Two novel nomograms for predicting the risk of hospitalization or mortality due to COVID-19 by the naïve Bayesian classifier method

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Abstract
Coronavirus disease 2019 (COVID-19) has become a global pandemic that has affected millions of people worldwide. The presence of multiple risk factors for COVID-19 makes it difficult to plan treatment and optimize the use of medical resources. The aim of this study is to determine potential risk factors for hospitalization or mortality in patients with COVID-19 via two novel naïve Bayesian nomograms. The publicly available COVID-19 National data published by the Mexican Ministry of Health through the “Dirección General de Epidemiología” website was analyzed. Univariable logistic regression was utilized to identify potential risk factors that may affect hospitalization or mortality in patients with COVID-19. The naïve Bayesian classifier method was implemented to predict nomograms. The nomograms were verified by the area under the receiver operating characteristic curve (AUC), classification accuracy (CA), F1 score, precision, recall, and calibration plot. A total of 979,430 patients (45.3 ± 15.9 years old, and 51.1% male) tested positive for COVID-19 from January 1 to November 22, 2020. Among them, 22.3% of the patients required hospitalization and 99,964 patients (9.8%) died. The most important risk factors to predict the probability of hospitalization and mortality were pneumonia, age, chronic kidney failure, chronic obstructive respiratory disease, and diabetes. The performance measures demonstrated good discrimination and calibration (hospitalization: AUC = 0.896, CA = 0.880; mortality: AUC = 0.903, CA = 0.899). Two novel nomograms to estimate the risk of hospitalization and mortality were proposed, which could be used to facilitate individualized decision-making for patients newly diagnosed with COVID-19.

KEYWORDS
COVID-19, hospitalization, mortality, nomogram, prediction, risk factor

1 INTRODUCTION

The coronavirus disease 2019 (COVID-19) was first observed in Wuhan, China in December 2019, and declared as a global pandemic on March 11, 2020.1 By the end of November 2020, more than 64 million confirmed cases including more than 1.4 million deaths were reported.2 The presence of comorbidities and older age are risk factors for hospitalization and mortality in COVID-19 patients.3 Some nomograms have been developed to determine risk factors for COVID-19 but the sample sizes were relatively small.4–6 Therefore, more comprehensive studies are needed to be developed and validated.
A nomogram is a graphical representation method that has been used in medicine to predict the probability of any disease or risk of death through risk factors. This method provides the identification of the most important risk factors and calculation of the individualized death through risk factors. This method provides the identification of used in medicine to predict the probability of any disease or risk of

Statistical models, especially logistic regression or Cox proportional hazards regression are generally used to build a nomogram. On the other hand, the naïve Bayesian classifier is a powerful classification technique to compose predictive models despite simple and easy calculations. It is based on Bayes' theorem with the assumption of conditional independence of features given the class. Although this feature seems to be a disadvantage, many studies have reported high conditional independence of features given the class. Let \( X \) be a set of attributes. Based on Bayes theorem,

\[
P(C = 1 | X) = \frac{P(C = 1) \prod P(x_i | C = 1)}{P(X)}
\]

\(1\) is the posterior probability of the target class. Therefore, the odds of \( C = 1 \) can be obtained as follows:

\[
\text{odds} = \frac{P(C = 1 | X)}{P(C = 0 | X)} = \frac{P(C = 1) \prod P(x_i | C = 1)}{P(C = 0) \prod P(x_i | C = 0)}
\]

\[
= \frac{P(C = 1)}{P(C = 0)} \prod P(x_i | C = 1) \prod P(x_i | C = 0)
\]

(2)

After taking log of odds, the Equation (2) transforms to logit,

\[
\logit P(C = 1 | X) = \log \left( \frac{P(C = 1)}{P(C = 0)} \right) + \sum_i \log \left( \frac{P(x_i | C = 1)}{P(x_i | C = 0)} \right)
\]

\[
= \log P(C = 1) + \sum_i \log \left( \frac{P(x_i | C = 1)}{P(x_i | C = 0)} \right)
\]

(3)

where LR is the likelihood ratio. The summation term of the right side of Equation (3) is used for the construction of a nomogram that relates the feature values to the point score. It estimates the ratio of posterior to prior probability given the feature value \( x_i \). Finally, to get \( P(C = 1 | X) \):

\[
P(C = 1 | X) = \frac{1}{1 + e^{-\log P(C = 1) - \sum_i \log LR(x_i)}}
\]

(4)

Equation (4) is the final probability value \( P(C = 1 | X) \) of \( C = 1 \) class when the attribute value is \( X \).

