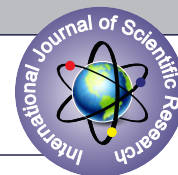


“ROLE OF CLINICO-PATHOLOGICAL AND RADIOLOGICAL IMAGING IN CASES OF COVID-19 PNEUMONIA DEVELOPING ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) “



Pulmonary Medicine

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ABSTRACT

SARS-COV-2 Disease (COVID -19) may result into moderate to severe /critical Pneumonia leading into Acute Respiratory distress Syndrome (ARDS).

ACUTE RESPIRATORY DISTRESS SYNDROME is a life threatening condition involving respiratory system which prevents adequate entry of oxygen into lungs and causes diffuse alveolar damage, altered immunological response, extensive micro-thrombus formation & ultimately leads into multiple organ dysfunctions and even Death .(1).

Research is still required to explore specific therapy of Covid-19 Pneumonia, early invention of vaccination, and prevent development of ARDS.

AIMS AND OBJECT—

AIM— Our main aim is to prevent development of ARDS in COVID-19 Pneumonia cases by early diagnosis, proper treatment like anti- viral therapy, steroids, provide breathing support and management of patients on the basis of grading of disease.

Many moderate to severe patients of Covid-19 pneumonia may develop acute respiratory Distress Syndrome (ARDS).

OBJECT— The main object in our study is to treat the patients of ARDS promptly and accurately on urgent basis by admitting them in ICU after accurate diagnosis clinically, by advising related Laboratory tests and HRCT CHEST scan for grading of ARDS so as to proper management and early treatment of cases accordingly.

The key factor in ARDS case is to maintain oxygen level. Our target should be to achieve oxygen level (SpO₂) by using high flow of oxygen, to avoid NIV and to use prone ventilation so as to adequate supply of oxygen into lungs and avoid low blood pressure, prevent shock, acute respiratory distress and multi organ failure and Death.

KEYWORDS

ARDS (Acute Respiratory Distress Syndrome), ICU (INTENSIVE CARE UNIT), Covid-19 Pneumonia, HFNO- HIGH Flow Nasal Oxygen, HRCT (High Resolution Computer Tomography).

INTRODUCTION/BACKGROUND OF RESEARCH PROJECT— Corona virus disease 2019 (sars-cov-2) is a novel disease diagnosed initially in Wuhan city of Hubei province of China in December 2019. (2)

On March 11, 2020, WHO declared covid-19 as a global pandemic due to its rapid spread in more than 212 countries within short period of times.

As of 22nd September 2020, Total covid-19 cases (31.62 millions) were reported globally while total deaths due to covid-19 were 9, 71, 715 and recovery rate 80.25 % and case fatality rate was 1.87%.

The worst affected countries due to covid-19 are USA, Italy, Russia, U.K, Brazil, India, South Korea, etc.

The sars-cov-2 infection causes viral pneumonia which may lead into Acute Respiratory Syndrome in severe and critically ill- cases.

There were combination of sign and symptoms developed due to simultaneously involvement of two processes, one from viral pneumonia and other due to developing ARDS.(3)

Though SARS and MERS also caused severe viral pneumonia and may lead into ARDS, The covid-19 pneumonia leading into ARDS presented as a global threat due to its highly contagious nature and having potential to mutate and infect non-immune populations.

The severity of covid-19 disease has been classified as (a) mild symptomatic (b) moderate symptomatic (c) Severely Symptomatic (d) critically ill patients. (4)

80% of total cases belongs to asymptomatic/mildly symptomatic and early moderate categories were cured after getting appropriate early treatment.

According to a study, 5 to 6% of total cases of covid-19 pneumonia

required admission in ICU which belong to severe and critically ill patients, usually above 50 years with/without co-morbidities.

The main indications of ICU (Intensive Care Unit) admissions related to Covid-19 Pneumonia are Acute Respiratory Distress Syndrome (ARDS), Shock, Sepsis, Superimposed infection, Cytokine storm syndrome, Acute Renal Failure, Acute Cardiac injury and Multi organ Failure, Death.(5)

The moderate covid-19 Pneumonia cases may turn into life threatening condition ARDS within 24 to 48 hours of illness. Usually the ARDS patients are treated in ICU.

Often ARDS patients are so sick, they are not in a position to explain the symptoms.

