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Computational methods for studying relationship between nutritional status and respiratory viral diseases: a systematic review

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Abstract

This study sought to identify the computational methods used in studying the relationship between nutritional status and human respiratory viral infections. Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline, we searched the PubMed database for studies that used computational approaches to investigate the nutritional determinants of respiratory viral infections. Sixty seven (67) studies were selected after screening an initial 1713 search hits against the study eligibility criteria. Our findings revealed that machine learning, neural network (and deep learning), mathematical models, and statistical methods were used by 83.58%, 26.87%, 13.43% and 92.54% respectively while 19.40% of studies use other unconventional methods. Furthermore, 16.42% and 71.64% studies use formerly created datasets and raw data respectively while 11.94% studies were performed without prior datasets. The outcomes of the selected studies showed that task related to prediction, identification, investigation, association and determination were performed by 20.90%, 8.96%, 40.30%, 10.93% and 14.93% of studies respectively. 1.49% each of the studies performed recommendation, risk reduction, management and screening. The findings of this review answered three research questions and provided guidance for some future contributions in the domain of studies related to nutritional status and respiratory viral disease.

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1 Introduction

Infectious diseases are caused by virus or bacteria and get transmitted person to person (van Seventer and Hochberg 2017). There are many types of infectious diseases, but infectious diseases related to digestive system and respiratory systems are very common. Infectious diseases basically spread to persons of a certain region or country or even to the whole world with very fast rate (Findlater and Bogoch 2018). The emergence of some infectious diseases creates either endemic or epidemic or pandemic. Endemic is the situation where the disease persists for very long time and people need to live with it. Epidemic is the condition where the disease spreads within certain region or country and pandemic is about worldwide spread of the disease (Silk and Fefferman 2021). An infectious disease can be purely new or one that evolved earlier. If the infectious disease that evolved earlier spreads infection in new location there is higher probability of getting controlled, but if the disease is a new one then it is cumbersome to control. In the situation of newly emerging infectious diseases, immunity and physical health status have to manage the infection. Immunity is greatly dependent on macro- and micro-nutrients. Macro-nutrients represent protein, fat, carbohydrate and water that require in large quantity while micro-nutrients represent vitamins and minerals that require in small quantity. The status of nutrition of our body is determined by the presence of these nutrients in terms of quantity. Adequate quantity of nutrients indicates normal-nutritional status while less or more quantity indicates malnutrition (Risch et al. 2023). Nutritional status and immunity have big roles to play in the management of infection. The relationship between nutritional status and immunity is well known and its role on infectious disease like COVID-19 is also established (Hussain and Borah 2022b; Im et al. 2020). People with malnutrition remain in the high risk zone and it is probable that during any pandemic like situation nutritional status of our body gets compromised due to non-availability of food and also due to other reasons (Mehta 2020; Hussain and Borah 2022c). Nutritional status, specifically malnutrition is considered to be one of the risk profiles similar to other comorbidity (Otero et al. 2021). That is why it is important to explore the correlation of nutritional status with infectious diseases.

The correlations of nutritional status with various types of infectious diseases are well studied from clinical perspectives, but not from computational perspectives (Cassotta et al. 2020). Application of computational aspects is much necessary in healthcare sector to cope up with this fast moving world especially for the developing countries like India. Computational aspects like machine learning (Hussain and Borah 2020a, b), neural network, deep learning, mathematical models, and other statistical methods have great potential to be applied in the healthcare sector for exploring various dynamics of diseases (Hussain et al. 2023; Hussain and Borah 2022a). Application of computational aspects in healthcare sector will surely boost the accessibility to healthcare facilities, efficiency, effectiveness, time management and cost management. Along with clinical aspects, computational aspects can be used and that will greatly help the clinicians in decision making and applying more appropriate diagnosis techniques.

The current study reviews the literature that uses computational aspects to analyse correlation of nutritional status or its components with respiratory viral diseases. This review is confined within 15 years of duration from 2007 to 2022. From 2007 to 2022 there were three pandemics/epidemics of medium or big size. In 2009, Swine flu emerged in United States and it was caused by a novel influenza virus called H1N1. Eventually it lasted for only one year and ended in the year 2010. In 2015, Middle East Respiratory Syndrome (MERS) occurred in the Republic of Korea by a virus called MERS-CoV and it is still

prevailing. In the year 2019, COVID-19 occurred all over the world. It was caused by a virus called SARS-CoV-2 and it is still prevailing all around (Hussain and Borah 2021). The virus is called SARS-CoV-2 because a similar kind of virus called SARS-CoV created another epidemic called Severe Acute Respiratory Syndrome (SARS) in China. That emerged in the year 2002 and ended in the year 2003.

The motivation behind this study is the recent pandemic caused by Coronavirus disease. Sudden occurrence of such a big pandemic was never expected and nobody was prepared for that. In the initial stage there were no medication, still the fatality rate was small. It was vulnerable to the patients having some other chronic and critical diseases. From the survival of patients without any comorbidity and fatality of the patients with other comorbidity indicated that immunity and nutritional status of body are playing important role, because existence of comorbidity eventually compromises the functions of immune system and nutritional status of our body. It is well known that immune system is greatly dependent on nutritional status (Pahwa and Sharan 2022; Noor et al. 2021). This motivated us to explore the correlation of nutritional status with infectious diseases and end up choosing to explore this relation from computational perspective.

Proceeding with our decision, we set the main aim of this systematic review as to identify and analyse the studies that are having computational methodological contributions on analysis of the correlation between nutritional status and respiratory viral diseases. There can be many viral diseases, but all do not create epidemic or pandemic. This study is confined within the viral diseases that create epidemic or pandemic and related to the respiratory system. The outcome of this review is expected to answer the research questions tabulated in Table 1.

2 Methods

To conduct this systematic review we followed the PRISMA guidelines updated in the year 2020 (Page et al. 2021; Moher et al. 2015). PRISMA is the recognized standard for evidence based reporting in systematic reviews and meta-analyses. This standard has 27 numbers of checklists and 4-phase flow diagram that are supposed to be followed for systematic review.

2.1 Information sources

We searched the PubMed database on 19th January 2023 to retrieve relevant literature published between January 2007 to December 2022.

