Etiology and Outcomes of ARDS in the Elderly Population in an Intensive Care Unit in North India

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ABSTRACT

Background: Whether age would impact the outcomes in subjects with acute respiratory distress syndrome (ARDS) remains unclear. Herein, we study the effect of age as a predictor of mortality in ARDS.

Materials and methods: We categorized consecutive subjects with ARDS as either ARDS_{elderly} (age >65 years) or ARDS_{nonelderly} (age ≤65 years) admitted to the respiratory intensive care unit (ICU) of a tertiary care hospital in North India between January 2007 and December 2019. We compared the baseline clinical and demographic characteristics, lung mechanics, and mortality between the two groups. We also analyzed the factors predicting ICU survival using multivariate logistic regression analysis.

Results: We included 625 patients (ARDS_{elderly} 140 (22.4%) and ARDS_{nonelderly} 485 (77.6%)) with a mean (standard deviation) age (56.3% males) of 40.6 (17.8) years. The ARDS_{elderly} were more likely (p = 0.0001) to have the presence of any comorbid illness compared to ARDS_{nonelderly}. The elderly subjects had significantly higher pulmonary ARDS than the younger group. The severity of ARDS was however, similarly distributed between the two study arms. There were 224 (35.8%) deaths, and the mortality was significantly higher (p = 0.012) in the ARDS_{elderly} than the ARDS_{nonelderly} (ARDS_{elderly} vs ARDS_{nonelderly} 45 vs 33.2%). On multivariate logistic regression analysis, the baseline sequential organ failure assessment scores, presence of pulmonary ARDS, and the development of new organ dysfunction were the independent predictors of mortality.

Conclusion: The outcomes in subjects with ARDS are dependent on the severity of illness at admission and the etiology of ARDS rather than the age alone.

Keywords: Acute respiratory distress syndrome, Elderly, Pneumonia, Respiratory failure, Sepsis.

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INTRODUCTION

Acute respiratory distress syndrome (ARDS) is associated with acute onset (<7 days) hypoxemic respiratory failure with bilateral opacities on chest radiograph, either due to the injury to the lung parenchyma or the pulmonary vasculature. 1 ARDS is subclassified as mild (200 < PaO_{2}/FiO_{2} ratio ≤300), moderate (100 < PaO_{2}/FiO_{2} ratio ≤200), or severe (PaO_{2}/FiO_{2} ratio ≤100) based on the degree of hypoxemia. 2 The mortality increases from 27% to as high as 45% with increasing severity of ARDS. 2 Apart from the severity of hypoxemia, several other factors affect ARDS outcomes, including the driving pressure, arterial PaCO_{2}, the strategy used for mechanical ventilation, and others. 3-7 There is limited information regarding the effect of age on mortality in ARDS. 5-10

Most clinical trials generally exclude elderly subjects with ARDS. In fact, major trials of ARDS do not address the issue of age-related mortality in ARDS. 5,11,12 Previous trials have merely mentioned the mean age in comparator groups and have not explored the mortality in the elderly. 7,11,12 With increasing global age, the proportion of elderly ARDS is likely to increase in the intensive care units (ICUs). 13 Although the principles of ARDS management are similar in elderly patients, the resolution of ARDS and the outcomes might be different in the elderly population. The elderly subjects have an age-related decline of the physiological reserve and a higher prevalence of comorbid illness. 14,15 These changes further enhance the stress due to acute illnesses, thereby increasing the risk of mortality in critically ill elderly patients. 15,16 We hypothesized that old age would independently affect the outcomes in subjects with ARDS. Our objective was to compare the clinical characteristics and the ICU outcomes of elderly (age >65 years) subjects with ARDS.

MATERIALS AND METHODS

We included all individuals diagnosed with ARDS admitted to the intensive care unit of Department of Pulmonary Medicine of our institute between February 1, 2001 and December 31, 2019. We use a specifically designed computer software to prospectively enter the patient data. 17,18 We calculated the acute physiology and chronic health evaluation (APACHE II) scores and sequential organ failure assessment (SOFA) scores using baseline values. Each subsequent day in respiratory intensive care unit (RICU) was calendar day timed from 8:00 a.m. to 8:00 a.m. of the next day. We calculated the delta SOFA as described previously. 19 We were granted a waiver for informed consent due to anonymized data’s retrospective use by the Institute Ethics Committee.
We used the American-European Consensus Conference criteria for acute lung injury and ARDS (before January 1, 2013) and Berlin definition (after 2013) for diagnosing ARDS. All the patient records were screened for study inclusion. We excluded repeat ICU admissions from the analysis. We used a low tidal volume strategy to ventilate all our patients. We used midazolam and atracurium during the initial 48–72 hours to facilitate mechanical ventilation. In addition we provided stress ulcer and deep venous thrombosis prophylaxis as per the ICU protocol. The subjects were given enteral nutrition.

