

## Research Article

### Effectiveness of Noninvasive Positive Pressure Ventilation in COVID-19 Patients with Severe Acute Respiratory Distress Syndrome

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#### Abstract

Results of invasive positive pressure ventilation (IPPV) in COVID-19 patients with Severe Acute Respiratory Distress Syndrome are discouraging despite its prompt use. However noninvasive positive pressure ventilation (NIPPV) is yet not a common practice internationally because of lack of global evidence advocating its effective use in severe cases of ARDS as well as dreadful concern about aerosol generation especially in patients having COVID-19 infection.

**Objective:** To determine whether, NIPPV application is effective and safe in COVID-19 Patients.

**Methods:** One hundred and thirty hemodynamically stable patients with severe ARDS as per Berlin definition (PaO<sub>2</sub>/FiO<sub>2</sub> ratio ≤ 100mm Hg), having GCS > 13, respiratory breathing index (RBI) < 105, and without any systemic complication were selected. They were managed with NIPPV in Corona Intensive Care Unit of Mayo Hospital/King Edward Medical University Lahore. A little innovation was done with the application of a specific orofacial interface, fitted with heat and moist exchanger (HME) at the interface and viral/bacterial filters at the expiratory limb of ventilatory circuit. Favorable outcome has been observed in 64% of treated cases in terms of improvement in PaO<sub>2</sub>/FiO<sub>2</sub> ratio, thus abating severity of ARDS from severe to mild category, in an average time span of 6 days. Remaining 36% of patients progressed to IPPV with definitive airway. During study period, 4.2% of healthcare workers (HCW) got infected with COVID-19. Associated complications of NIPPV application were claustrophobia (13.8%), nasal crusting (6.9%), aspiration (6.1%) and barotrauma (0.7%).

**Conclusion:** In carefully selected patients, use of noninvasive positive pressure ventilation with the application of HME and viral/bacterial filters is an effective, preferable and safe modality of choice to provide respiratory support, thus obviating the need for IPPV. However further larger studies are needed to confirm our recommendations.

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**Key Words:** Noninvasive positive pressure ventilation; invasive positive pressure ventilation; severe acute respiratory distress syndrome in COVID-19; respiratory breathing index; patient self-inflicted lung injury

## Introduction:

Noninvasive ventilation (NIV) refers to the administration of mechanical ventilation without using a definitive airway (endotracheal tube or tracheostomy tube). NIV may be delivered by means of positive-pressure and negative-pressure techniques: where positive pressure is directly applied to airways to augment inflation of lungs while negative pressure is applied externally to the abdomen and thorax to draw air into the lungs through the upper airway<sup>3</sup>. Among these two modalities, noninvasive positive pressure ventilation (NIPPV) is the most commonly employed noninvasive technique nowadays in the setting of acute respiratory failure. Administration of NIPPV via an anaesthesia mask dated back to 1940s, when Motley et al used it in the treatment of acute respiratory failure caused by pneumonia, pulmonary edema, near-drowning, Guillian-Barre syndrome and acute severe asthma. Its utility lessened with the advent of invasive positive pressure ventilation (IPPV), until it re-emerged in 1980 when it was successfully used to treat conditions like obstructive sleep apnoea and respiratory failure in patients with neuromuscular diseases<sup>4,5</sup>. Thereafter use of NIPPV has witnessed a tremendous worldwide expansion in terms of spectrum of diseases that it can successfully manage and the achievable goals<sup>6</sup>. We tried to exploit noninvasive positive pressure ventilation to assist spontaneous breathing remaining as close to normal physiology as possible. In the absence of any absolute contraindication, NIPPV offers same physiological benefits as IMV delivered via endotracheal intubation (ETI) while avoiding IPPV's detrimental complications such as upper airway trauma, ventilator associated pneumonia, ventilator induced lung injury, bio-trauma, critical illness polyneuropathy and myopathy and continuous need for sedation to name a few. On the other hand it offers some added benefits over invasive ventilation such as permitting airway clearance through effective coughing, swallowing, oral patency, intermittent ventilation, normal feeding, communication, nebulization, physiotherapy and expectation<sup>7,8,9,10</sup>.