2.2 Search strategy

We formulated search queries that primarily consist of name of the disease or its pathogen; computational aspects that are supposed to be there in the document; and the terms related to nutrition. We formulated three types of search queries as follows:

- <Computational aspect> AND <Disease or pathogen> AND Nutritional status
- ((<Disease or pathogen>[Title/Abstract]) AND (Nutrition[Title/Abstract])) AND (<Computational aspect>[Title/Abstract])

Table 1 Research questions (RQs) to address

RQ#	Research question	Expectation
RQ1	Is it feasible to integrate computational aspects with the studies of nutritional status and respiratory viral diseases?	To find if nutritional status can be associated with viral diseases related to respiratory system, and to find what type of techniques or models or tools are feasible/available for this
RQ2	What type of data do we need to study the association between nutritional status and respiratory viral diseases?	To find relevant datasets or data, used performance metrics; and also to check if the study can be performed without datasets or data
RQ3	Is there any contribution of nutritional status on the optimization of infectiological parameters?	To find if there are models/techniques that work on optimization of infectiological parameters, and to find if nutritional status has any significant contribution on optimization

- ((AB=(<Disease or pathogen>)) AND AB=(Nutrition) AND AB=(<Computational aspect>)

The first and second search queries are for PubMed database. The first query is unrestricted and it searches everywhere in the document. On the other hand the second search query is restricted to search the title and abstract of the document. The third query is for Web of Science core collection. The search is restricted to search the abstract. We found that PubMed has almost all the articles retrieved from Web of Science. So we end up considering only PubMed. In the above search queries <Disease or pathogen> takes the values "COVID-19", "SARS-CoV-2", "Coronavirus", "Middle East Respiratory Syndrome", "MERS-CoV", "Swine flu", "H1N1" and "Influenza virus H1N1"; <Computational aspect> take the values "Machine learning", "Deep learning", "Genetic algorithm", "Mathematical model", "Computational model" and "Neural network". The formulated search queries are available in Online Resource 1.

2.3 Screening and selection process

Using the search strategy we retrieved articles for three respiratory viral diseases namely Coronavirus, Middle East Respiratory Syndrome and Swine flu emerged in between 2007 and 2022. The retrieved articles undergone preliminary screening for eligibility check. The initial screening checked the title, abstract and keywords. After initial screening the qualified articles were checked for eligibility criteria mentioned in Sect. 2.4. The articles satisfying the inclusion criteria were considered for further processing.

2.4 Eligibility criteria

The study inclusion criteria are as follows:

- Journal articles having relation between respiratory viral diseases (COVID-19, Middle East Respiratory Syndrome, Swine flu or their pathogens) and Nutritional status or its components (Macro-nutrients: carbohydrate, fat, protein, water or Micro-nutrients: vitamins, minerals) and Computational aspects (Machine learning, Deep learning, Genetic algorithm, Mathematical model, Computational model, Neural network).
- The articles should have methodological or outcome based or result oriented contribution.

Similarly, the criteria used for excluding studies from the review are as follows:

- Review articles, hypothetical studies, and preprint; articles dealing with species other than human, articles with purpose and contextual mismatch, articles written in any language other than English, articles for which full text could not be downloaded, symposium papers, conference papers, and book chapters.
- Non-availability of information about any computational aspects, name of those viral diseases or their pathogens, and status of the nutrition or any component of nutritional status.

2.5 Data extraction and data synthesis

To extract the data from each of the selected studies, we used an excel spreadsheet to collate information including "Disease name", "Title and First authors", "Year", "Journal/Publisher", "Impact Factor", "Technique/Model/Tool", "Dataset/Data", "Performance metrics", "Outcome", "Methodological contribution", "Nutritional status or its component" and "Limitation". All the selected articles included in this excel spreadsheet have been provided with a reference number as well. The extracted data are available in the Online Resource 2.

After data extraction, we proceed for data synthesis. The basic concept of synthesizing data is to combine the facts and figures to formulate a response to answer the research questions. Collection of a number of studies having similar kind of results and comparable viewpoints help in providing the evidence and answering the research questions. We scrutinized and evaluated both quantitative and qualitative data. Quantitative data include number of studies in various category, studies included from different years, number of studies using various techniques, number of studies using same dataset, values of various performance metrics, number of studies with similar kind of outcome. The qualitative data include the assessment of the models, techniques, tools based on their relevance, strength, weakness and type. We used various techniques to synthesize the collected data. To get a clear view we used a number of visualization technique like- Pie chart and Bar chart. We also used tables for better presentation and summarizing the results.

3 Results

3.1 Study selection

The studies were finally selected following a 4-phase process suggested by PRISMA. Figure 1 is prepared based on the 4-phase flow diagram suggested in PRISMA guidelines.

This work identified 1713 numbers of studies, out of which 1250 studies were for COVID-19, 419 studies were for Middle East Respiratory Syndrome and 44 studies were for Swine flu. After initial screening we could keep 103 (6.01%) numbers of articles for eligibility check. Rest 1610 (93.99%) numbers of studies were excluded. Out of those 1610 articles, 59 numbers of articles were review articles; 96 numbers of articles missed our keywords like- name of the disease, used computational aspects and status of nutrition; 168 articles were discussing different context other than infectious disease and nutritional status; 4 articles were found to be a preprint; 1272 numbers of articles redundantly appeared for different search queries. We also excluded 11 numbers of studies due to other reasons like being a conference or symposium paper.