We recorded the following information: (a) demographic profile; (b) etiology of ARDS; (c) baseline APACHE II and SOFA scores; (d) daily SOFA score including the maximum SOFA score attained during RICU stay; (e) duration of mechanical ventilation; (f) worst values of the following physiologic and ventilator parameters recorded daily including PaO_{2}/FiO_{2} ratio, positive end-expiratory pressure (PEEP), plateau pressure (Pplat), driving pressure (Pplat minus PEEP) and peak inspiratory pressure (PIP) (Ppeak); (g) ICU and hospital length of stay (LOS); and (h) final outcome.

We categorized subjects with age >65 years as ARDSelderly and those with age ≤65 years as ARDSnonelderly based on previous studies and the World Health Organization definition of the elderly. We compared the ICU outcomes between elderly and nonelderly subjects with ARDS. We also investigated parameters that predicted mortality in subjects with ARDS.

**Statistical Analysis**

We used statistical software package (SPSS for MS-Windows, version 22.0, IBM Inc., Armonk, New York, United States) to perform statistical analysis. We used the Chi-square test and the Student’s t-test (or Mann–Whitney U test), or analysis of variance (or Kruskal–Wallis) for comparing the differences between categorical and continuous variables, respectively. We have described the normally and non-normally distributed data as mean with standard deviation (SD), and median (interquartile range), respectively. We performed a multivariate logistic regression analysis to identify the factors affecting survival. The variables found significant (p <0.1) on the univariate analysis were entered in a multivariate logistic regression model to derive adjusted odds ratio and confidence limits. The level of significance was expressed as probability values (p value) and the odds ratio (95% confidence intervals(CIs)). We constructed survival curves to study the effect of the category of ARDS on RICU stay using Kaplan–Meier curves. We used the log-rank test to study the differences between the survival curves. We used the mixed model technique for repeated measurements analysis of variance to compare the trends in lung mechanics (static lung compliance, PaO_{2}/FiO_{2} ratio) and ventilatory parameters (PIP, PEEP, plateau pressure, and driving pressure); the within-groups factor was the time (baseline to day 5 of RICU stay), and the between-groups factor was age (ARDSelderly vs ARDSnonelderly). We considered a p-value of less than 0.05 to be statistically significant.

**Results**

We admitted 780 subjects with ARDS during the study period. We included 625 (ARDSelderly 140 [22.4%] and ARDSnonelderly 485 [77.6%]) subjects for further analysis. We excluded the remaining subjects due to survival for <24 hours, ambiguity in the diagnosis and etiology of ARDS, and the presence of insufficient information. The mean (SD) age of the study population (males, n = 352 [56.3%]) was 40.6 (17.8) years and was significantly higher in the ARDSelderly (67.3 vs 32.9 years). Serum glucose was significantly higher in the ARDSelderly (ARDSelderly vs ARDSnonelderly; mean ± SD, 150.5 ± 98.7 vs 129.3 ± 79, respectively; p = 0.009) at admission (Table 1). Comorbid illnesses were frequent in the ARDSelderly (p = 0.0001) than ARDSnonelderly. The mean ± SD APACHE II score at baseline was not different between the two arms (ARDSelderly vs ARDSnonelderly 19.2 ± 7.8 vs 18.4 ± 8.2, respectively; p = 0.327). We did not find any difference in the APACHE II score even after recalculating the APACHE II score without age (ARDSelderly vs ARDSnonelderly 16.4 ± 8.9 vs 17.4 ± 7.9, respectively; p = 0.238). We found no difference in the severity of illness at admission (baseline SOFA score) between the two groups (Table 1).

