

# A Survey on Using Immunopathogenesis to Predict Nipah Virus using Machine Learning Techniques

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**Abstract**—Viral disease can occur through direct contact with immunopathogenesis. The consecutive reappearance of the Nipah virus is one of the human-zoonotic viruses relevant to the Hendra virus (*HeV*) which spreads due to the impact of *Pteropus* bats/flying foxes or unprotected pets and causes a serious attack and encephalitis. First, the *NiV* was reported in Malaysia in 1998. Subsequently, lung disease was recently discovered in the Kerala district. According to WHO statistics, the identification of zoonotic disease, one of the main challenges and cause of numerous outbreaks, coincide with the season of the sap harvest, that is, from winter to spring. The huge family of *Henipavirus* extends new species of deadly disease called Nipah by the novel *Paramyxovirus* pathogen. The goal of this work is to predict and diagnose virus by knowing the effectiveness of machine learning as soon as possible due to lethality. In current medical care, PCR or serology works effectively to diagnose the virulent, in which the body is rapidly transformed through the blood immunity cells, which it infects with asymptomatic symptoms. This document aims to summarize the machine learning technique, which is one of the main areas in the field of data analysis, although it plays a more important role in many real-time applications; the healthcare sector analyses the multiple machine learning algorithms for disease prediction and/or solution analysis. The minor inconvenience of the healthcare sector may take some time to clarify the test result. From a medical point of view, there are no syringes and there are no validated drugs available against the Nipah virus. So far, the result reaches a high mortality. Here, the summary of Nipah reports to stimulate researchers to observe the disease in the first phase with high precision and also tracks the drugs associated with Nipah. Machine learning algorithms are very essential in the medical society to isolate the virus of suspicious and emergency cases using ML predictor.

**Keywords**—blood immunity, diagnosis, *HeV*, healthcare, WHO, immunity, Kerala, machine learning, Nipah virus, outbreaks, *paramyxovirus*, *Pteropus* bat

## I. INTRODUCTION

Nipah infects through the animals which is an intractable pulmonary disease. Initially the disease comes from the Malaysian country in the period 1998-1999 (Nipah River village), after this caused several outbreaks. This RNA related disease first infects the unprotected animals and it spreads the multiple modes of transmission can be either, animal to human or in the person-to-person transmission. In Malaysia (1998-99), approximately 250 suspected cases were identified through the clinical result. Simultaneously the disease caused multiple outbreaks recently this was identified from the Kerala district (Calicut) peoples in May'18. World Health Organization (WHO) takes the initiative to trace the virus as much faster due to the high mortality range. At first, NiV infects through various hosts

such as, mammals (*genes Pteropus*), African green monkeys, pigs, horse, dog, and cat, also infect to the reason of unrelated close contact. According to the WHO, the incubation period of this NiV disease may range from 6-21 days. Multiple machine learning algorithms and techniques has helped to identify the disease through the cluster analysis. Machine learning is a large area, thus the techniques are very much efficient, commonly used in the clinical industry.

However, till now any other therapeutic as well as syringes are not available in the medical places as well as country. NiV is the combination of RNA and Ribavirin. Generally any virus first must attack the blood cells if they have a low level immune parameter. Human cells have N number of compounds in the inhibitor. In other words, NiV initially could affect dendritic cells among various blood cell communities [3]. The BSL-4 agent laboratory has a license to test the pathogen. This Biological Safety Level-4 is a one of the highly integrated testing lab has the efficiency requirement to diagnose the difficult disease. Actually, this lab contains high level security to analyze the result during the testing period. A domestic animal has the responsibility to distribute such kind of disease effectively. Several technical oriented methodologies have been carried out to trace such type of virus, but getting low response results only. This work is carried out by multiple researchers have proposed their techniques by the influence of Machine Learning techniques/algorithms for to get the efficient accuracy level. A hypothesis of machine learning has much efficient to predict the intractable diseases. This survey establishes the overall data about the Nipah gathered from various medical related articles, WHO and National Centre for disease control (NCDC). NiV is one of the species among Hendra virus or the Ebola virus or Henipavirus or Marburg virus or filovirus [5]. In India, up to one hundred twelve species of bats were identified from these thirty one species were affected by the Nipah [5]. Mostly the disease was diagnosed by either Serology or through PCR medical tests. We searched many prediction models as well as techniques to diagnose the Nipah from the multiple research articles. Many of them have discussed about the early prediction system using static data, but WHO wants to stop this infinite disease problem, is needed to find the optimized prediction model.