The qualified 103 numbers of articles were further assessed for eligibility. Out of those 103 articles, we further excluded 36 numbers of studies. Out of those 36 articles, 13 articles were excluded due to mismatch in purpose; 6 articles were excluded as those were proving a hypothesis; 3 studies were not about human; 1 talked about virtual nutrition; 1 discussed about economic aspects, 1 talked about worker management; for
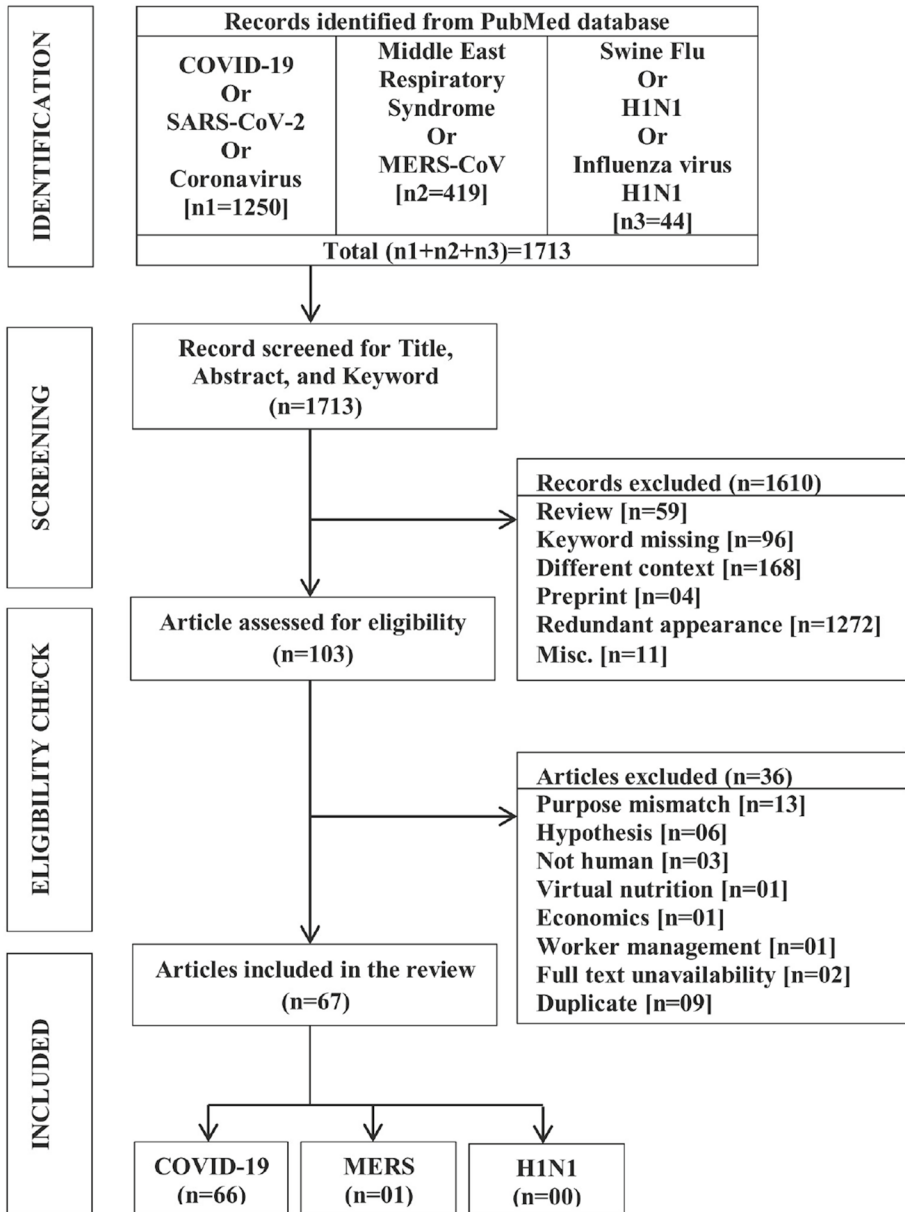
Fig. 1 Procedure followed for the article consideration

2 articles we could not find full text; and 9 articles were found to be duplicate of each other. Finally, we could keep 67 numbers of studies that fulfilled our requirements. Out of those 67 studies, 66 were about COVID-19, 1 about MERS, and no articles were found eligible in case of H1N1.

3.2 Year wise distribution of the studies

In the interval from 2007 to 2022, there were three outbreaks of infectious disease namely Swine flu, MERS and COVID-19.

Swine flu emerged in the year 2009, MERS emerged in the year 2015 and COVID-19 emerged in the year 2019 and still it is present. The selected studies belong to the years 2015, 2020, 2021 and 2022. The articles from other years could not qualify the selection criteria. Figure 2 shows the year wise distribution of the selected studies. The highest number of studies that is 32 (48%) belong to the year 2021 followed by 24 (36%) numbers belonging to the year 2022, 10 (15%) numbers from the year 2020 and the lowest number that is 1 (1%) study belong to the year 2015.

3.3 Computational methodologies

The models or techniques or tools used by the selected studies can be categorized as machine learning techniques, neural network and deep learning techniques, mathematical models, statistical models and tools, and miscellaneous models and tools. Figure 3 shows the overall use of the computational aspects by the selected studies.

We find that 83.58% studies use machine learning techniques; 26.87% studies use neural network and deep learning techniques; 13.43% studies use mathematical models; 92.54% studies use statistical methods and tools; and 19.40% of studies use miscellaneous methods and tools. The cumulative percentage will not be 100 as a single study may use multiple techniques, models and tools.

Fig. 2 Year wise distribution of the articles

Year wise distribution of the selected studies

■ 2015 ■ 2020 ■ 2021 ■ 2022

Fig. 3 Computational aspects used by the studies
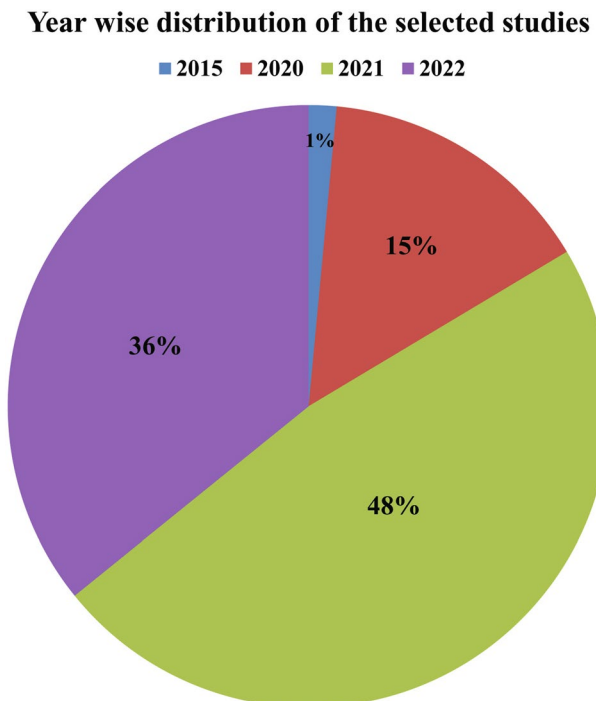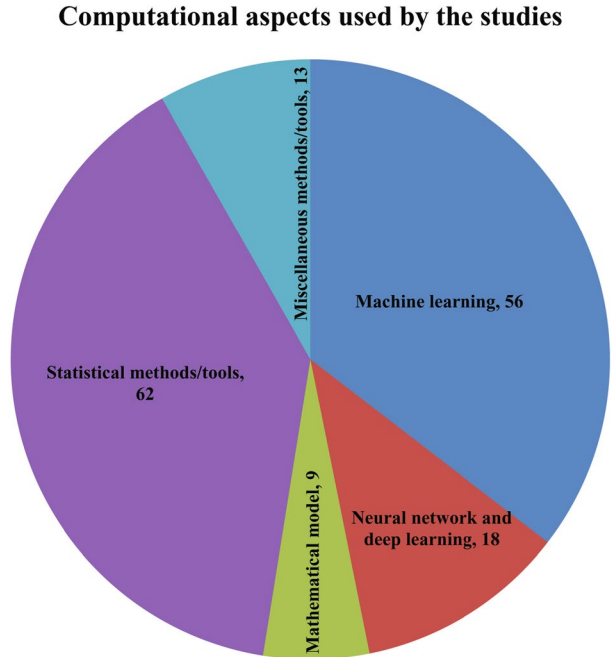
Computational aspects used by the studies

Table 2 lists the individual machine learning techniques and the studies that use those models.

