

COVID-Associated Respiratory Distress Syndrome (CARDS) in Pregnancy; What Makes it so Different?



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Infection with the novel coronavirus (nCoV-2) results in severe pneumonia known as COVID-19 disease. A good portion of infected patients develop severe form of acute respiratory distress syndrome (ARDS) that is associated with a high mortality rate. Almost all physicians around the world are familiar with the concept of ARDS, its diagnosis and treatment. However, COVID-19 associated respiratory distress syndrome (CARDS) especially in pregnant women has different features with many unanswered questions (1). Patients with CARDS although meet the Berlin criteria for ARDS, they generally present an atypical form of this syndrome. Gattinoni et al described two different types of CARDS as high elastance (H) and low elastance (L), which are usually distinguishable with computerized tomographic (CT) scanning (2). The almost constant presence of ground-glass opacity and crazy-paving pattern in the CT scan images of COVID-19 patients show an interstitial pneumonia in these patients (3). The ground-glass opacities can be due to the combination of mild edema of the alveolar septi, hyperplasia of the interstitium and partial filling of airspaces, although the crazy-paving pattern may correlate with intralobular and interlobular hyperplasia (Table 1) (4). It seems that lymphopenia, hypercoagulation and low grade inflammation is a classic description of this disease. So, endothelial activation, direct viral invasion of tissues and immunosuppression is a major reason for organ dysfunction in COVID-19 rather than hyperinflammation (5). Recent studies showed that inflammation imbalance and coagulopathy, clearly resulted in severity of disease in COVID-19 critically ill patients which predisposes to the development of microthrombosis, disseminated intravascular coagulation, and multi-organ failure evidenced in severe CARDS. Regarding the pathophysiology of this disease, it is clear that the effects of coagulation activation go beyond clotting and interaction between coagulation and inflammation can significantly affect disease progression and lead to poor outcome. So measuring local and

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systemic inflammatory responses by corona virus can be used as to guide the standard treatment. Immune factors contributing to CARDS can be described as adaptive immune response to Corona virus, Extensive pulmonary macrophage activation and pulmonary immunovascular coagulopathy.

Regarding treatment in early stage, the key issue is the overcome the disrupted vasoregulation with improved oxygenation, early intubation, effective sedation, and/or paralysis which may interrupt that (6,7). If lung edema increases in the patient with type L because of the disease progression and/or Patient self-induced lung injury, the normal lung shrinks more, and the type H phenotype progressively develops. Progression to this type is meaning increased mortality (8).

Recent studies showed that immunosuppression, endothelial activation, and direct viral-mediated tissue damage, rather than hyperinflammatory injury, mediate COVID-induced organ dysfunction.

CARDS represents an ongoing global threat, as this virus family has the potential to mutate and infect non-immune populations. Physicians should be aware that CARDS in pregnancy is a serious complication of COVID-19, which requires early detection and appropriate management. We should emphasize that until we understand the complete nature of nCoV-2 infection and identify appropriate treatment strategies, advanced levels of supportive respiratory care remain the fundamental of managing CARDS patients. Although post-mortem examination is not generally carried out for safety reasons in known COVID-19 victims with high



Table 1. Different characteristics of ARDS and CARDS

	Acute Respiratory Distress Syndrome	COVID-Associated Respiratory Distress
Risk Factors	Higher APACHE-II, MODS, Oxygenation index	Older age, comorbidities like diabetes, hypertension and cerebrovascular diseases
Obesity	↓ Mortality	↑ Mortality
Pregnancy	↑ Mortality	↓ Mortality
Types	High elastance	High elastance Low elastance
Radiologic findings	Bilateral diffuse Patchy infiltration Comparable with clinical findings	Uni- or bi-lateral Ground glass opacification Noncomparable with clinical findings
Autopsy findings	Diffuse alveolar damage, Pulmonary edema, Lymphatic interstitial pneumonia	Diffuse alveolar damage, pulmonary edema, vascular damage (vasculitis), direct viral damage, thrombotic microangiopathy with extensive fibrin deposition
Pulmonary vascular permeability index & extravascular lung water index	Decreased	May vary
Inflammation	Hyperinflammatory	Hypo/Hyperinflammatory
Shunt fraction	May vary	Increased
Therapeutics ECMO	Extracorporeal membrane oxygenation is considered as rescue therapy (↓ 60-day mortality with moderate ↑ risk of bleeding)	Extracorporeal membrane oxygenation has not been useful.
Prone Position	Recommended as rescue therapy (↓ mortality)	Recommended as early application of prone position (Co-operative prone positioning)
Corticosteroids	Low dose, short duration	High dose/low dose, short duration?
NIPPV	Not recommended	Recommended to delay intubation
High-Flow Nasal Oxygen	Not useful	Has been effective
Immunotherapy	Not so effective based on the limited evidence	A potentially strong therapeutic effect with ongoing trials
Mortality	30-40%	>50%

virus load, autopsy findings could shed more light into the pathogenesis of this potentially fatal disease. Pregnant patients with COVID-19 show an ARDS phenotype, with heterogeneity in respiratory mechanics, aeration loss related to the degree of hypoxemia, and inter-individually variable recruitability (9). Finally CARDS in pregnancy consists of totally clinical, physiologic and immunologic profile compared to ARDS which should be considered in therapeutic and diagnostic approaches. It seems that CARDS reflects immunosuppression and features compatible with vascular disease instead of routine ARDS or cytokine storm syndrome.

Ethical Issues

Not applicable.

Conflict of Interests

None.

Authors' contributions

AM: hypothesis, manuscript drafting. NDN: manuscript editing. All authors read and approved the final format of manuscript.

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