ARDS<sup>11</sup> characterized by acute onset illness ( $\leq 7$  days) with refractory hypoxemia, bilateral pulmonary infiltrates, and normal echocardiography is associated with a high mortality. The conventional standard care for patients with ARDS include early

institution of IPPV with low tidal volume, high positive end-expiratory pressure and plateau pressure  $\leq 30$ cm H<sub>2</sub>O to ensure lung protective strategy based on the concept to avoid ventilator induced lung injury to already damaged lungs<sup>12</sup>. The benefits and harms of NIPPV in ARDS have neither been systematically evaluated nor it has been used as a modality of choice particularly in severe subgroup of ARDS. Available literature is scarce and is based on relatively small samples, that too consisting of heterogeneous patient population. This same trend of preferring invasive ventilation over NIPPV has been followed internationally, for patients with ARDS secondary to COVID-19 pneumonia (CARDS), mainly due to lack of evidence regarding its efficacy and its dreadful risk of aerosolization.

This study was conducted with the aim of determining efficacy of NIPPV in patients suffering from severe ARDS (PaO<sub>2</sub>/FiO<sub>2</sub> ratio  $\leq 100$ mm Hg) secondary to CARDS. We used noninvasive mode of invasive positive pressure ventilator (Spont/CPAP-PS mode) with a little innovation of use of specialized orofacial interface (BMC F2 NV1/NV2) fitted with HME filter at interface and bacterial/viral filters at expiratory limb of circuit to minimize risk of aerosolization. Our primary objective was to determine the proportion of patients, both L- and H-phenotypes, with severe CARDS, who were successfully managed with NIPPV in the background of available international data, reflecting poor outcome of COVID-19 pneumonia patients, especially of L-phenotype, when managed with invasive ventilation.

## Methods:

After taking permission from Ethical Committee, this descriptive case series was conducted in Corona Intensive Care Unit of Mayo Hospital Lahore from 1st April 2020 to 30th August 2020, where patients are being managed by a multidisciplinary team consisting of pulmonologists, intensivists and medical specialists.

The Primary Outcome Measure stepping down of NIPPV therapy once severe CARDS improve to mild CARDS i.e. PaO<sub>2</sub>/FiO<sub>2</sub> ratio  $\geq 200$ mm Hg and  $\leq 300$ mm Hg, leading to shifting of patient from ICU to HDU.

Secondary Outcome Measures are discharge from hospital after resolution of respiratory symptoms and two consecutive negative COVID-19 PCR reports in the absence of any other complication.

Inclusion Criteria are as follows:

RT-PCR proven COVID-19 pneumonia in an adult patient of either sex, Fulfilling criteria of severe ARDS as per Berlin Diagnostic Criteria (2012) i.e. PaO<sub>2</sub>/FiO<sub>2</sub> ratio  $\leq$  100mm Hg, GCS  $>$  13, Hemodynamically stable patient i.e. mean arterial pressure (MAP)  $>$  65mm Hg without any vasopressors and/or arrhythmias, Respiratory breathing index  $<$  105

Exclusion Criteria are as follows:

Patients with severe ARDS due to causes other than COVID-19 pneumonia, GCS  $<$  13, Hemodynamically unstable patient i.e. either mean arterial pressure (MAP)  $<$  65mm Hg or  $>$  65mm Hg with vasopressors and/or arrhythmias, Respiratory breathing index  $>$  105