We find that 11.94% of studies use boosting algorithms (XGBoost=4.48%, Ada-Boost=2.99%, GBoost=2.99%, HGBoost=1.49%); Linear discriminant analysis is used by 1.49% of studies; 16.42% studies use tree based algorithms (Decision tree=4.48%, Random forest=10.45%, Extra-trees=1.49%); Ensemble-based multi-criteria decision making is used by 1.49% of the studies; Support vector machine is used by 10.45% of the studies; K-nearest neighbor is used by 7.46% of the studies while 34.33% of the studies used regression algorithms (Linear regression=8.96%, Logistic regression=25.37%).

Table 3 lists the neural network and deep learning techniques used by the studies.

We find that classical neural network models are used by 7.46% of the studies; Multilayer perceptron is used by 5.97% of the studies; classical deep learning techniques are used by 2.99% of the studies; 4.48% of the studies use convolutional neural network; 2.99% use long short term memory; 1.49% each by deep neural network and autoencoder.

Similarly, Table 4 lists out the individual mathematical models used by the studies.

It has been seen that normal mathematical models are used by 5.97% of the studies; 1.49% each of the studies use statistical marginalized two-part models, SEIR model, mathematical linear programming model and optimization-based mathematical programming model while 2.99% studies use SIR model.

Like the previous cases, Table 5 lists out various statistical methods and tools that are used by the selected studies.

It was found that SPSS was used in 8.96% of studies; polynomial mixed-effects regression model was used by 4.48% of studies; 11.94% studies use cox analysis (Uni- and multivariate cox regression analysis=5.97% and Cox proportional hazards models=5.97%); Kaplan-Meier method is used by 11.94% of the studies; t-test is used by 13.43% of the studies; Mann–Whitney method is used by 8.96% of the studies; 20.90% studies use

Table 2 Machine learning techniques used by the studies

Machine learning techniques	
Model/Tool	References
XGBoost	Jolley et al. (2022), Bendavid et al. (2022) and Chowdhury et al. (2022)
AdaBoost	Chowdhury et al. (2022) and Shams et al. (2021)
GBoost	Aktar et al. (2021) and Ref5
HGBoost	Chowdhury et al. (2022)
Linear Discriminant Analysis	Willette et al. (2022)
Decision Tree	Aktar et al. (2021), Ren et al. (2022) and Ref28
Random Forest	Aktar et al. (2021), Chowdhury et al. (2022), Song et al. (2022), Ren et al. (2022), Jafari et al (2022), Tang et al. (2021) and Martinez et al (2022)
Support Vector Machine	Aktar et al. (2021), Chowdhury et al. (2022), Schiaffino et al. (2021), Song et al. (2022), Ren et al. (2022), Tang et al. (2021) and Martinez et al (2022)
K-Nearest Neighbor	Aktar et al. (2021), Chowdhury et al. (2022), Ren et al. (2022), Tang et al. (2021) and Martinez et al (2022)
Linear Regression	Shams et al. (2021), Faradina et al. (2021), Osuna-Padilla et al. (2021), Martinez et al (2022), Eslamian et al. (2022) and Rahayu and Timotius (2022)
Logistic Regression	Bendavid et al. (2022), Chowdhury et al. (2022), Song et al. (2022), Vu et al. (2021), Li et al. (2021a), Katz et al (2021), Xue et al. (2020), Zhou et al. (2021), Mostaghim et al. (2020), Larrazabal et al. (2021), Ma et al. (2021), Cosgrove and Wharton (2021), Rouget et al. (2021), Bedock et al. (2021), Osuna-Padilla et al. (2021), Werneck et al. (2021) and Dror et al. (2022)
Ensemble-based multi-criteria decision making (MCDM)	Chowdhury et al. (2022)
Extremely Randomized Trees (Extra-Trees)	Chowdhury et al. (2022)

XGBoost Extreme Gradient Boosting, *AdaBoost* Adaptive Boosting, *GBoost* Gradient Boosting, *HGBoost* Histogram-based Gradient Boosting

Table 3 Neural network and deep learning techniques used by the studies

Neural network and deep learning techniques	
Model/Tool	References
Classical Neural Network	Song et al. (2022), Saldivar-Espinoza et al. (2022), Laponogov et al. (2021), Martinez et al (2022)) and Deschasaux-Tanguy et al. (2021)
Multilayer Perceptron (MLP)	Chowdhury et al. (2022), Schiaffino et al. (2021), Jafari et al (2022) and (Saldivar-Espinoza et al. (2022)
Classical Deep Learning	Aktar et al. (2021) and Sciannameo et al. (2022)
Convolutional Neural Network	Bendavid et al. (2022), Sciannameo et al. (2022) and Khozeimeh et al. (2021)
Long Short Term Memory	Bendavid et al. (2022) and Sciannameo et al. (2022)
Deep Neural Network	Basu and Sen (2022)
Autoencoder	Khozeimeh et al. (2021)

Table 4 Mathematical models used by the studies

Mathematical models	
Model/Tool	References
Normal Mathematical model	Hozé et al. (2021), Hussain and Borah (2022b), Pham (2022) and Novosad et al (2020)
Statistical marginalized two-part models	Kamyari et al. (2021)
SIR	Jiang et al. (2020) and Fujiwara et al. (2022)
SEIR	Jiang et al. (2020)
Mathematical linear programming model	Castañón et al. (2020)
Optimization-based mathematical programming model	Dalal (2022)

SIR Susceptible-infectious-recovered, *SEIR* Susceptible-exposed-infectious-recovered