Niv and HeV viruses, which do not change in the system, cause harm to human beings of paramixovirus-bred animals. Both are transmitted by bats [38] or paternal bats. According to current research report, Nipah can increase its symptomatology within 5 to 14 days, causing people to die. Many viruses initially infect the human immune system, including rotavirus, rubella, cedar, henipavirus, hepatitis,

poliomyelitis, mumps, flu, in particular. Each virus adds its negative proteins to the blood cells, which make the human being, feel so tired once the virus is affected. Tissues may have the possibility of being damaged due to cellular infection or may increase the level of pathogens [40].

## II. DATA COLLECTION

We conducted a literature survey and the information are collected from the various digital sources, Medical oriented articles such as MDPI, PubMed, Hindawi, and also from the Scopus indexed journals. Most of the medical articles, are case study reports which are represented in the term of ‘Diagnosis and Infection’, ‘Vaccine Development’, ‘A rare and Intractable disease’, ‘Nipah virus Analysis’, ‘Prioritizing surveillance of Nipah virus in India’. Simultaneously, other current case reports were collected from the World Health Organization and NCDC. Recently [1], the awareness camp has been organized against Nipah by the Kerala Medical College and hospital. The intention of the camp is to create an awareness of the hospital workers. Generally, in the medical history the positive fruit bats are denoted by the name of *Pteropus medius*.

Moreover, all the case study reports and the results were generated by the use of PCR and serology methods, by testing the human specimens. And for the further research, the sample collection guidelines [17] can be given by (NCDC) National Institute of Virology, Pune. The laboratory, find a viral disease based on the human’s blood molecules and IgM antibody detection through the medical test ELISA. The following section describes how machine learning techniques are used in the medical field.

## III. RELATED WORKS

Nipah is an unpredictable and severe respiratory infection, which transmit from one who has NiV+. This deadly virus may cause coma and encephalitis to the people or even fatality. Due to the reason of deadly virus many researchers are trying to find the vaccination of this disease. Currently any approved vaccines are not available and the treatments were none. Aditi and M. Shariff [2] has taken a systematic review of Nipah virus infection. The study report contains the biological information about the Nipah agents and immunopathogenesis diagnosis, which will carry in the hospital industry. For this the authors have conducted a literature survey from the Cochrane library, Google scholar and PubMed, viz. Use of various research articles, information has been gathered. Antibody detection techniques are also explored and the case type definition will also be defined with the help of NCDC. Rodolphe pelissier et al., [3] represent the Nipah regards the immunopathogenesis. During the NiV infection, people may face the unbalanced problem and the authors have clearly demonstrated the protein expression system which is closely related to the human immunopathogenesis.

The natural reservoir has some host to spread the Nipah through the respiratory route or throat swabs sometimes. Jorge D. Mello-Roman et al., [12] represents the case study report of dengue disease which is carried out in the Paraguay. The combination of Artificial Neural Network (ANN) and Support Vector Machine has been much helpful for to diagnose dengue disease at the early stage. The machine learning techniques are much more effective and assist in the medical diagnosis. ANN and SVM are two classification models are used to identify the dengue disease with a high

accuracy level. SVM obtains the accuracy result in above 90% not only accuracy also specificity and sensitivity of the dengue disease were observed, when comparing with other models.