One hundred and thirty patients admitted in Corona Intensive Care Unit of Mayo Hospital Lahore, fulfilling inclusion criteria were selected. Appropriately sized orofacial interface (BMC F2 NVI/NV2), fitted with HME and viral/bacterial filters, were attached to an invasive ventilator to establish a sealed and safe system. On invasive ventilator, non-invasive mode was selected to provide Bi-level positive airway pressure. Inspiratory positive airway pressure (IPAP)/PS was set between 10-25cm of H<sub>2</sub>O to ensure adequate tidal volume and to reduce work of breathing. Tidal volume greater than 10ml/kg was avoided to prevent patient induced self inflicted lung injury (P-SILI). PS was also adjusted as per carbon dioxide levels in cases of type II respiratory failure. Expiratory positive airway pressure (EPAP)/PEEP was maintained above atmospheric pressure for lung recruitment to prevent alveolar collapse on expiration and to improve oxygenation. It ranged from 6-15cm of H<sub>2</sub>O. FiO<sub>2</sub> up to 100% was titrated in order to achieve SpO<sub>2</sub>  $>$  90%. Parameters assessed include oxygen saturation as measured by pulse oximetry (SpO<sub>2</sub>), PaO<sub>2</sub>/FiO<sub>2</sub> ratio, arterial blood gases, RBI, hemodynamics, GCS and patient comfort using a numerical rating scale (0, totally uncomfortable, to 10, fully comfortable). These were recorded every four hourly for the first 48 hours and then thrice

daily. Deterioration in either RBI, hemodynamic status, or GCS led to stepping up of therapy i.e. prompt intubation with definitive airway without any further delay. Stepping down from NIPPV and shifting from ICU to HDU occurred as soon as PaO<sub>2</sub>/FiO<sub>2</sub> ratio improved from severe to mild category, along with stable cardiovascular and neurological status and absence of any other systemic complication.

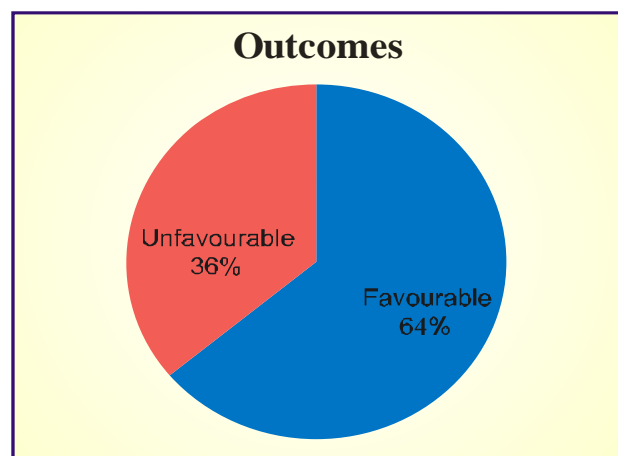


**Figure 1:** BMC F2 NVI/NV2 Face Mask

### Results:

**Table I:**

Outcomes	N	%age	P-value
Favorable	84	64.6	0.001
Unfavorable	46	35.3	



**Figure 2:** Outcomes of NIPPV application

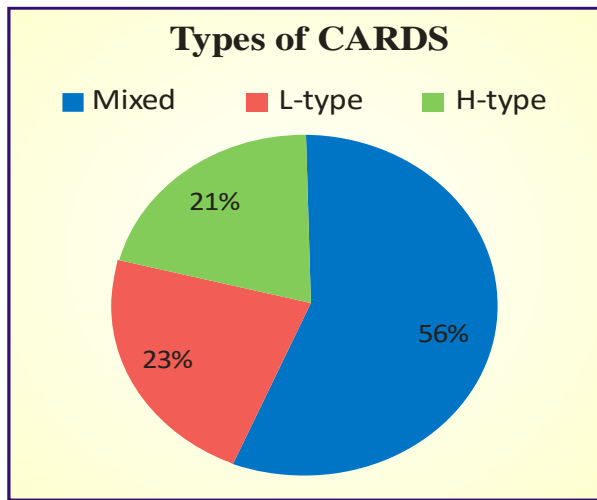


Figure 3:

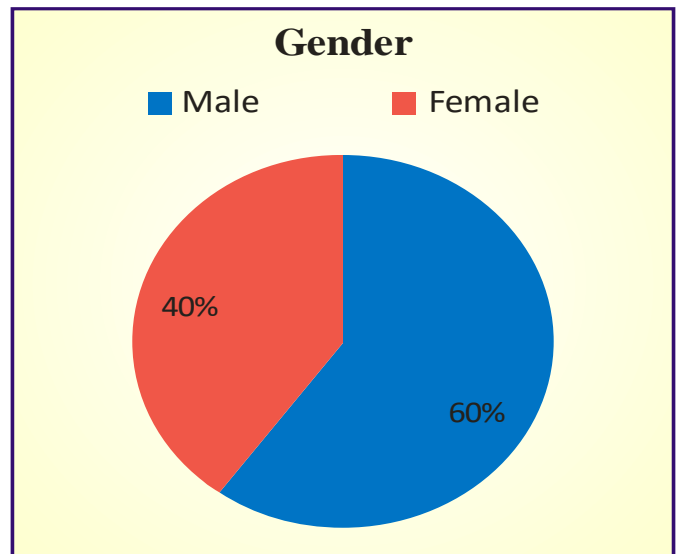


Figure 6: Gender distribution

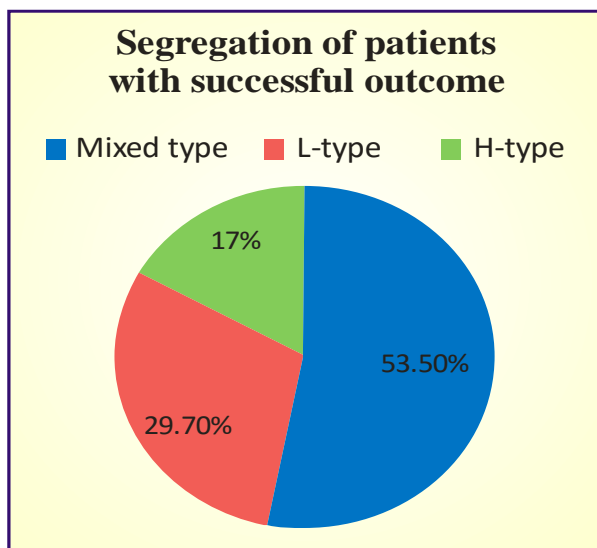


Figure 4: Segregation of patients with successful outcome

**Table 2: Complications of NIPPV application**

Complications	N	%age
Claustrophobia	18	13.8
Nasal crusting	9	6.9
Aspiration	8	6.1
Barotrauma	1	0.7

**Discussion:**

COVID-19 has been ravaging country after country and continent after continent the year round. So far, millions have been infected and have surrendered their precious lives to the lethal SARS CoV-2. The predicament took a sinister turn when Solidarity trial under the aegis of the UNO concluded that none of Hydroxy-chloroquin, lopinavir, interferon-beta 1a, and remdesivir proved effective in significantly reducing mortality, initiation of mechanical ventilation, and length of hospital stay<sup>13</sup>. Though the Moderna, Pfizer and Oxford vaccine hold great promise in giving hope of 90% protection against the deadly disease, yet demand & supply and logistic problems stare in the face, more so for low-income countries like ours. The management of CARDS posed challenges in terms of clinical management, availability of trained human resource and ample infrastructure. The proposed pathophysiological mechanisms include hypoxemic respiratory failure, cytokine release syndrome, macrophage activation syndrome and COVID-19 related hyper coagulability. In our study