Table 5 Statistical methods/tools used by the studies

Statistical methods/tools	
Model/Tool	References
SPSS	Willette et al. (2022), Zhou et al. (2021), Faradina et al. (2021), Ma et al. (2021), Karahan and Katkat (2021) and Dancer et al. (2015)
Polynomial mixed-effects regression models	Perrar et al. (2022), Tallon et al (2022) and Wu et al. (2021)
Uni- and multivariate Cox regression analyses	Recinella et al. (2020), Merino et al. (2021), Annweiler et al. (2021) and Bennouar et al (2021)
Cox proportional hazards models	Anderson et al. (2020), Subramanian et al. (2021), Brenner et al. (2020) and Reis et al. (2021)
Kaplan–Meier method	Li et al. (2021a), Osuna-Padilla et al. (2021), Recinella et al. (2020), Annweiler et al. (2021), Brenner et al. (2020), Bennouar et al (2021), Reis et al. (2021) and Linneberg et al. (2021)
t-test	Li et al. (2021a), Mahmudiono et al. (2022), Doganci et al. (2020), Dror et al. (2022), Subramanian et al. (2021), Annweiler et al. (2021)), Karahan and Katkat (2021), Linneberg et al. (2021) and Dancer et al. (2015)
Mann–Whitney test	Li et al. (2021a), Pérez-Cruz et al. (2021), Dror et al. (2022), Karahan and Katkat (2021), Linneberg et al. (2021) and Dancer et al. (2015)
Chi-squared test	Li et al. (2021a), Mahmudiono et al. (2022), Faradina et al. (2021), Doganci et al. (2020), Larrazabal et al. (2021), Ma et al. (2021), Bedock et al. (2021), Li et al. (2021b), Pérez-Cruz et al. (2021), Subramanian et al. (2021), Annweiler et al. (2021), Karahan and Katkat (2021), Linneberg et al. (2021) and Dancer et al. (2015)
Fisher's exact test	Faradina et al. (2021), Larrazabal et al. (2021), Bedock et al. (2021), Pérez-Cruz et al. (2021) and Dancer et al. (2015)
R	Xu et al. (2021), Anderson et al. (2020)
STATA	Anderson et al. (2020)

SPSS Statistical package for the social sciences, *STATA* Statistics and data

Table 6 Other models/tools used by the studies

Miscellaneous methods/tools	
Model/Tool	References
Gene Multiple Association Network Integration Algorithm, Enrichr enrichment analysis tool, GLay clustering	Maigoro et al. (2022)
AutoDock, PyMOL	Xu et al. (2021)
Cytoscape	Xu et al. (2021) and Liu et al (2022)
Geriatric Nutritional Risk Index (GNRI)	Recinella et al. (2020)
Malnutrition Universal Screening Tool (MUST)	Eslamian et al. (2022)
Markov Chain Monte Carlo (MCMC) method	Brenner et al. (2020)
Shapiro–Wilk and Levene tests, Kruskal–Wallis H test	Redwood-Brown et al. (2021)
Pearson correlation	Basu and Sen (2022)
ANOVA, Kruskal–Wallis test	Dror et al. (2022)
HealtheDataLab	Tallon et al (2022)
Kolmogorov–Smirnov test	Karahan and Katkat (2021)
Dp-ucMGP	Linneberg et al. (2021)
GC-MS analysis, PASS (Prediction of Activity Spectra for Substances), Lipinski's rule of five	Siddiqui et al. (2022)

Chi-square test; 7.46% studies use Fisher's exact test; R is used by 2.99% of the studies while 1.49% studies use STATA.

Table 6 lists out other models and tools that are used by the selected studies.

It is found that 1.49% each of the studies use Gene Multiple Association Network Integration Algorithm, Enrichr enrichment analysis tool, GLay clustering, AutoDock, PyMOL, Geriatric Nutritional Risk Index (GNRI), Malnutrition Universal Screening Tool (MUST), Markov Chain Monte Carlo (MCMC) method, Shapiro-Wilk and Levene tests, Kruskal-Wallis H test, Pearson correlation, ANOVA, Kruskal-Wallis test, HealtheDataLab, Kolmogorov-Smirnov test, Dp-ucMGP, GC-MS analysis, PASS (Prediction of Activity Spectra for Substances), Lipinski's rule of five while 2.99% of the studies use Cytoscape.

Overall we find that statistical methods and tools are used by highest number of studies followed by machine learning techniques. Neural network and deep learning techniques are also been used by significant number of studies. Uses of mathematical model in the studies are found to be comparatively less than other models and techniques.

3.4 Datasets used by the studies

Out of the 67 selected studies 59 (88.06%) numbers of studies used formerly created private or publicly available datasets or raw data from the communities or healthcare organizations. Table 7 lists the details about the formal datasets along with the corresponding references. These are the datasets used by 18.64% of the total studies using data.

We have not included the raw data that were used by 81.36% of the studies that use data. The data are basically some patients, protein data, food based molecules, CT images, satellite images, blood samples, miRNA samples, metabolomics data, food supply, socio-economic parameter data and drug data. The complete list is available in Online Resource 2. Out of that 67 studies, 8 (11.94%) numbers of studies do not use any kind of datasets or

Table 7 Datasets used by the studies

Dataset	Detail	Reference
N3C data	National COVID Cohort Collaborative's (N3C) electronic health record repository (n=1793604)	(Jolley et al. 2022)
MIMIC-III	Detailed clinical information for over 60,000 stays in ICUs at the Beth Israel Deaconess Medical Center in Boston, Massachusetts	(Bendavid et al. 2022)
Cambridge, Coswara, Virufy, and NoCoCoDa	Cough datasets: Cambridge- by The University of Cambridge; Coswara- by Indian Institute of Science (IISc), Bangalore; Virufy- labeled with COVID-19 status, obtained through PCR testing and patient demographic data; NoCoCoDa- includes coughing events during or after the critical phase of COVID-19 patients recorded through public media interviews	(Chowdhury et al. 2022)
MGB database	1495 patients with age 65 and above (44 features)	(Song et al. 2022)
COVID-19 Healthy Diet Dataset	Includes different types of foods from 170 countries around the world as well as obesity, undernutrition, death, and COVID-19 data as percentages of the total population	(Shams et al. 2021)
GISAID database	877,086 SARS-CoV-2 genomes until 19 April 2021 and 4,616,059 SARS-CoV-2 genomes from 6 January 2022	(Saldivar-Espinoza et al. 2022)
UF i2b2 patient registry	Population of 987,849 patients, 887- positively diagnosed with COVID-19, 31950- diagnosis of vitamin D deficiency, and 87- both vitamin D deficiency and COVID-19	(Katz et al 2021)
GEO database	Blood expression profiles of 15,379 genes in acute respiratory infection samples	(Tang et al. 2021)
TCMSP database	12541 natural bioactive constituents of plants	(Xu et al. 2021)
Cerner Real-World Data^{TM}	116,370 adults with confirmed COVID-19 infection, 93,098 (80.0%) did not have diabetes; 22,470 (19.3%) had T2D; and 802 (0.7%) had T1D	(Tallon et al 2022)
THIN database	UK primary care database (The Health Improvement Network, THIN): 1012944 registered women	(Subramanian et al. 2021)

data. These are the studies that analyse different aspects of respiratory viral diseases using mathematical model.