2 | MATERIALS AND METHODS

2.1 Dataset

In this study, the publicly available COVID-19 dataset was used released by the Mexican Ministry of Health via the "Dirección General de Epidemiología" website (https://www.gob.mx/salud/documentos/datos-abiertos-152127). A total of 2,559,993 patients (over 18 years) were admitted to the hospitals on suspicion of COVID-19 in Mexico between January 1 and November 22, 2020. Twelve risk factors (features) were included in the analyses that were age, gender, smoking status, the presence of pneumonia, diabetes, obesity, hypertension, cardiovascular, chronic obstructive respiratory disease (CORD), chronic kidney failure, immunosuppressed, and asthma.

2.2 Naïve Bayesian classifier

The naïve Bayesian classifier determines the probability for a particular class by using Bayes' theorem and assumes that the attribute values are independent of each other. Let \( C \) be a dependent binary variable where 0 indicates the other class and 1 the target class, \( X = \{x_1, x_2, ..., x_n\} \) be a set of attributes. Based on Bayes theorem,

\[
P(C = 1 | X) = \frac{P(C = 1) \prod P(x_i | C = 1)}{P(X)}
\]

(1)

Let \( x_i \) show attribute values where \( i = 1, 2, ..., n \) is the number of attributes and \( j = 1, 2, ..., m \) is the number of categories for each attribute. LR\( (x_{ij}) \) values are obtained as follows:

\[
LR(x_{ij}) = \frac{P(x_i | C = 1)}{P(x_i | C = 0)}
\]

(5)

By using Equation (5), the points of each attribute \( a_i \) are calculated as follows:

\[
a_i = \frac{\log LR(x_{ij})}{\max \log LR(x_{ij})} \times 100.
\]

(6)

In Equation (6), the denominator describes the largest attribute value among the absolute values of the log-likelihood ratios of all attribute values, which means the most important attribute values for target class \( C \). The numerator describes the log-likelihood ratio of the \( j \)th category in attribute \( i \). As a result, the points line is constructed by Equation (6).

By using Equation (6), \( a_i \) for each category of attribute values can be calculated. The total points value is obtained by summing the
points of the corresponding categories (Equation 7) and so, the total points line can be drawn.

\[
\text{Total } a_i = \frac{\sum \log \text{LR}(x_i)}{\max_i |\log \text{LR}(x_i)|} \times 100. \tag{7}
\]

The probabilities corresponding to the total points’ values are obtained by substitution of Equation (7) into Equation (4).

\[
P(C = 1 | X) = \frac{1}{1 + e^{-\log \text{LR}(C = 1) \cdot \text{Total} \cdot a_i / \max_i |\log \text{LR}(x_i)|}}. \tag{8}
\]

### 2.4 Evaluation of the performance of the nomogram

A stratified 10-fold cross-validation method was implemented through the data training process. For this purpose, the data was divided into 10 folds. Onefold was considered as a test subset and ninefold as a training subset. Five different discrimination metrics were used which are ROC curve, CA, F1 score, precision, and recall. Among them, the ROC curve is plotted against the 1-specificity for various cut-off points. As the curve close to the upper left corner of the graph, the probability of a true positive test result is higher than the probability of a false-negative test result. AUC, defined as the integral of the area between the ROC curve and the (1-specificity) x-axis, is utilized to assess the accuracy. The AUC differs between 0.5 and 1.0, where 0.5 denotes bad discrimination and 1 denotes perfect discrimination.\(^{12}\) CA is the ratio of the correctly predicted observations to the total number of predictions. Precision is calculated as correctly predicted positives divided by the total predicted positives. The recall is the number of true positive observations divided by the total number of true positives and the number of false negatives.

Finally, the F1 score is the weighted average of precision and recall metrics. Calibration of the nomograms was assessed by calibration plots that are drawn by observed probabilities against predicted probabilities calculated with the nomogram. As the observed outcomes are close to the predicted outcomes, this means that there is a concordance between curves.\(^{13}\) Finally, decision curve analysis (DCA) was performed to assess the clinical usefulness of the nomograms. The graph shows the clinical net benefit according to various threshold probabilities. The net benefit is calculated as follows:

\[
\text{Net benefit} = \text{True positive rate} - \frac{\text{False positive rate} \times \text{Threshold probability}}{1 - \text{Threshold probability}}.
\]

There are two reference lines for "intervention-for-all patients" (light gray line) and "intervention-for-none" (thin black line) in the graph. A nomogram should be found superior to both references to justify being used in clinical practice.\(^{14}\)