Gaurav Sharma, Seema Bawa et al., [4] uses a hybrid machine learning models for predicting the T-cell Lymphotropic virus. This is coming under the category of retrovirus, was identified in 1980. For T-cell Lymphotropic virus prediction, machine learning algorithms like Random forest, K-Means and Feature selection method have been used. And some heuristic techniques were also has been used to process and evaluate the performance of the hybrid model. The results are explored and analyzed by the K-fold cross validation techniques and AUROC method. The hybrid models are trained and evaluated by the use of optimal features. Then for prediction of HBsAg seroclearance, the authors [20] expresses the various machine learning models such as Extreme gradient boosting (XGBoost), Random forest (RF), Decision tree (DT) and Logical regression (LR). The specificity of the predictive model will be calculated by above four ML models/algorithms.

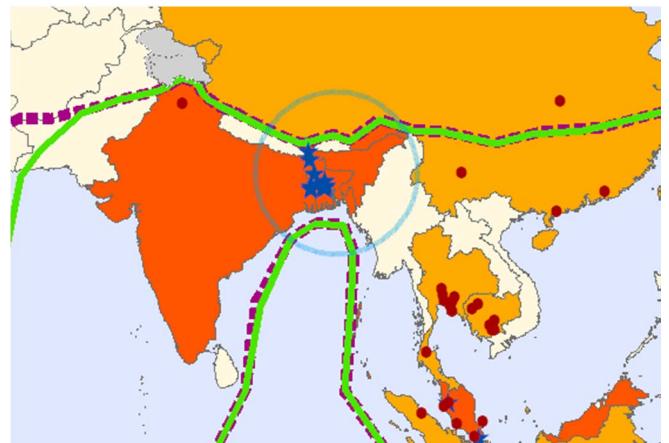


Fig. 1. Nipah outbreak in India

The above illustration can be captured from the <https://www.who.int/csr/disease/nipah/en/>. Akanksha Rajput, Archit Kumar and Manoj Kumar [9] developed an “anti-Nipah” web server. For this the authors gather the data from the various research articles (PubMed) and patents. All the information is integrated with the QSAR model with the help of Machine learning model. The web source contains all the virus information as well as NiV inhibitors resource. In which, this is a new initiative computational tool but they don’t provide any methodology for this computational work. Sayantan Banerjee, Nitin Gupta et al., [8] explained about an intractable disease. Overall outbreaks of NiV were described. It also details how and where Nipah infects the human body and some lab tests. And they provide some basic prevention for the disease. Poojitha Amin, Nikhitha R. Anikireddypally et al., [13] described about the health monitoring system. Author offers a new system architecture which is categorized into five phases such as, data collection, data pre-processing, transformation, and evaluation and user notification. The author takes the initiative and built the health oriented mobile application called fitbit into the wearable smart device by the use of ensemble classifiers. This application will help the client can monitor their health condition and it provides the alert while the user at the risk state. The data can be persisted into Mongo database.

[31] comparing the SVM and ANN algorithm for predicting hemodialysis using machine learning techniques with the help of medical method spectroscopy, SVM is claimed as an ideal method.

Stephen and Wenfeng [42] compared and used the three widely used classification and prediction methods, as well as algorithms like RF, SVM, and ANN for predicting kyphosis disease. They compared their widely used classification algorithms (RF, SVM and ANN) with other machine learning algorithms. The three algorithms mentioned above are very effective ML algorithms which are very commonly used in the medical industry and therefore are exceeded with a level of accuracy greater than 80% during cross validation.

N. Rajathi et al., [43] discussed the mosquito borne virus and the early prediction model. The main symptoms of dengue disease are vomiting, severe fever, joint pain, bleeding and a high body fatigue rate. The main goal of the work is to detect the dengue virus in the initial stage of virus infection using ML classification techniques and different algorithms such as Naïve Bayes, J48, RF, REP (reduce error pruning), SMO (sequential minimal optimization), LWL (logically weighted learning), ZeroR and Adaboost. Finally, they compared these classification algorithms to find out which one is providing high precision among them in viral disease prediction. Hepatitis is also one of the harmful diseases caused by the virulent virus and also attacks the part of the liver. [44] will approach the forecast using the ANFIS method, which is hybrid.