3.5 Performance metrics used by the studies

We found that the selected studies used many performance metrics to measure the performance of the used model or techniques. Table 8 lists out the common performance metrics with definition and the references to the studies.

The percentage wise use of performance measures are shown in Fig. 4

The plot shows that AUC has been used by maximum number of studies. Precision and Recall are the second highest used performance metrics followed by Accuracy. ROC, Absolute Errors and Specificity are also being used by significant numbers of studies. The Absolute Errors contain Mean Absolute Errors (MAE), Mean Square Errors (MSE), Root Mean Square Errors (RMSE) and Mean Absolute Percentage Error (MAPE). Other metrics like- R2 metrics, Nomogram, MCC, Quadratic mean, Log loss function, 20-fold cross validation, Plant-Based Diet Score are included under miscellaneous category.

3.6 Outcome of the studies

Out of the 67 studies some studies have common outcome in terms of the performed task. The used data and the context may be different but the ultimate computational task that the studies perform is similar. Figure 5 plots the ultimate outcomes of the studies with the number of studies yielding that outcome.

We found that 20.90% of the studies performed tasks related to prediction; 8.96% of the studies performed identification; 40.30% of the studies worked on investigation; 1.49% each of the studies performed recommendation, risk reduction, management, screening; finding some kind of association was performed by 10.45% of the studies while 14.93% of the studies worked on determination. Highest numbers of studies performed investigation followed by prediction. A significant numbers of studies performed task related to determination followed by identification and association.

3.6.1 Methodological contribution

The selected studies performed the targeted task using different types of methodology.

The methodological contributions of the studies can be summarized as "model development", "existing model use" and "tool use". Figure 6 shows the segment wise methodological contributions. It is found that 8.96% of studies used machine learning models; 4.48% studies used statistical model and mathematical model was used in 13.43% of studies. Similarly, 40.30% studies use existing machine learning model and 41.79% studies use existing statistical models. Likewise, 11.94% studies use healthcare specific tools and 2.99% studies use statistical tools. Most of the studies use existing machine learning and statistical models. The complete list of methodological contributions is available in Online Resource 2.

3.6.2 Presence of different components of nutritional status

To justify the aim of this review, it is inevitable to have the presence of various components of nutritional status in each of the selected studies.

Table 8 Performance measures used in the studies

Performance measure	Definition	Studies
Accuracy or model score	Accuracy is defined as the ratio of correctly predicted examples by the total examples	(Aktar et al. 2021), (Jafari et al 2022), (Khozeimeh et al. 2021), (Tang et al. 2021), (Martinez et al 2022)
Precision	This is also called as Positive predictive value. The ratio of correct positive predictions to the total predicted positives. Out of all the positive predicted, what percentage is truly positive	(Aktar et al. 2021), (Bendavid et al. 2022), (Chowdhury et al. 2022), (Schiaffino et al. 2021), (Jafari et al 2022), (Martinez et al 2022)
Recall or sensitivity	Probability of Detection or True Positive Rate. The ratio of correct positive predictions to the total positives examples. Out of the total positive, what percentage are predicted positive	(Willette et al. 2022), (Chowdhury et al. 2022), (Schiaffino et al. 2021), (Saldivar-Espinoza et al. 2022), (Vu et al. 2021), (Martinez et al 2022)
F1-Score	F-score is basically the harmonic mean of precision and recall. It takes both false positive and false negatives into account. Therefore, it performs well on an imbalanced dataset	(Aktar et al. 2021), (Ren et al. 2022)
AUC	It stands for Area Under ROC Curve. It measures the entire two dimensional area under ROC curve	(Jolley et al. 2022), (Willette et al. 2022), (Aktar et al. 2021), (Bendavid et al. 2022), (Chowdhury et al. 2022), (Schiaffino et al. 2021), (Song et al. 2022), (Saldivar-Espinoza et al. 2022)
ROC	It is a graphical plot that measures the performance of a classification model at all classification thresholds	(Bendavid et al. 2022), (Jafari et al 2022), (Xue et al. 2020), (Bennouar et al 2021)
Absolute Errors	Absolute error is the magnitude of the difference between predicted value and true value. Used types- MAE, MSE, RMSE, MAPE	(Shams et al. 2021), (Sciannameo et al. 2022), (Basu and Sen 2022)
Specificity	This is also called as True negative rate. The ratio of correct negative predictions to the total predicted true negative and false positive	(Willette et al. 2022), (Saldivar-Espinoza et al. 2022), (Martinez et al 2022)
Misc	Some other performance measures: R^2 metrics, Nomogram, MCC, Quadratic mean, Log loss function, 20-fold cross validation, Plant-Based Diet Score	(Willette et al. 2022), (Aktar et al. 2021), (Shams et al. 2021), (Xue et al. 2020), (Tang et al. 2021), (Merino et al. 2021)