### 2.5 Statistical analysis

Logistic regression analysis was performed by IBM SPSS (Version 23). Nomograms, ROC curves, and discrimination measures were obtained by Orange software version 3.27.1. Calibration curves and DCA were plotted using R software version 4.0.0 ("rms" and "rmda" packages, respectively). Continuous variables were expressed as mean ± standard deviation and categorical variables summarized with frequency and percentage. A two-sided p value of less than .05 was considered statistically significant.
3 | RESULTS

A total of 2,559,993 suspected cases of COVID-19 (over 18 years) were admitted to the hospitals in Mexico between January 1 and November 22, 2020. A total of 979,430 patients (38.3%) were diagnosed with COVID-19. Among them, 22.3% hospitalized, and 9.8% of individuals died. The mean age of the patients was 45.3 ± 15.9 years, and 51.1% of them were male. Descriptive statistics of hospitalization and mortality status of COVID-19 patients are summarized in Table 1.

Univariable logistic regression showed that gender, age, the presence of pneumonia, diabetes, CORD, asthma, immunosuppressed, hypertension, cardiovascular, obesity, chronic kidney failure, and smoking were associated with risk of hospitalization (Model 1) or mortality (Model 2) due to COVID-19 (all p < .001). The most important risk factor for both models was pneumonia. Accordingly, there was a 57.06-fold and 22.20-fold increase in the risk of hospitalization and mortality, respectively (Table 2).

Two nomograms for predicting the probability of hospitalization or mortality were constructed via the naïve Bayes classifier method. A typical nomogram comprises a point line (topmost line, range from −100 to 100) to calculate each risk factor’s point, straight lines for each risk factor, a total point line, and finally a probability line. As the importance of an attribute (risk factor) increases, the length of the point line is longer. Attribute values for each risk factor in the nomogram are assigned points via the point line \( a_{ij} \). The probability of the risk is estimated by summing points of attribute values (total \( a_{ij} \)) and is matched to the probability through total the point line, and the probability line.15

In the current study, the risk factors were sorted in order of absolute importance (the length of the point line) in the nomograms. Accordingly, the most important risk factors to predict the probability of hospitalization were pneumonia (yes: 100 points), age (>55: 40 points), chronic kidney failure (yes: 62.75 points), CORD (yes: 54.71 points), diabetes (yes: 40 points) (Figure 1A). Similarly, the most important risk factors to predict the probability of mortality were age (>55: 47.86 points), pneumonia (yes: 74.12 points), chronic kidney failure (yes: 69.69 points), CORD (yes: 61.35 points), and diabetes (yes: 43.87 points) (Figure 2A).

The calibration curves verified a good consistency for predicting mortality and the perfect consistency for predicting hospitalization (Figures 1C and 2C). The discrimination of the constructed nomogram evaluated with the AUC, CA, F1, precision, and recall metrics showed an almost excellent performance (Table 3). The clinical usefulness of the nomograms was evaluated by DCA. The analysis revealed that both nomograms had higher net benefit than "intervention-for-all-patients" or "intervention-for-none" as well as the nomogram in predicting hospitalization had more benefit than in predicting mortality (Figures 1D and 2D).

4 | DISCUSSION

In this study, two novel nomograms for predicting the risk of hospitalization and mortality in COVID-19 patients were developed and validated. Although various nomograms have been developed by studies on COVID-19, we have analyzed a larger sample size (979,430 patients) via the naïve Bayesian classifier technique.16-18 The predictive validity of the nomograms was verified with calibration and discrimination.

Although many studies have utilized logistic regression analysis for building nomograms, the naïve Bayesian nomogram has

### TABLE 2

Univariable logistic regression analysis predicting hospitalization (Model 1) and mortality (Model 2)