#### IV. NIPAH: A POISONOUS DISEASE

Initially, the zoonotic disease (NiV) is an emerging bat borne pathogen comes from the Malaysian country in the period of 1998-99. In which, this caused a several outbreaks; however, we don't have any predication and/or prognosis model to identify the disease Nipah. This is a natural reservoir, can be transmitted through the animals and also some close relationship. Hygienic is only of the main problem to occurring, such type of disease. If the person has low immunity cells contained in the human epithelial cells, the disease may easily occur. As per the World Health Organization (WHO), the total fatality rate is 75% in May 2018 [9]. Actually India met several Nipah outbreaks, one of the recently occur in Kerala. The main reason of this disease is, one is due to un-hygienic and another one is the raw date palm juice.

The fruit can be contaminated by infected animals as well as mammals (flying fox) and this will be transmitted through the infected animal's urine. There are countless variety bats in this world. *Pteropus giganteus* [34] is one of the flying fox species in which they cause the Nipah disease. It could not have any accurate symptoms. The disease may start with the side effect of an unpredicted high fever rate, drowsiness, dizziness, shortest breath with a cough, encephalitis, vomiting, myalgia, sore throat, and with other neurological signs. In the medical industry, against Nipah none of them have found any vaccine or treatments were found. After the large study, the horse vaccine (sG and HeV-sG) will be developed [2] and it is approved by the America, which is based on G glycoprotein, the vaccine was simply called as *Equivac* thus it is against for the *Hendra* virus HeV.

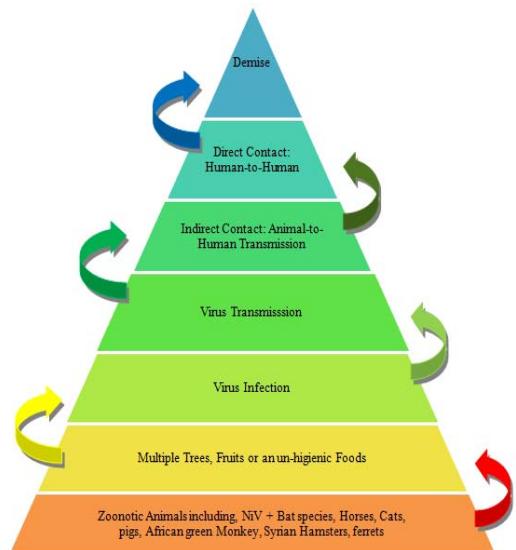


Fig. 2. Nipah Pyramid

##### A. History of Nipah

Traditionally the virus Nipah can be identified by immunohistochemistry of squirrel monkeys and African green monkeys through their respiratory route lungs and kidney. The Nipah causes several outbreaks: In Malaysia and Singapore, the peoples were attacked by the high encephalitis in the year of 1998 to 1999. Consecutively, it spreads to pigs (pig farm). In 2014, this will cause another outbreak in the Philippines, attacks via the horses. Here the patients were infected by the horse meat consumption and had a close relationship with the horse. Thus the bat-bone pathogen (Nipah) transmitted through the close and animal relationship. In south Asia, the transmission of disease and the infected RNA will be detected in the saliva of patients [2]. This infects not only from the bats, also by alcohol consumption made from the raw date palm. The virulent disease initially affects the human nervous system and can spread, including the respiratory vascular system and the immune system. Several studies report that cerebral encephalitis are the initial reason for leading to higher mortality. Inoculated zoonotic are spreading the virulent, so the virulent NiV disease was initially isolated in Malaysia. In addition, the epithelium is that the human blood vessel assumes the responsibility of protecting the immune cells of the virus, or also protects the immune system from the blood. Then Nipah attacks the epithelium through the respiratory tract. Day by day the ship could suffer density losses if the virus is really present in the body. This NiV can be classified into two forms of groups [37], such as NiV-M and NiV-B. Both virulent types are isolated from human resources like through throat swabs.

##### B. Nipah Bat Species

Some of the NiV+ bats [5] are viz, *Hipposideros ater*, *coelops frithii*, *Rhinolophus luntus*, *Pteropud medius*, *Hipposideros Pomona*, *Hipposideros larvatus*, *Hipposideros diadema*, *Chaerophon plicatus*, *Saccoaimus* and *Megaderma spasma*. From these, 90<sup>th</sup> percentile of similarity NiV+ bat species was detected in the countries, Asia, Australia through the medical test methods serology or PCR. Few of the similarities based NiV+ species are, *Taphozous*

melanopogon, Rousettus aegyptiacus, Chaerophon plicatus, etc.