The treating physician can observe difficulty in breathing, falling spo₂ level <90% at room air, RR >30/minutes, Low B.P, Rapid breathing, cardiac irregularity, and Multi- organ failure.

ARDS can be suspected if there is new or worsening respiratory symptoms within short period after known clinical insult with evidence of respiratory failure and oxygen impairment.

Three Categories of ARDS are summarized as:-

- 1. Mild ARDS—**
200mg Hg <Pao₂/Fio₂ < 300 mg with PEEP/CPAP > 5 cm H₂O
- 2. Moderate ARDS—**
100 mg Hg <Pao₂/Fio₂ < 200 mg with PEEP > 5 cm H₂O
- 3. Severe ARDS—**
Pao₂/Fio₂ < 100 mg Hg with PEEP > 5 cm H₂O

When Pao₂ is not available, spo₂/fio₂ < 315 suggests ARDS (including in non-ventilated patients).

The main purpose of treatment is to provide breathing support as well as to cure the cause of ARDS.

The overall treatment may involve to suppress viral load, reduce inflammation and removal of fluid from the lungs so as to prevent alveolar damage.

There may be need of ventilator to deliver high flow of oxygen & continued pressure positive end expiratory pressure (PEEP) to get the normal level of Spo₂.

There may be mild, moderate or severe amount of lung damage which may be transient or permanent.

Many patients during POST- ARDS period may have problems in maintaining quality of normal healthy life due to development of pulmonary fibrosis.

In some patients having severe Covid-19 pneumonia that gets worse and develop ARDS within short period of time.

Covid-19 ARDS appears to have worse prognosis than ARDS from other causes.

The risk factors for poor prognosis depends upon old age >50 years, presence of comorbidities such as Diabetes, Hypertension, COPD, Cardio-vascular disease, etc.

The vascular enlargement was reported in most of the cases of covid-19 ARDS.

The Morbidity and mortality from covid-19 ARDS is due to respiratory failure or respiratory failure combined with cardiac failure, myocardial damage, pulmonary embolism, multi organ failure leading to death in some critically ill patients.

MATERIAL & METHODS:-

STUDY AREA AND PARTICIPANTS ----

This Retrospective study was conducted on Covid-19 positive cases confirmed by RT-PCR Method (CORADS- 6) admitted in isolation ward of G.S.Medical College and Hospitals, Pilkhuwa. Initially, most of them having mild symptoms were kept in isolation ward and discharged after treatment for 10 days. Few of them did not respond to treatment and showed progression of disease, hence these patients were transferred from isolation ward to Intensive care unit (ICU) after clinical assessment, Laboratory reports & Radiological investigations.

Out of total 563 confirmed cases admitted in isolation ward under medicine department for appropriate treatment, only 51 cases were shifted to ICU on the basis of laboratory Tests and HRCT Chest investigations and clinical severity assessment, those patients developed moderate to severe symptoms of ARDS (Acute Respiratory Distress Syndrome).

SAMPLE SIZE --- Our sample Size was limited to total 51 cases of moderate to severe cases of covid-19 Pneumonia transferred from isolation ward into ICU due to clinical impairment and further progression of disease with development of sign and symptoms of Acute Respiratory distress syndrome.

These patients were tested for CRP, Ferritin, LDH, d-Dimer, IL-6, etc. and depicted deranged values.

All the patients were undergone HRCT Chest to assess C T. Severity Score which is a semi-quantitative method to detect involvement of lobes of both lungs and extent of alveolar damage and further categorization into mild, moderate and severe types of ARDS.

HRCT scan chest imaging features includes multiple patchy areas of ground glass opacities/consolidation located peripherally involving predominantly bilateral lower lobes (Superior and posterior basal segments) initially, and later on may involve Right mid, left lingual and both upper lobes (Multilobar involvement) with intra lobular, inter lobar and pleural thickening, giving rise to CRAZY-PAVING pattern. (6).

Depending upon the severity, the patients are treated with antiviral, steroid, oxygen therapy on prone position for mild and moderate categories of patients (7).

Most of the patients were discharged after successful treatment while remaining patients under severe and critically ill types were referred for higher centers (Level 3) for advanced treatment.

INCLUSION CRITERIA--

Moderate to Severe Symptoms of Respiratory Distress, sPo₂ <90, RR > 30 minutes

Raised values of CRP, FERRITIN, LDH, d-Dimer and CT SEVERITY Score 8 or more on HRCT Chest.