The elderly subjects had significantly higher pulmonary ARDS than the younger counterparts, who were more likely to suffer from extrapulmonary ARDS. The most common cause of ARDS in the elderly was community-acquired pneumonia (47%, 66/140), while sepsis (43.5%, 211/485) was the most common cause of ARDS in the younger subjects. There was no difference in the baseline PaCO_{2}, PaO_{2}/FiO_{2} ratio, and static lung compliance or the severity of ARDS between the two study arms. Most of the subjects were managed with positive pressure ventilation (noninvasive ventilation or invasive mechanical ventilation); the type of ventilatory support was similar between the two study groups. The mean ± SD plateau pressure (ARDSnonelderly vs ARDSelderly 24.3 ± 6.2 vs 22.3 ± 5.9; p = 0.004) and applied PEEP (ARDSnonelderly vs ARDSelderly, 8.4 ± 4.6 vs 7 ± 3.3; p = 0.012) were significantly higher in the ARDSnonelderly arm than ARDSelderly. However, there was no difference in the baseline peak airway pressures and the driving pressures (Table 1). There was no difference in the trends of PaO_{2}/FiO_{2} ratio between the two groups during the initial 5 days of RICU stay (Fig. 1). The plateau pressure reduced significantly with time (days 0 through 5) in both the groups and were significantly lower in the ARDSelderly compared to the ARDSnonelderly at all time. The driving pressure reduced during the RICU stay in ARDSelderly while it increased in ARDSnonelderly during RICU stay. There were no significant differences in other parameters between the two groups. We found no difference in the duration of ICU and hospital LOS between the two groups. There were 224 (35.8%) deaths, and the mortality was significantly higher (p = 0.012) in the ARDSelderly compared to ARDSnonelderly (ARDSelderly vs ARDSnonelderly 45 vs 33.2%).

In the univariate model, the factors that predicted survival included female gender, presence of comorbid illness, baseline serum glucose, baseline SOFA score, delta SOFA, PaCO_{2}, PaO_{2}/FiO_{2} ratio, use of invasive mechanical ventilation, peak airway pressure, pulmonary ARDS, ARDSelderly and the severity of ARDS (Table 2). However, in the multivariate logistic regression analysis, the only variables that predicted outcome were the baseline SOFA score, the development of new organ dysfunction (delta-SOFA score), and pulmonary ARDS (Table 2).

We plotted the survival curves for patients with ARDSelderly and ARDSnonelderly vis-à-vis the RICU stay (Fig. 2). The mean RICU stay in patients with ARDSnonelderly was 9.3 days (95% CI, 8.5—10 days; range 1–64 days) vs 10.6 days (95% CI, 3.1—12.1 days; range 1–47 days) days in patients with ARDSelderly and was not statistically different in the two groups (log-rank test, p = 0.284).

**Discussion**

This study highlights that while the elderly subjects had greater comorbid illnesses and more pulmonary ARDS than the younger subjects, they did not experience higher mortality than their younger counterparts. Only a few studies have investigated the effect of age...
on outcomes in subjects with ARDS$^8,9,21,22$ Notably, some of these studies were conducted before the landmark ARDSnet trial$^7,8$. Thus, a better understanding of the etiology and factors predicting outcomes in elderly subjects with ARDS is required. The proportion of elderly subjects with ARDS in our study was 22% and was lower than the previous studies (up to 60%).$^8,9,22$ The lower prevalence of elderly subjects in our study could be due to the lower life expectancy of the Indian population compared to the western countries. It could also be due to a general perception of poor outcomes and physicians’ reluctance to admit the elderly to the ICU.$^{14}$

The common etiology of ARDS in the elderly subjects was pneumonia, while sepsis was the most common cause of ARDS in younger individuals. In general, the incidence of pneumonia is higher in the elderly than in the young and is associated with higher mortality.$^{11,23,25}$ Even in the current study, the presence of pneumonia and pulmonary ARDS was an independent predictor of mortality. The elderly subjects required lower PEEP and driving pressure than the younger individuals, possibly due to the difference in ARDS etiology between the two arms. It has been previously shown that a higher PEEP is required for ARDS in Elderly