AUC Area under the ROC curve, *ROC* Receiver operating characteristics curve, *MAE* Mean Absolute Error, *MSE* Mean Square Error, *RMSE* Root Mean Square Error, *MAPE* Mean absolute percentage error
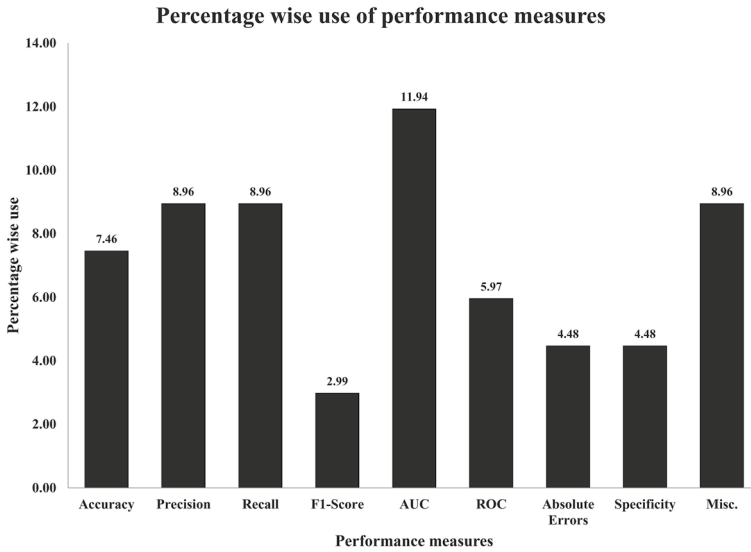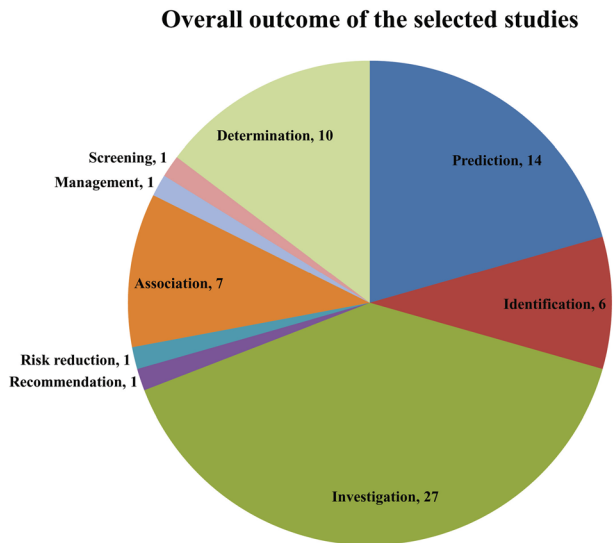
Percentage wise use of performance measures

Fig. 4 Percentage wise use of performance measures

Fig. 5 Overall outcome of the selected studies

Overall outcome of the selected studies

The components of nutritional status either in the form of macro-nutrients or micro-nutrients or other associated indicators should be present somewhere in the experimental setup of the studies. Figure 7 shows the presence of different components of nutritional status in the studies. It was found that the component of nutritional status were present inside the dataset for 7.46% of studies; BMI related presence, food and diet related presence, macro-nutrient (protein, fat, carbohydrate, water) related presence, micro-nutrient (vitamins and minerals) related presence, demographics related presence and obesity related
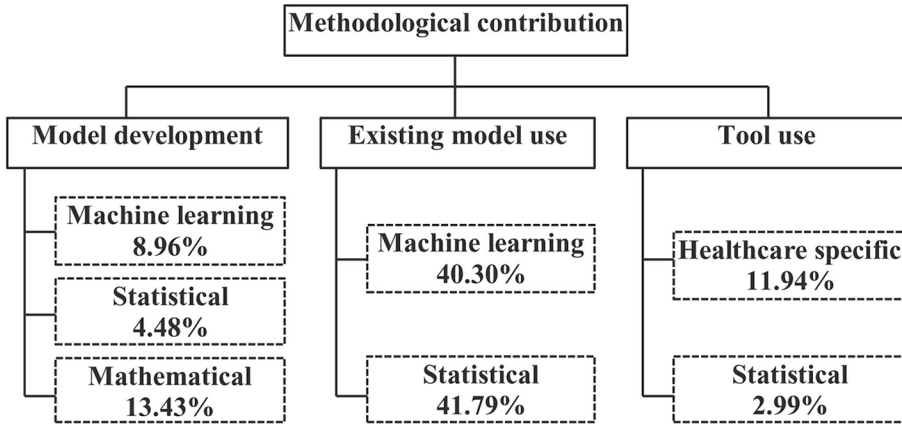
Fig. 6 Methodological contributions of the selected studies

Fig. 7 Presence of various components of nutritional status in the selected studies

presence were found in 11.94%, 13.43%, 11.94%, 28.36%, 2.99% and 4.48% of studies respectively. The components were present as blood profile data in 5.97% of studies and in 7.46% studies it was present in other form. The presence was directly mentioned in 38.81% studies. The details about the presence of different components of nutritional status for each of the individual studies are available in Online Resource 2.

4 Discussion

The main intention of this systematic review was to analyse the studies related to nutritional status and respiratory viral disease that use computational aspects. We further intended to get answers to some research questions listed in Table 1. The individual research questions are addressed in the subsequent sections.

4.1 RQ1: Is it feasible to integrate computational aspects with the studies of nutritional status and respiratory viral diseases?

This research question is about the feasibility check if different computational aspects like artificial intelligence techniques, mathematical models, statistical methods and tools can be used in the studies related to nutritional status and its association with respiratory viral diseases. All the studies included in this review deal with some kind of computational aspect,

nutritional status or component of nutritional status and viral diseases of respiratory system. Now, out of the selected 67 numbers of studies, 66 numbers of the studies belong to the disease called Coronavirus disease 2019 and 1 study belongs to the disease called Middle East Respiratory Syndrome and no study for Swine flu. Swine flu emerged in the year 2009 and Middle East Respiratory Syndrome emerged in the year 2015. During that period, use of computational aspects in healthcare sector was very limited. Though the use of computational aspects in the healthcare sector evolved in early 20's, its use was very limited. It got a bit boost around the year 2013. After that its use continuously grew and during the time of Coronavirus disease it got a sharp boost. As a result, we could get a significant number of studies that uses computational aspects in the studies related to the viral disease and nutritional status or its components. So, by looking into the current boost in the use of computational aspects for healthcare, we can infer that the use of computational aspects in the studies of nutritional status or components and its correlation with respiratory viral diseases is quite feasible. There are ample scopes for exploring correlations of nutritional status or its components with viral diseases of respiratory system by using computational aspects.

4.2 RQ2: What type of data do we need to study the association between nutritional status and respiratory viral diseases?

From the selected studies we found that out of 67 articles 59 (88.06%) numbers of studies worked on processing existing data that were basically collected from the communities or healthcare institutions. 8 (11.94%) numbers of studies did not work on existing collected data. 16.42% studies used formerly created private or publicly available datasets while 71.64% studies used raw data collected from different communities and healthcare organizations. So, to study the association between nutritional status or its components and respiratory viral diseases, either of the ways (using existing data or without using existing data) can be adopted. It depends on what type of study is planned. The outcome of the studies show that various types of studies can be performed that correlate nutritional status or its components and different aspects of viral diseases infecting respiratory system. The most common types of outcomes the works showed are- investigation, prediction, determination, identification, association, screening, management, risk reduction, and recommendation. If we plan to work on investigation, we may prefer raw data like hospital admitted patients, cohort of population. For prediction related works we will prefer large amount of existing historical data or datasets. For works related to determination and identification, we may prefer raw data. For finding some kind of association, we may use mathematical models or combination of both model and existing data. For screening basically raw data will be preferred. For management, risk reduction and recommendation, existing data will be preferred. So, overall we can say that the study related to the association between nutritional status or its components and various aspects of respiratory viral diseases can be performed using datasets or using raw data or even without using existing data.

