Study to identify predictor of hypoxia in COVID-19 infection: A single-center, retrospective study

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ABSTRACT

Background: Given the limited availability of critical care resources in our country, it is important to identify reliable predictors of hypoxia in patients with COVID-19 infection. We thus sought to compare differential predictive values of demographic, clinical, and laboratory measures and identify predictor for hypoxia in COVID-19 infection. Materials and Methods: This is a single-center retrospective analysis of patient admitted at AIIMS Patna between 15th June and 15th Aug. All the patients who had oxygen saturation less than 94% grouped under hypoxic group while ≥94% in non-hypoxic group at room air. Statistical analysis: Logistic regression model used to determine the predictor of hypoxia in COVID-19 infection. Results: Total 73 were used for analysis. Study patients had a mean age of 55.05 ± 12.7 year, of whom 78.08% were male (57/73). 39 (53.42%) patients were found hypoxic at time of admission while 34 (46.56%) were non-hypoxic. Presence of dyspnoea significantly found more frequently in hypoxic patients (P = 0.0003). Patients with O2 saturation of less than 94% have more likely to have diabetes (P = 0.002) and hypertension (P = 0.02). Analysis of laboratory variables showed that leucocytosis (P = 0.007) and neutrophilia (P = 0.01) were significantly higher in hypoxic group compare to non-hypoxic group. Univariate regression model showed patient with any one comorbidities, diabetes, or hypertension was found as strong risk factor for hypoxia after COVID-19 infection (P < 0.05). Conclusion: This is the first study to identify predictor of hypoxia in COVID-19 infection. Among lab variable, leucocytosis, neutrophilia, lymphocytopenia, and CRP (>27.5 mg/L) were found as predictor of hypoxia in COVID infection.

Keywords: Comorbidity, COVID-19, hypoxia, inflammatory marker

Introduction

In December 2019, an outbreak of coronavirus disease 2019 (COVID-19), which was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), broke out in Wuhan, China. The World Health Organization (WHO) declared it a significant threat to international health. Studies showed that 14% of COVID-19 associated pneumonia cases are severe, and 5% of infected patients require intensive care. COVID-19 affect multiple system but the respiratory system is affected most commonly and severely affected. So, measuring of respiratory function would more likely relate to outcomes, particularly in a rapidly progressive disease condition. Therefore, it focused particularly on dyspnoea and systemic oxygenation as potential prognostic biomarkers. Given the limited availability of critical care resources in our country and as most of the patients are home quarantine after infection, it is important to identify simple but reliable predictors of hypoxia in patients with COVID-19 infection. We thus sought to compare differential predictive values of demographic, clinical, and laboratory measures and identify predictor for hypoxia in COVID-19 infection.

Materials and Methods

This is a single-center retrospective cohort study. After ethical approval (AIIMS/Pat/IEC/2020/552), we enrolled all patients...
with COVID infection, diagnosed by RT-PCR and got admitted in pulmonary and urology ward at AIIMS Patna between 15th June and 15th Aug.

Inclusions criteria
1. All the confirmed case of COVID-19 infection by RT-PCR and discharged in stable condition
2. Age >15 years

Exclusion criteria
1. Patient who expire during hospitalization
2. Patient who were transferred to ICU

All the patients who were admitted and treated according to treatment guideline released by Government of India.\[4\] The following data were collected from the case history and available clinical investigation of the patients by manual as well as electronic data recordkeeping system: (i) demographic parameters (age, sex) of the patients; (ii) presenting symptoms and duration of symptoms; (iii) presence of comorbidities [hypertension, diabetes, coronary artery disease, malignancy, neurologic diseases, chronic obstructive pulmonary disease, bronchial asthma, chronic kidney diseases (CKDs), chronic liver disease (CLD), etc.]; (iv) any available investigations (complete blood count, liver and kidney function tests, electrolytes). All the patients who had oxygen saturation less than 94% grouped under hypoxic group while ≥94% in non-hypoxic group at room air.