Table 1: Baseline characteristics, ventilatory parameters, and outcomes of patients with ALI/ARDS$_{elderly}$ and ALI/ARDS$_{nonelderly}$

| Parameters | Total (n = 625) | ARDS$_{elderly}$ (n = 140) | ARDS$_{nonelderly}$ (n = 485) | p value |
|------------|----------------|-----------------------------|-----------------------------|--------|
| **Demographic profile** | | | | |
| Male gender, n (%) | 352 (56.3) | 86 (61.4) | 266 (54.8) | 0.177 |
| Age, in years | 40.6 ± 17.8 | 67.3 ± 7 | 32.9 ± 11.4 | 0.0001 |
| Any comorbidity, n (%) | 176 (28.2) | 83 (59.3) | 93 (19.2) | 0.0001 |
| **Laboratory parameters** | | | | |
| Plasma glucose | 134 ± 84.2 | 150.5 ± 98.7 | 129.3 ± 79 | 0.009 |
| Hemoglobin, g/dL | 10.9 ± 3 | 11.1 ± 2.9 | 10.9 ± 3 | 0.451 |
| Serum albumin, mg/dL | 2.3 ± 2.5 | 2.3 ± 1.4 | 2.3 ± 2.8 | 0.855 |
| **ICU severity scores** | | | | |
| Baseline APACHE II score | 18.6 ± 8.1 | 19.2 ± 7.8 | 18.4 ± 8.2 | 0.324 |
| Baseline APACHE II score without age | 17.2 ± 8.2 | 16.4 ± 8.9 | 17.4 ± 7.9 | 0.238 |
| SOFA score at admission | 7.8 ± 3.6 | 7.2 ± 3.3 | 7.9 ± 3.7 | 0.058 |
| Delta-SOFA score | 2 ± 2.9 | 2.2 ± 3.1 | 1.9 ± 2.9 | 0.370 |
| **Respiratory parameters** | | | | |
| PaCO$_2$ | 39.1 ± 13.8 | 39.3 ± 14.7 | 39.1 ± 13.5 | 0.881 |
| PaO$_2$-FiO$_2$ ratio | 167.9 ± 67.8 | 171.9 ± 69.9 | 166.8 ± 67.2 | 0.430 |
| Cstat at RICU admission, mL/cm H$_2$O | 25.3 ± 12.1 | 27.6 ± 12.3 | 24.8 ± 12 | 0.109 |
| **Type of respiratory support** | | | | |
| Oxygen supplementation | 140 (22.4) | 40 (28.6) | 100 (20.6) | 0.094 |
| Noninvasive ventilation | 25 (4) | 8 (5.7) | 17 (3.5) | 0.515 |
| Invasive mechanical ventilation | 460 (73.6) | 92 (65.7) | 368 (75.9) | 0.089 |
| **Ventilator parameters** | | | | |
| PIP, cm of H$_2$O | 28 ± 8.1 | 26.8 ± 7.6 | 28.3 ± 8.2 | 0.087 |
| Plateau pressure, in cm of H$_2$O | 23.9 ± 6.2 | 22.3 ± 5.9 | 24.3 ± 6.2 | 0.004 |
| PEEP, cm of H$_2$O | 8.2 ± 4.4 | 7 ± 3.3 | 8.4 ± 4.6 | 0.012 |
| Driving pressure, cm of H$_2$O | 5.3 ± 3.9 | 6.1 ± 4 | 5.7 ± 3.9 | 0.421 |
| **Type of ARDS** | | | | |
| *Extrapulmonary ARDS | 312 (49.9) | 48 (34.3) | 264 (54.4) | 0.0001 |
| *Pulmonary ARDS | 313 (50.1) | 92 (65.7) | 221 (45.6) | 0.440 |
| **Severity of ARDS** | | | | |
| Mild | 209 (33.4) | 52 (37.4) | 157 (32.4) | 0.440 |
| Moderate | 306 (49) | 62 (44.6) | 244 (50.3) | 0.421 |
| Severe | 110 (17.6) | 26 (18.6) | 84 (17.3) | 0.421 |
| **Outcomes** | | | | |
| Mortality, n (%) | 224 (35.8) | 63 (45) | 161 (33.2) | 0.012 |
| ICU length of stay, in days | 9.6 ± 8.8 | 10.6 ± 8.9 | 9.3 ± 8.8 | 0.121 |
| Hospital length of stay, in days | 18.9 ± 48 | 22.7 ± 59.6 | 17.8 ± 44.1 | 0.283 |