#### C. Adaptive Immunity

NiV belongs to *Henipavirus* family, which is classified into major clades, genotype B found in Bangladesh and genotype M found in Malaysia and Cambodia [6]. In May 2018, the clinical specimens like serum, urine and throat swab can be collected from 3 suspected NiV peoples for the clinical verification. The collected samples were compared with secondary case people's specimens. Using nested RT-PCR amplification and ELISA find out the Nipah primers denoted by the medical term like, CGTGGTTATCTTGAACCTATGTACTTCAG-3'. The specimens are tested in the highly integrated medical laboratory BSL-4.

Literally, the genome contains six structural proteins related to the RNA, which are Nucleocapsid protein, Phosphoprotein, matrix protein, fusion protein, glycoprotein and large protein, which is shortly defined by the 3'-N-P-M-F-G-L-5'. However the research team finds N gene (bat) is relatively matched with the human sequence (Kerala). According to the report of NCDC [2], the affected peoples are ensured by seizure with fever, heavy headache with fever or shortness of breath. These symptoms of case type are declared as a suspected case. The probable case is defined by the similar specimen diagnosis and NiV+ cases are confirmed by the laboratory test (PCR or ELISA).

#### D. Clinical Detection Methodology

Epithelial has the low-quantity compound, in which the cell will initially be present in the urine [37]. Urinalysis helps isolate any virus, from its range of intervals. Using human specimens like the samples of throat swab, tissue samples and urine or CSF, the virus can be tested in the medical industry laboratory. Some of the effective clinical testing methods are,

TABLE I. MEDICAL TEST TYPES

S. No	Name of the Methodology	Method Description
1	PCR (Polymerase Chain Reaction)	Used in molecular biology help to make numerous copy of the RNA. It is a sensational [38], used to detect virus-driven genes in an exciting medical field.
2	ELISA (Enzyme Linked Immunosorbent Assay)	Used to find the infected antibody from the blood or for serological diagnosis
3	Virus isolation	Specific clinical test method. The BSL-4 laboratory is necessary for to test the collected specimens
4	Serum Neutralization Assay	Gold standard test due to the need of Bio-Safety level 4 laboratory requirements
5	Histopathology	It can also refer as Immunohistochemistry. The tests were done during the post mortem [38].
6	Serological Assay	It is used to find the virulent virus antigens.

#### E. Vaccine Development

Traditionally the virus Nipah can be identified by the research on "anti-Nipah" syringes have been carried out in

many countries. However, despite of number of vaccines has been developed for Nipah, and this will be tested in the animal models [2]. After that, the developed vaccine will be supported for the animals and for both HeV and NiV. According to the report of [33], Dr. Schnell and their colleague have worked together and found an effective vaccine against the Nipah virus, but it couldn't be conducted a proper testing, due to oriented with all deadly viruses. This needs perfect platform to test the vaccine with the clinical help. The real-time data are collected from the <http://dhs.kerala.gov.in/index.php/publichealth.html>.

The report will be collected from the [32] through the online search. According to this 2019 report, many of the humans will be dying by the case of fever. Nipah also causes asymptomatic fever with cough with a high rate of specificity. The total fatality rate will also high due to the fever. The normal fever could not cause a fatality. While comparing with other viral disease/infection, the mortality range will be lower, whereas fever causes the high impact. The knowledge representation of the fatality range is given below.