Statistical analyses
Continuous data are reported as median and interquartile range (IQR), and categorical data are expressed as frequency and percent-age. Student t-tests and Chi-square were used to compare continuous and categorical data between patients with SpO2 values less than 94% vs SpO2 values of 94% or greater after oxygen supplementation. Clinical and lab characteristics of hypoxia and non-hypoxia COVID-19 patients were compared, and we used a logistic regression model to determine the predictive factors of hypoxia in COVID-19 infection.

Results
Total 94 adult patients were admitted in given period while 73 were used for analysis. 21 patients either transferred to ICU or expire or data could not be retrieved. Study patients who had a mean age of 55.05 ± 12.7 year, of whom 78.08% were male (57 of the 73 patients). 39 (53.42%) patients were found hypoxic at time of admission while 34 (46.56%) were non-hypoxic. Male predominance is slightly higher in non-hypoxic group (82.35%) than hypoxic patients (74.35%). Fever (68.1%), cough (59.6%) and shortness of breath (71.9%) were the most common presenting symptoms. Dyspnea significantly found more frequently in hypoxic patients (51.28 vs. 11.76%, \(P = 0.0003\)). Patients with O2 saturation of less than 94% have more likely to have diabetes (38.46% vs. 17.64%, \(P = 0.002\)), hypertension (41.02% vs. 26.47% \(P = 0.02\)), and hypothyroidism (12.82% vs. 0% \(P = 0.03\)). Analysis of laboratory variables showed that Leukocytosis (\(P = 0.007\)) and neutrophilia (\(P = 0.01\)) were significantly higher in hypoxic group compare to non-hypoxic group. Among blood inflammatory marker, only CRP (>27.5 mg/dl) was significantly higher in hypoxic patients (\(P = 0.05\)). Inflammatory marker like serum LDH, procalcitonin, and Interleukin-6 were higher in hypoxic group but statistically not significant (\(P > 0.05\)) [Table 1]. When we compare absolute value of Lab parameters, Total leukocyte count, Neutrophil, serum ferritin, and LDH were significantly elevated in hypoxic group (\(P < 0.05\)) [Table 2].

We used univariate regression model to analyze predictors of hypoxia in COVID-19 infection. Patient with any one comorbidities, diabetes, or hypertension was found strong risk factor for hypoxia after COVID-19 infection (\(P < 0.05\)). Presence of dyspnea was also found as strong risk factor for occurrence of hypoxia. Among lab variable, Leukocytosis, neutrophilia, lymphocytopenia, and CRP (>27.5 mg/L) were found as predictor of hypoxia in COVID infection (\(P < 0.05\)) [Table 3].

Discussion
The clinical spectrum of COVID-19 infection varied from asymptomatic infection to mild upper respiratory tract symptoms, and severe viral pneumonia with respiratory failure and even death.\[3\] Patients with a mild disease may not initially require hospitalization, and advised for home isolation with close monitoring of dyspnea and oxygenation. Patients are classified under moderate category when respiratory rate of more than or equal to 24 and oxygen saturation (SpO2) of less than 94% on room air (range 90–94%).\[4\] Such group of patients or severe disease generally require hospitalization and oxygenation. It is important to identify, which patients will developed severe disease or hypoxia after COVID infection. Hypoxia on admission has been identified as predictor of in-hospital mortality.\[6\] This study was design to identify the risk factor for hypoxia after COVID infection. 53.42% of our study patients developed hypoxia with O2 saturation of less than 94% and require oxygen supplementation. Fever and cough were found more frequently in hypoxic group but statistically not significant (\(P < 0.05\)). There was significantly higher proportion of patients in hypoxic group who had dyspnea (\(P < 0.05\)). Previous study also found dyspnea as indicators of severe COVID-19 disease.\[9\] It is very important to understand by primary care physician that severity of hypoxia at time admission can vary, depending upon time of presentation, which are affected by their awareness of warning signs, transportation issue, hospital fear, and other limitations to timely access to emergency medical care. So it is very important to encourage patients with COVID-19 infection to attend the hospital early in the course of disease. Hypertension was found as most common comorbidity followed by Diabetes which is similar to other study.\[10\] Hypoxic patients were found more likely to have Diabetes and hypertension (\(P < 0.05\)).