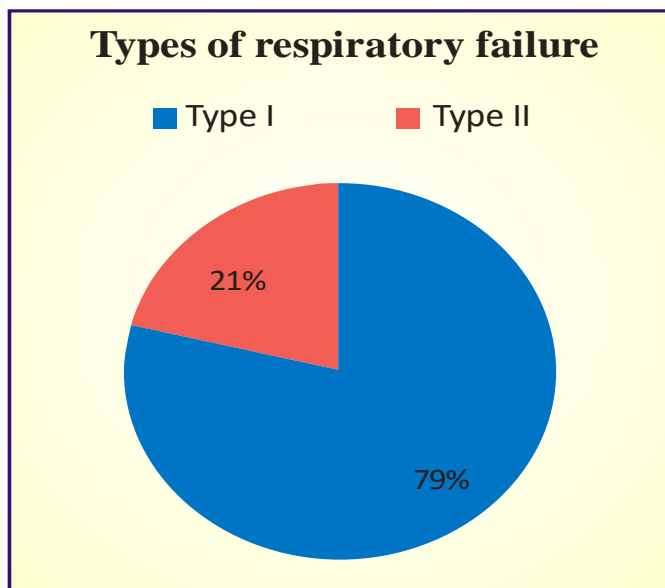


Figure 5: Types of respiratory failure

we dealt with cases of hypoxemia leading to severe CARDS i.e. PaO<sub>2</sub>/FiO<sub>2</sub> ratio  $\leq$  100mm Hg as per Berlin definition. Literature review suggested that subgroups of ARDS most likely to benefit from NIV are not yet agreed upon. However LUNG SAFE STUDY which graded ARDS patients using NIV according to PaO<sub>2</sub>/FiO<sub>2</sub> ratio as mild, moderate and severe found out that worsening ARDS categories were associated with more prolonged and aggressive invasive ventilatory support, and worse patient outcomes<sup>10</sup>. In the same study, success rates of NIV in severe ARDS was found out to be 53% which is 11% less as compared to our results, but neither did they collect data on the type of interface used for NIPPV, which was potentially an important determinant of NIPPV success<sup>14</sup> nor their study population was homogenous like ours as far as the cause of ARDS is concerned

Success rate of NIPPV in our study is 64% as determined by primary outcome measure i.e. stepping down of NIPPV therapy once severe CARDS improved to mild CARDS leading to shifting of patient from ICU to HDU (Figure 2). We opted for preferred use of NIPPV after failing non re-breather mask (NRM) along with awake prone positioning and found this modality to be more safe and effective than high flow nasal cannula (HFNC). NIPPV has several anticipated advantages over HFNC, mostly used elsewhere in the world<sup>15</sup>. NIPPV delivered high PEEP and high FiO<sub>2</sub> with more certainty. The circuit was fitted with filters to ensure safety of healthcare workers against risk of aerosolization, the most feared aspect of HFNC as well as conventional NIPPV. NIPPV unlike HFNC also addressed type 2 respiratory failure simultaneously. It effectively reduced work of breathing thus avoid fatigability and P-SILI. Real time non-invasive monitoring of respiratory parameters were made possible by attaching NIPPV circuit to a ventilator. Moreover, prompt conversion to invasive mechanical ventilation was possible without shifting of patient to another setup, whenever needed. And last, but not the least, it was far more economical as compared to HFNC as ventilators were already available in the ICU and only provision of interfaces and protective filters had to be

ensured, which too, were re-used after cleaning and disinfecting in resource limited set ups.

As far as clinical phenotypes of COVID-19 are concerned, gattinoni et al. described two phenotypes Type L and Type H (typical ARDS)<sup>16</sup>. These types are clearly distinguishable by CT scan but can also be predicted by imperfect surrogates such as response to PEEP and respiratory system compliance. In Type L patients, there is low elastance, low ventilation to perfusion (VA/Q) ratio, low lung weight and low lung recruitability, while Type H is characterized by high elastance, high right-to-left shunt, high lung weight and high lung recruitability. Transition from Type L to Type H may be due to pathological evolution of COVID-19 on one hand, while injurious effects of patient self inflicted lung injury (P-SILI) on the other<sup>17</sup>. However certain researchers proposed that L and H types are two ends of the spectrum and that most patients could not be classified as either the L- or H-subphenotype<sup>18</sup>. Our study findings were in accordance with this proposition. Our study population consisted of 73 patients (56.1%) with mixed-phenotype CARDS, 30 patients (23%) with L-phenotype CARDS while 27 cases (20.7%) were of H-phenotype (Figure 3). We applied NIPPV to all phenotypes. Among 84 patients (64%) with successful outcome, 45 patients (53.5%) were of mixed-phenotype, 25 patients (29.7%) were of L-phenotype while rest of the 14 patients (17%) were of H-phenotype (Figure 4). Reviewed literature suggested that the use of IPPV with high PEEP is rather detrimental for L-phenotype of COVID-pneumonia where parenchymal involvement is less severe as compared to H-phenotype. In our study, we observed same pattern i.e. L-phenotype being more responsive to NIPPV therapy. To determine whether this beneficial effect in curtailig progression of L- and mixed-phenotype CARDS was due to in time avoidance of P-SILI by NIPPV therapy need further larger sized studies.