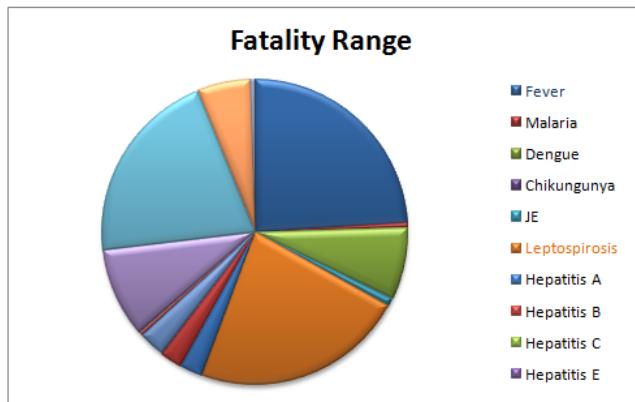


Fig. 3. Disease-based mortality range

#### V. MACHINE LEARNING

Machine learning technology allows the computer to generate the knowledge of past experience. Machine learning (ML) provides several prediction algorithms for the multiple identification purpose. The most widely used forms of prediction in the healthcare sector include: Random Forest (RF), support vector machine classifier (SVM), Naïve Bayes, Artificial Neural Network (ANN) and various cross validation techniques thanks to its greater accuracy. Predicting NiV is a huge task and is also one of the best challenges for the clinical industry during asymptomatic virulent disease. The machine learning is a highly sophisticated technique capable of predicting disease from any type of summary data and, therefore, a subfield of AI. Compared to other applications, ML has a strong relationship with the fields of computer science and statistics. Today, Machine Learning plays a vital role in various real-time applications such as marketing analysis, medical fields, robotics industry, malware filtering, online fraud detection and even safety-related industries. For each situation, knowledge of Machine Learning is required to active the result. Machine Learning is broad and could be a multi-disciplinary field [18]. ML allows ANN to collect the

training set from the various sources. For any prediction work, ML is needed to get the exact result. In the healthcare sector, it will predict disease based on the specificity of multiple ML algorithms. Many ML-based predictive algorithms have been developed for disease identification [19]. Each of them has its own calibration to diagnose the disease based on the definition of the problem. Machine Learning was designed to develop a unique computer program with the principle of accessing data for the purpose of learning. At first, Machine Learning originated by Samuel in the 1950s [22] and [23]. The primary of Machine Learning is the ability to predict that the machine can learn synthetic information on its own. The health sector concentrates the application of machine learning for the four emerging reasons, such as disease diagnosis, disease prevention, essential and useful prognosis, the best treatment and the best research. Also ML provides efficient tools for prediction, especially in the health care industry in medical imaging and computer aided diagnosis.

#### A. Approaches of Machine Learning

In healthcare prediction, the supervised, unsupervised and reinforcement learning models are widely used ML methods. The efficient learning algorithm [45] are used for both data analysis and decision making problems. This will be described below.

- *Supervised Learning:* This is one of the learning methods, in which the prediction can be done by the use of labeled data. Here the supervised algorithms are called classification and prediction. After learning data, the supervised algorithm will predict the result and it compares the predicted output with the original label.
- *Unsupervised Learning:* Here, this is opposed to supervised learning. This does not require any label to predict the result, unlike supervised. It learns and forms the groups of data which are similar, like a cluster.
- *Reinforcement Learning:* Mostly used by the business decision applications. The reinforcement learning method is used to train the data based upon the past data, if the error occurs in the output. It will work under the principle of user's feedback. The user can train the machine through providing feedback until the original prediction is done.

#### B. Machine Learning Techniques

Learning techniques [4] are used to predict and identify the accuracy using various classification algorithms. Decision Tree, Random Forest, Neural Network, and Support Vector Machine are widely used classification techniques. Naive Bayes is also one of the effective techniques most probably used in the health related applications for prediction. The main intention of the ML algorithms is, to learn the raw data, to identify the problem and to find the new data which is predicted. The frequently used Machine learning methods are [20],

- *Logistic Regression Model:* This classification method was developed by David Cox. The most used regression model for statistical and for scientific study. This is used to correlate the relationship between the two different variables using a logistic function.
- *Decision Tree:* Another widely used classification model is a Decision Tree, which also handles both numerical and categorical variables for finding the non-linear parameters. This non-parametric supervised learning follows a greedy method used to split up the values in a tree like manner.
- *Support Vector Machine (SVM):* This statistically based approach [31] is applicable to both the classification and regression problem. It is a classification technique used to separate the data and to create the set of hyperplanes among the number of datasets, especially for high dimensional data due to handle multiclass problem. In other words [31], it evaluates the max distance of each data point and concludes a best hyperplane. Using SVM classification, we can overcome the misclassification. Basically, the overall performance of the SVM classifier [12] is calculated by the kernel functions linear, Guassian and polynomial. In which, this will be denoted by the symbol of hyperparameter  $\gamma$ . The eminent and frequently used SVM classification [38] and regression model is one of the leading medical methods used in human genome problems.