Biochemical analysis showed that Leukocyte count and neutrophils were significantly higher in hypoxic group compare to non-hypoxic
This study finds out important risk factor for hypoxia in COVID-19 infection. We found comorbidity such as diabetes, hypertension, and lab variable like leucocytosis, neutrophilia, Lymphopenia, and inflammatory marker like higher CRP associated with development of hypoxia.

There are certain limitations of the study. Firstly, considering this was a single-center, retrospective study with limited sample size, avoiding bias regarding patient distribution is considered difficult. Longitudinal observational study would be more reliable for identification of risk factors for hypoxia. Another limitation was inability to carry out a multivariable analysis to account for the presence of several symptoms, comorbidities, and potential confounders.

**Conclusion**

This is the first study to identify predictor of hypoxia in COVID-19 infection. Patient with any one comorbidities, diabetes, or hypertension was found strong risk factor for hypoxia after COVID-19 infection.
Among lab variable, Leucocytosis, neutrophilia, lymphocytopenia, and CRP (>27.5 mg/L) were found as predictor of hypoxia in COVID infection. It is important to identify hypoxia in early stage to reduce mortality in resource limited setting.

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Table 2: comparison of lab variable between hypoxic and non-hypoxic covid 19 infection

| Laboratory variable | Hypoxic covid 19 infection (n=39) | Non-Hypoxic covid 19 infection (n=34) | P |
|---------------------|----------------------------------|--------------------------------------|---|
| Haemoglobin         | 11.46±2.0                        | 10.39±2.01                           | NS |
| TLC                 | 10.32±4.56                       | 7.54±4.54                            | 0.006 |
| Platelet            | 214.42±97.58                     | 187.56±97.54                        | NS |
| Neutrophil          | 82.55±11.00                      | 74.82±10.93                          | 0.002 |
| Lymphocyte          | 13.18±7.95                       | 19.60±9.71                           | 0.01 |
| STB                 | 1.17±3.07                        | 2.42±2.83                            | NS |
| ALT                 | 116.53±108.37                    | 106.87±106.62                       | NS |
| AST                 | 106.43±75.29                     | 81.90±74.77                          | NS |
| Urea                | 65.37±86.10                      | 96.00±86.10                          | NS |
| Creatinine          | 1.98±2.92                        | 4.05±4.02                            | NS |
| CRP                 | 107.79±89.82                     | 66.79±89.97                          | 0.05 |
| Ferritin            | 966.94±804.09                    | 577.70±807.52                       | 0.04 |
| LDH                 | 891.94±290.94                    | 735.53±293.55                       | 0.02 |
| PCT                 | 1.08±1.50                        | 0.28±1.39                            | NS |
| D-Dimer             | 2.00±2.78                        | 1.02±2.80                            | NS |

Table 3: Univariate regression analysis to identify risk factor for hypoxia after covid 19 infection

| Risk factor                  | OR (95% CI) | P     |
|------------------------------|-------------|-------|
| Age >60 years                | 1.34 (0.55-3.27) | NS    |
| Any one comorbidity          | 3.26 (1.21-8.73) | 0.01  |
| DM                           | 2.91 (0.9781-8.69) | 0.05  |
| Hypertension                 | 3.30 (1.16-9.38) | 0.02  |
| Fever                        | 1.26 (0.51-3.10) | NS    |
| Dyspnoea                     | 7.89 (2.33-26.67) | 0.0009 |
| Leucocytosis                 | 4.48 (1.43-14.02) | 0.01  |
| Neutrophilia                 | 3.22 (1.21-8.52) | 0.01  |
| Lymphopenia                  | 6.12 (1.77-21.15) | 0.004 |
| Ferritin (>500 ng/ml)        | 2.43 (0.93-6.34) | 0.06  |
| CRP (>27.5)                  | 2.53 (0.98-6.54) | 0.05  |
| PCT (>0.2 ng/ml)             | 2.61 (0.8717-7.83) | NS    |

OR odds ratio, NS Not significant, Laboratory data (Total Leukocyte count, Lymphocyte, Ferritin and CRP were dichotomized based on conventional clinical cut off values.

Conflicts of interest
There are no conflicts of interest.

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