*Includes sepsis, acute pancreatitis, multiple transfusions, and malaria; *Includes community-acquired pneumonia, aspiration pneumonia, vasculitis, tuberculosis, fat embolism, drowning, and paraquat poisoning; *Includes diabetes mellitus, hypertension, chronic renal failure, chronic liver disease, immunosuppression, and malignancy. APACHE II, acute physiology and chronic health evaluation II; ARDS, acute respiratory distress syndrome; Cstat, static lung compliance; PaCO$_2$, partial pressure of carbon dioxide in arterial blood; PaO$_2$, partial pressure of oxygen in arterial blood; PaO$_2$-FiO$_2$ ratio, the ratio of partial pressure of arterial blood to the fraction of oxygen in inspired air; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; SOFA, sequential organ failure assessment.
**Table 2: Comparison of parameters between survivors and nonsurvivors**

| Parameters                        | Survivors (n = 401) | Nonsurvivors (n = 224) | p value | Crude OR (95% CI) | Adjusted OR (95% CI) |
|-----------------------------------|---------------------|------------------------|---------|-------------------|----------------------|
| **Female gender, n (%)**          | 189 (47.1)          | 84 (37.5)              | 0.023   | 0.67 (0.48–0.94)* | 0.76 (0.5–1.2)       |
| Comorbid illness†                 | 95 (23.7)           | 81 (36.2)              | 0.001   | 1.8 (1.3–2.6)*    | 1.5 (0.9–2.5)        |
| **Laboratory parameters**         |                     |                        |         |                   |                      |
| Plasma glucose                    | 126.2 ± 76.7        | 148.1 ± 94.7           | 0.002   | 1 (1–1.01)*       | 1 (0.99–1)           |
| Hemoglobin, g/dL                  | 11 ± 3              | 10.9 ± 3.1             | 0.905   | 0.99 (0.9–1.1)    | 0.99 (0.9–1.1)       |
| Serum albumin, mg/dL              | 2.3 ± 2.5           | 2.3 ± 2.6              | 0.686   | 1.01 (0.9–1.1)    | 1.01 (0.9–1.1)       |
| **ICU severity scores**           |                     |                        |         |                   |                      |
| SOFA score                        | 7.2 ± 3.4           | 8.8 ± 3.8              | 0.0001  | 1.1 (1.1–1.2)*    | 1.1 (1.1–1.2)*       |
| Delta-SOFA score                  | 1.4 ± 2.1; 0 (0–2)  | 3.2 ± 3.7; 2 (0–5)     | 0.0001  | 1.2 (1.1–1.3)*    | 1.4 (1.3–1.5)*       |
| **Respiratory parameters**        |                     |                        |         |                   |                      |
| PaCO₂                             | 41.8 ± 16.3         | 37.6 ± 11.9            | 0.0001  | 1 (1.01–1.03)*    | 1 (0.9–1)            |
| PaO₂/FIO₂ ratio                   | 175.7 ± 67.7        | 154 ± 65.9             | 0.0001  | 0.99 (0.99–1)*    | 0.99 (0.99–1)        |
| Cstat at RICU admission, mL/cm H₂O| 24.4 ± 10.9         | 25.8 ± 12.8            | 0.300   | 0.99 (0.97–1)     | 0.99 (0.97–1)        |
| **Type of respiratory support**   |                     |                        |         |                   |                      |
| Noninvasive support†              | 119 (29.7)          | 46 (20.5)              | Reference | Reference       |                      |
| Invasive mechanical ventilation   | 282 (70.3)          | 178 (79.5)             | 1.6 (1.1–2.4)* | 1.3 (0.7–2.2)    |                      |
| **Ventilator parameters**         |                     |                        |         |                   |                      |
| Peak airway pressure, cm of H₂O   | 27.3 ± 7.9          | 29.1 ± 8.3             | 0.012   | 1.03 (1–1.1)*     | 1 (0.9–1)            |
| Plateau pressure, in cm of H₂O    | 23.6 ± 5.8          | 24.5 ± 6.8             | 0.138   | 1.02 (0.9–1.1)    | 1.02 (0.9–1.1)       |
| PEEP, cm of H₂O                   | 8.1 ± 4.7           | 8.3 ± 3.9              | 0.702   | 1.01 (0.9–1.1)    | 1.01 (0.9–1.1)       |
| Driving pressure, cm of H₂O       | 5.9 ± 4.1           | 5.8 ± 3.6              | 0.102   | 0.99 (0.94–1)     | 0.99 (0.94–1)        |
| **Type of ARDS**                  |                     |                        |         |                   | 0.016                |
| Extrapulmonary ARDS               | 215 (53.6)          | 97 (43.3)              | Reference | Reference       |                      |
| Pulmonary ARDS                    | 186 (46.4)          | 127 (56.7)             | 1.5 (1.1–2.1)* | 2 (1.3–3.1)*     |                      |
| **Category of ARDS**              |                     |                        |         |                   | 0.012                |
| ARDSnonelderly                    | 324 (80.8)          | 161 (71.9)             | Reference | Reference       |                      |
| ARDSelderly                       | 77 (19.2)           | 63 (28.1)              | 1.6 (1.1–2.4)* | 1.4 (0.8–2.4)    |                      |
| **Severity of ARDS**              |                     |                        |         |                   | 0.001                |
| Mild                              | 150 (37.5)          | 59 (26.3)              | Reference | Reference       |                      |
| Moderate                          | 194 (48.5)          | 112 (50)               | 1.5 (1–2.1)* | 1.5 (0.9–3.3)    |                      |
| Severe                            | 56 (14)             | 53 (23.7)              | 2.4 (1.5–3.9)* | 1.7 (0.9–2.5)    |                      |