4.3 RQ3: Is there any contribution of nutritional status on the optimization of infectiological parameters?

Infectiological parameters indicate three main aspects of infectious diseases namely susceptibility, infection and recovery. In the situation of pandemic, to ensure intact of productivity and mitigation of loss, the management will try to provide facilities such that

more and more numbers of susceptible individuals can be allowed to perform day-to-day activities. At the same time the managerial team will focus on minimizing the number of infections and maximizing the recovery. During the situation of pandemic nobody has control over the spread of it. So, the team engaged with the management of pandemic will prefer to have some optimal number of susceptible population, infected population and recovered population within a particular area such that necessary services can be delivered effectively and mitigation measures can be deployed. Usually the approximate number of population within an area is known to the authority. Considering the population of that area to be susceptible, the management can decide how much will be deployed at a time. The disease dynamics can give an idea about the number of infection and recovery. To ease this task, optimization algorithms can be used to get optimal number of susceptible population, infected population, and recovered population within a known range. The optimization may be boosted or impacted by the status of nutrition. A recent study by Hussain and Borah (2022b) mathematically established the relationship among nutritional status, immunity and the infectiological parameters of Coronavirus disease 2019. According to this study, normal nutritional status has positive impact on immunity and the combination of normal nutritional status and strong immunity greatly impacts on increasing the deployment of susceptible individuals, reducing the infection and increasing the recovery. Likewise, malnutrition has negative impact on immunity and the combination of malnutrition and weak immunity impacts on decreasing the deployment of susceptible individuals, increasing the infection and decreasing the recovery. The former is expected and the latter is not expected in the situation of pandemic. So, overall it can be said that optimization of infectiological parameters are impacted by the status of nutrition.

4.4 Future scope and guidance

The current review shows path to some broad areas where new contributions can explore a lot of information. That will eventually add values to the healthcare sector. Some of the gaps where the researchers and healthcare professionals can think about contributing are as follows:

- The overall use of computational aspects shows that mathematical models are used by comparatively less numbers of studies. Alongside the studies from clinical perspectives, the studies can be performed from mathematical perspective as well. Study from mathematical perspectives will open up so many dynamics of diseases and those will be easy to understand and to apply in practical applications.
- For development of artificial intelligence models very large amount of data is needed. The more the training data the better for the model. Application of artificial intelligence techniques will help healthcare sector in so many ways like cost reduction, time reduction, easy accessibility. So, researchers can think about collecting clinical data and create datasets. It is a bit tough to get medical and healthcare data because the authorities show disagreement in revealing patient data. There are scopes for collecting healthcare data and creating datasets.
- Nutritional status of our body has association with all functionalities. All the happenings of our body can be directly or indirectly integrated with nutritional status or its components. So, association of nutritional status or its components with different types of diseases (infectious or non-infectious) can be studied.

- The outcomes of the selected studies show that there are ample scope in the studies related to management, risk reduction and recommendation. There are many managerial, risk reduction and recommendation tasks associated with both infectious and non-infectious diseases. Researchers can think about studies related to recommending risk reduction activities and optimal management of various aspects associated with diseases.

4.5 Limitations

Though we have reviewed the articles by following standard guidelines, yet there are some limitations. Firstly, we have retrieved the records only from PubMed. Though this database is considered to be one of the best databases for articles related to medical science, yet there are possibilities that in other databases we could find some high quality relevant studies. That would have improved the outcome of this review. Secondly, the year wise distribution of the selected studies shows that most of the studies are from three different years only. Though we have searched for articles within a range of fifteen years, yet the selected articles reflect the contribution from four years only. Searching other relevant databases could have provided studies covering more years. Thirdly, we considered limited numbers of computational aspects during the searching of articles. Use of more computational aspects could have retrieved more relevant studies and that could eventually improve the outcome of this review.

Apart from the limitations of the review process, identification of limitations and related gaps from the selected studies are vital for possible scientific contributions. Most of the studies listed out the limitations either as a separate section or as a part of discussion or even as in conclusion that was left for future work. A very small numbers of studies did not mention the limitations in the text. For those studies we identified the limitations. The complete list of limitations for each individual studies are available in Online Resource 2. The limitations were primarily related to various aspects of the concerned study. It is difficult to bring the limitations under some category as the limitations are too different from one another. However some limitations are found to be related to small sample size, imbalanced data, dependence on single parameter, early stage data collection, confinement within a limit, possible biased manual data collection, not using real data and testing on limited numbers of models.

5 Conclusions

Computational aspects in the studies of nutritional status and infectious disease can open up possibilities to easy understanding of various relations and associations. This systematic review tried to extract data from the articles related to the use of various computational aspects on the studies of nutritional status or its components and viral diseases of respiratory system. The review was confined within the years 2007 and 2022. The pre-set eligibility criteria allowed to keep only 67 numbers of studies out of 1713 records retrieved from PubMed. The selected studies were outcome based and mainly worked on investigation, prediction, determination, identification, association, screening, management, risk reduction, and recommendation. The studies used computational aspects like machine learning techniques, neural network and deep learning techniques, mathematical models, statistical methods and tools. Some of the studies contributed by developing machine

learning, statistical and mathematical models. A significant numbers of studies used existing machine learning and statistical models. A few studies used healthcare specific tools and statistical tools. Some of the studies used existing data and some of the studies did not use existing data. Maximum number of studies used raw data collected from some communities and healthcare organizations. Some of the studies used formerly created private or publicly available datasets. This review clearly answered the research questions about feasibility of the use of computational aspects with the studies about nutritional status or its components and viral diseases infecting respiratory system, types of data requirement and its necessity, and about the impact of nutritional status on optimization of infectiological parameters. This review also opened up a few gaps where researchers and healthcare professionals can think about possible contributions.

6 Supplementary information

Two online resource files namely "ESM_1" and "ESM_2" are associated with this study. Online Resource 1 consists of primary keywords/terms and search queries that were used to retrieve the records while Online Resource 2 consists of characteristics of the included studies.

Data availability Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

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