RBI has been considered a sensitive indicator to anticipate successful extubation in invasively ventilated patients<sup>19</sup>. However, we used it to intubate a patient as soon as he/she showed signs of exhaustion while on NIPPV. RBI > 105 for consecutive 3-4 hours is considered a sign of early exhaustion, and IPPV was

initiated in such patients without any further delay. In recent literature, P-SILI is considered an important phenomenon in progression and worsening of lung injury in patients of respiratory failure. It is caused by intense respiratory effort yielding swings in transpulmonary pressure, abnormal increase in transvascular pressure, an intra-tidal shift of gas between different lung zones and diaphragmatic injury<sup>20</sup>. Close monitoring of RBI also helped us in predicting P-SILI before progression of lung injury to an irreversible/critical stage.

Majority of COVID-19 cases develop type I respiratory failure and same is the case with our study where patients with type I respiratory failure constituted 79% of study population. However patients vulnerable to hypoventilation such as patients with COPD, obesity, overlap syndrome (OSA with COPD), asthma-COPD overlap syndrome (ACOS) as well as fatigued ones are at higher risk of developing type II respiratory failure and this type of patients constituted 21% of our patients (Figure 5). NIPPV proved to be equally effective in treating this patient population who developed type II respiratory failure CARDS.

Despite adopting all possible precautionary measures, 4.2% of healthcare workers attending patients recruited in our study got infected with COVID-19. Unavailability of proper negative pressure environment in ICU during first two months of our study period was main contributing factor to this transmission. However, all of them recovered uneventfully with in due course of time

Male gender is more affected gender in our study (Figure 6), a finding comparable to international data.

Any intervention has its complications and so is the case with application of NIPPV. Reviewed international literature mentioned a number of complications ranging in severity from mild to life threatening ones. We mainly had to cope with complications like claustrophobia, aspiration, nasal crusting/dryness/ulceration, and barotrauma (Table 2). Incidence of claustrophobia (13.8%) in our study was comparable to international data. Patient reassurance, mild seda-

tion, use of manual mask application and starting with a prudent ventilatory support i.e. lowest possible PS were some steps which we found useful in addressing it. Nasal crusting/ulceration was another frequently encountered complaint (6.9%) and was ameliorated by using water instead of air to fill face-mask cushions and re adjusting mask straps. Aspiration occurred in just 6.1% cases and can be avoided by placing patient in propped up position (30-45°), waiting at-least two hours after a meal before applying NIPPV and not applying PS > 20cm H<sub>2</sub>O. Barotrauma occurred in one patient only (0.7%) which was effectively managed with insertion of small bore chest drain.

Biggest limitation of our study is the absence of a comparative control group. Furthermore, L- and H-phenotypes related outcomes necessitate large-scale randomized controlled trials of moderate and severe COVID-19 patients with NIPPV.

### Conclusion:

In carefully selected patients, use of noninvasive positive pressure ventilation with the application of HME and viral/bacterial filters is an effective, preferable and safe modality of choice to provide respiratory support in severe CARDS, thus obviating the need for IPPV. However further larger studies are needed to confirm our recommendations.

**Ethical Approval:** Given

**Conflict of Interest:** The authors declare no conflict of interest

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