outcome prediction, and management, is consistent

with our findings. They reported that comprehensive patient data from healthcare settings with varying socioeconomic backgrounds, such as primary care and low- and middle-income countries, may enhance ML-CDSS capacity to make recommendations tailored to different clinical situations. The examination of ML-CDSS has revealed several current gaps that need to be filled to determine the potential benefits of these tools for patients and doctors.<sup>65</sup>

We identified a confounding variable (other surgeries) in our included studies. The majority of these surgeries were tracheotomies or combined trauma treatments, which may indicate more serious starting circumstances in HAVM patients.<sup>58</sup> In this regard, Bådholm and colleagues, in their study, aimed to evaluate the effect of the consistency of the number of cells in the cerebrospinal fluid sampled from external ventricular drains, with and without patient repositioning, on infection diagnostics. They concluded that in serially taken samples, there was a considerable variation in the counts of cerebral spinal fluid cells, and repositioning also significantly affected the change in mixed effect models. Diagnostics for external ventricular drain-related infections were complicated by this shift, which was seen to be bigger at higher numbers and to occur in both directions.<sup>66</sup> A recent systematic analysis by Peetluk and colleagues sought to critically assess prediction models created to forecast the outcomes of tuberculosis treatment among individuals with pulmonary tuberculosis. They found that while most ML models performed well (*c*-statistic/AUROC >0.7), all of them were shown to have a considerable risk of bias due to weak methodologic techniques, missing data exclusion, insufficient reporting, inadequate validation, and a lack of calibration evaluation. Model comparisons were hampered by population heterogeneities, such as differing predictor and outcome definitions and inclusion/exclusion policies for people with multidrug resistant and younger ages. Hence, there may be other confounding variables in this matter. Therefore, it is suggested that future studies investigate other confounding variables in the use of ML algorithms to diagnose and predict meningitis.<sup>67</sup>

The majority of the included studies (56%) were carried out in low- and middle-income countries (LMICs), according to the results of our systematic review.<sup>46-48,50,56,57,60,61</sup> This can become a strong point for improving primary care services and thus improving their economies, especially due to the unequal distribution of resources and health care provision in LMICs. It is also critical to identify the agents of disease spread to implement control and prevention measures, as the identification of these factors can yield forecasts that help policymakers make informed decisions about vaccination purchases, public awareness campaigns, and health professional training programs.

## 4.2 | Strengths and limitations

This study has several strengths. First, this study followed recommendations for systematic review methods.<sup>32,33</sup> Second, we reviewed all studies that used different types of ML algorithms to diagnose and predict different types of meningitis. Third, the

country filter was not applied to the literature search. Therefore, studies from all LMICs and high-income countries (HICs) were eligible for this review.

It is important to talk about any potential methodological restrictions placed on this systematic study. First, our review exclusively included English-language studies. As a result, this evaluation did not consider relevant publications written in other languages. Second, studies with various demographics and kinds of meningitis patients (i.e., with various medical problems and age groups) were included in this review. As a result, there can be a number of discrepancies in the findings of each research study. For example, an algorithm may be more effective in detecting one type of meningitis than other types of meningitis. Therefore, it was unable to properly explain the conclusive results and carry out a meta-analytical study due to the variety of background elements, including the type of algorithm, the type of meningitis disease, and the ensuing performance reports. Additionally, these restrictions prevented us from doing a meta-analysis.

## 5 | CONCLUSION

The study's findings demonstrated that, across all included investigations, ML algorithms proved to be a useful method for streamlining diagnosis, forecasting outcomes for risk categorization, and enhancing resource efficiency by anticipating patient or service volume and identifying risk factors. The role of ML algorithms in improving disease diagnosis was more significant than disease prediction and prevalence. Meanwhile, the use of combined methods can optimize differential diagnoses and facilitate the decision-making process for healthcare providers.

### AUTHOR CONTRIBUTIONS

**Kosar Ghaddarpouri:** Conceptualization; data curation; investigation; writing—original draft. **Maryam Ghaddarpouri:** Data curation; formal analysis; investigation. **Atefeh Sadat Mousavi:** Data curation; formal analysis; investigation. **Seyyedeh Fatemeh Mousavi Baigi:** Formal analysis; investigation; methodology; writing—original draft. **Masoumeh Rezaei Sarsari:** Data curation; formal analysis; investigation. **Fatemeh Dahmardeh Kemmak:** Data curation; formal analysis; investigation. **Mohammad Reza Mazaheri Habibi:** Conceptualization; investigation; methodology; project administration; supervision; writing—review & editing.

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### CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

### DATA AVAILABILITY STATEMENT

The article and its Supporting Information contain the data sets that this work uses to support its conclusions.

### TRANSPARENCY STATEMENT

The lead author Mohammad Reza Mazaheri Habibi affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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