*Statistically significant; †Include oxygen supplementation and noninvasive ventilation; ‡Includes diabetes mellitus, hypertension, chronic renal failure, chronic liver disease, immunosuppression, and malignancy. APACHE II, acute physiology and chronic health evaluation II; ARDS, acute respiratory distress syndrome; Cstat, static lung compliance; PaCO₂, partial pressure of carbon dioxide in arterial blood; PaO₂, partial pressure of oxygen in arterial blood; PaO₂/FIO₂ ratio, the ratio of partial pressure of arterial blood to the fraction of oxygen in inspired air; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; SOFA, sequential organ failure assessment.

In our study, higher severity of illness at baseline (SOFA score) was independently associated with a higher odds of death. Another factor that predicted mortality in our study was the delta-SOFA score, which signifies the development of new organ dysfunction. An increase in delta SOFA has been previously shown to be associated with an increase in ICU mortality and follows a linear pattern.29

Intuitively, the presence of comorbid illness should affect outcomes in elderly subjects. However, the presence of comorbid illness did not impact the clinical outcomes in the current study. In a previous study, the mere presence of comorbidity was not associated with higher mortality in subjects with ARDS.30 However, a Charlson’s comorbidity score of >4 predicted higher mortality.30 In another study, comorbid illness, such as COPD, chronic steroid use, and presence of diabetes mellitus, was not associated with a higher mortality.31 The presence of hyperglycemia has been associated with poor outcomes in critically ill subjects.32 The elderly subjects in the current study had significantly higher plasma glucose levels. However, on a multivariate logistic regression analysis,
higher plasma glucose at admission did not predict mortality, possibly due to better glucose control in the ICU after admission.31

Our study has a few limitations. The study was single-centered with the inherent flaws of a retrospective study design. We used an arbitrary cutoff value of 65 years. The number of very old subjects (>80 years) was less; thus, the results of this study may not be applicable to this age-group. The use of an arbitrary age cutoff is likely to ignore the within-age group heterogeneity in organ reserves, functional
ability, and the ability to tolerate the various treatment. Thus, future studies may consider using an objective measure of frailty, which is more likely to represent the biological age. Finally, we do not have the follow-up details of subjects after discharge from the hospital.

In conclusion, the outcomes in elderly subjects with ARDS are dependent on the severity of illness at admission, the occurrence of new organ dysfunction, and the etiology of ARDS rather than the age. More studies are needed to confirm our findings.

**Author Contributions**

Inderpaul S Sehgal—conceived the idea, performed the statistical analysis, drafted and revised the manuscript, and is the overall guarantor

Ritesh Agarwal—provided intellectual content to the manuscript, drafted and critically revised the manuscript for intellectual content

Sahajal Dhooria—drafted and critically revised the manuscript for intellectual content

Kuruswamy T Prasad—drafted and critically revised the manuscript for intellectual content

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