| Variables                  | Model 1 (n = 979,430) |        |        |        | Model 2 (n = 218,399) |        |        |        |
|----------------------------|-----------------------|--------|--------|--------|-----------------------|--------|--------|--------|
|                            | Odds ratio            | 95% Confidence interval | p Value | Odds ratio | 95% Confidence interval | p Value |
| Pneumonia (Ref: no)        | 57.06                 | 56.18  | 57.95  | <.001   | 22.20                 | 21.85  | 22.55  | <.001  |
| Chronic kidney failure (Ref: no) | 6.98                 | 6.77  | 7.20  | <.001   | 6.42                 | 6.23  | 6.62  | <.001  |
| CORD (Ref: no)             | 5.39                  | 5.20  | 5.58  | <.001   | 5.05                 | 4.87  | 5.24  | <.001  |
| Diabetes (Ref: no)         | 4.53                  | 4.48  | 4.58  | <.001   | 4.44                 | 4.38  | 4.51  | <.001  |
| Hypertension (Ref: no)     | 3.85                  | 3.81  | 3.89  | <.001   | 4.35                 | 4.29  | 4.41  | <.001  |
| Cardiovascular (Ref: no)   | 3.74                  | 3.64  | 3.86  | <.001   | 3.78                 | 3.66  | 3.91  | <.001  |
| Immunosuppressed (Ref: no) | 3.29                  | 3.17  | 3.43  | <.001   | 2.97                 | 2.84  | 3.11  | <.001  |
| Gender (Ref: female)       | 1.62                  | 1.61  | 1.64  | <.001   | 1.77                 | 1.75  | 1.80  | <.001  |
| Obesity (Ref: no)          | 1.60                  | 1.58  | 1.62  | <.001   | 1.60                 | 1.57  | 1.62  | <.001  |
| Age                        | 1.07                  | 1.07  | 1.08  | <.001   | 1.08                 | 1.08  | 1.09  | <.001  |
| Smoking (Ref: no)          | 1.04                  | 1.02  | 1.06  | <.001   | 1.08                 | 1.05  | 1.10  | <.001  |
| Asthma (Ref: no)           | 0.85                  | 0.82  | 0.87  | <.001   | 0.77                 | 0.73  | 0.81  | <.001  |

Abbreviations: CORD: chronic obstructive pulmonary disease; Ref: reference.
several advantages. First, the naïve Bayesian nomogram considers negative and positive influences of the point values of risk factors (range between −100 and 100). Conversely, the logistic regression nomogram depicts only negative influence over risk factors. Second, the naïve Bayes nomogram may be used in the presence of missing data in contrast to the logistic regression method. Finally, the Bayesian nomogram is based on simple calculation and principles compared to the logistic regression nomogram. Therefore, naïve Bayes nomogram has been preferred in recent years.\textsuperscript{11,19}

The results demonstrated that pneumonia and age factors had the greatest influence on hospitalization (range, −35 to 100) and mortality (range, −100 to 50), respectively. On the other hand, the smallest influencing factor was smoking status for both nomograms. The most significant risk factor was pneumonia for hospitalization (100 points) and mortality (74.12 points). Coronavirus can affect
multiple organs but the most common indication for hospitalization is viral pneumonia. Otherwise, some studies have reported that COVID-19 causes a higher mortality rate in individuals aged 50 years or older. In the United States, the mortality was ranging from 3% to 11% among persons aged 65–84 years, 1%–3% among persons aged 55–64 years. Another study examining COVID-19 reports from 16 countries showed that individuals aged 65 years or older had about 62 times and those aged 55–64 years had about 8.1 times
higher mortality rate compared with individuals ages 54 years or younger.24

This study indicated that common comorbidities were associated with COVID-19 related hospitalization and mortality. Although the presence of chronic kidney failure, CORD, cardiovascular, immunosuppressed risk factors increased the risk of COVID-19 for hospitalization or mortality, the absence of these risk factors had little or no effect. Conversely, the absence of diabetes, hypertension, obesity decreased the risk for both conditions. These comorbidities have been associated with COVID-19 in previous studies.25-28

In accordance with the literature,29 our results showed that being male increased the risk of mortality. Interestingly, according to our analysis, the presence of asthma appears to be a risk-reducing factor, but its influencing factor was very small. Indeed, the relationship between asthma and COVID-19 is still uncertain.30 Smoking does not seem to have a notable increasing or decreasing effect on risk factors in this study. Surprisingly, Farsalinos et al.31 stated that nicotine may be considered as a potential treatment option.

This study has some limitations. The dataset lacks some information such as laboratory results and treatment of comorbidities, which could have been useful to better understand the clinical pattern of COVID-19. In conclusion, the proposed Bayesian nomograms can be used to assess patients with COVID-19 symptoms and to facilitate medical decision-making.

CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are openly available in the Mexican Ministry of Health via the "Dirección General de Epidemiología" at https://www.gob.mx/salud/documentos/datos-abiertos-152127.

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How to cite this article: Karaismailoglu E, Karaismailoglu S. Two novel nomograms for predicting the risk of hospitalization or mortality due to COVID-19 by the naïve Bayesian classifier method. *J Med Virol*. 2021;93:3194-3201. https://doi.org/10.1002/jmv.26890