- *Artificial Neural Network:* This is also referred to as computational networks. Multilayer perceptron and Radial basis functions are the two different neural networks, and it is a supervised learning method. MLP consists three different layers such as the input layer, hidden layer and output layer.

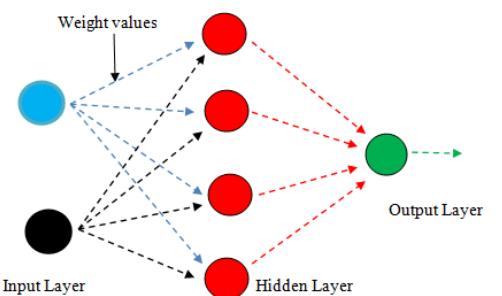


Fig. 4. MLP Architecture

The threshold value can be trained with the influence of propagation network. This architecture is completely interconnected with the neurons and each of them has its own weight values used to train the machine. The basic model diagram of MLP is shown in the figure 4.

### C. Model Evaluation

The performance of the overall trained will be measured [4] by using various machine learning parameters.

- *Accuracy:*

$$\text{Accuracy} = \frac{\text{TP}}{\text{TP} + \text{FN}} * 100$$

- *Recall:*

$$\text{True Positive Rate} = \frac{\text{TP}}{\text{TP} + \text{FN}}$$

- *Specificity:*

$$\text{True Negative Rate} = \frac{\text{TN}}{\text{TN} + \text{FP}}$$

- *Precision:*

$$\text{Positive Predicted Value} = \frac{\text{TP}}{\text{TP} + \text{FP}}$$

- *Negative Predicted Value (Ratio):*

$$\text{Ratio} = \frac{\text{TN}}{\text{TN} + \text{FN}}$$

- *F1 score:*

$$\text{Average} = \frac{2 * \text{PPV} * \text{TPR}}{\text{PPV} + \text{TPR}}$$

Where, TP and FP are true positive and false positive and TN and FN are true negative and false negative.

### CONCLUSION

NiV causes several outbreaks in south and southeast area as much as harmful. Through this paper, we will able to discover the facts of machine learning, not only in the pharmaceutical industry, but also in many fields such as intrusion detection and finance. However, its help is increasingly being used in the medical industry by the name of disease prognosis. Although it is very difficult to detect an immediate or an illness in the medical fields, predicting it with a variety of machine learning aids is a boon in today's computerized world. The prominence of the WHO is to defuse the mitigation of disease transmission. The Nipah virus causes much illness in the human blood cells and also attacks the blood immune system. The poisonous virus detected by the RT-PCR and urine test so far in the pharmaceutical industry, various researchers have found that animals with this type of disease appear very year. But no clear signs of it have been found.

Secondary the disease leads to high mortality. Against Nipah an effective prophylaxis are unavailable due to the lack of human scientific study. Multiple prediction models have been developed for many viral diseases. Finding an anti-virus drug can be challenging in the medical field, according to new virus studies. On the other hand, there is no doubt that such a poisonous disease can be predicted using a computer based machine learning techniques. Future studies will carry this work and we will focus on to articulate such ML predictor model to diagnose or to predict the viral disease and also focus to find the clinical signs of the virulent disease using learning algorithms in healthcare application. And also need to confer the prevention to the peoples which is more beneficiary for the uninfected people.

Further, this paper summarizes the NiV disease and its medical detection methods. It is known that the human body has a variety of immunity compounds, no matter what kind of viruses, it first mixes with a gene, such as RNA, or other low-efficiency or low potency antibodies.

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