Patients need of Oxygen Therapy and On Ventilation Support on Clinical Assessment

Not responding to treatment in Isolation Ward.

EXCLUSION CRITERIA--

Covid-19 patients with mild symptoms with SpO₂ >95, RR 20/minute

Patients responding to normal Treatment

Pneumonia cases due to other causes

STUDY DESIGN--

To Detect cases of ARDS (Acute Respiratory Distress Syndrome) in isolation ward and shifted to ICU on the basis of clinical assessment, laboratory tests, and Radiological Investigations like HRCT Chest with C T Severity Score more than 8 to 15, to evaluate extent of pulmonary involvement.

OUR study includes RT-PCR Test confirmed, 51 Covid-19 patients who developed symptoms of Acute Respiratory Distress Syndrome shifted to ICU for Further Management.

Study Period--From 01 July 2020 to 30th September 2020.

DATA COLLECTION --From CMS office through MRD department, clinical data from Medicine and Lab Data from pathology and HRCT Chest Scan data from Radio-Diagnosis Department.

Criteria for Referral to Higher Centers--

1. Patients above 50 years with co-morbidities and not responding to given treatment
2. Further deterioration of patient clinically & radio -logically as increased C T Severity score on Follow up HRCT Chest.
3. Non-resolving Pneumonia after vigorous treatment,
4. Poor prognosis and further clinical deterioration.

Table 1: Demographic characteristics

Age group (in years)	Male	Female	Total	Percentage
25-40	10	01	11	21.57
40-50	15	02	17	33.33
50-60	07	01	08	15.69
60-70	07	02	09	17.65
>70	05	01	06	11.76

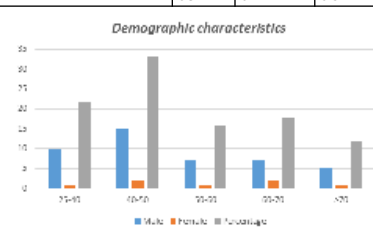
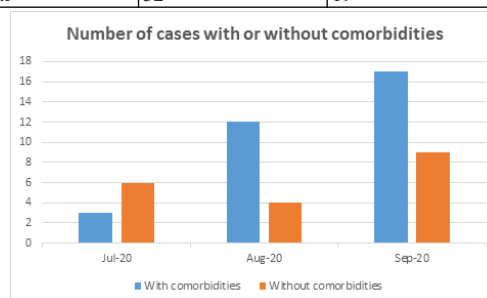


Table 2: Number of cases with or without comorbidities

Number of Patients	With comorbidities	Without comorbidities
July 2020	03	06
August 2020	12	04
September 2020	17	09
Total	32	19



Informed Consent –

The Informed Consent is not required because it is a retrospective study in which patient identity is not disclosed in any manner and data is collected from medical records.

STATISTICAL ANALYSIS – The parameters will be recorded and data collected will be analyzed by using standard statistical methods, according to demographic characteristics will be compiled using student

T-test and chi-square test as appropriate. The statistical test is significant at $p < 0.05$ at 5% level of significance.

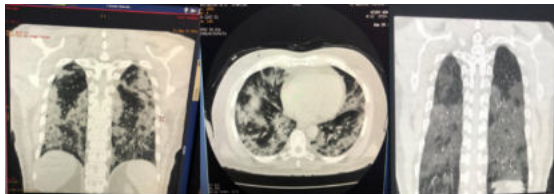
RESULTS –

During three months study period, 51 patients full filling all Berlin criteria of covid-19 were found confirmed cases developed ARDS. The median age was 52.5 (25 to 80 years). 44 patients (86.27%) were Male And 7 (13.7 %) were females. All the patients were tested for CRP, S.Ferritin, D-dimer and IL-6 at the time of Admission in ICU.

HRCT scan Chest was advised for all the patients to assess semi-quantitative analysis of extent of pulmonary damage and involvement of multiple lobes of both lungs due to Covid-19 pneumonia and measured as CT severity scoring.

The COVID-ARDS findings are summarized as follows—
Table 5.

Sex	Covid-19 ARDS	percentage
Male	44/51	86.27 %
Female	07/51	13.72 %
Age years	25---80	52.5 mean age
ARDS severity		
MILD	28/51	54.90 %
MODERATE	11/51	21.5%
SEVERE	12/ 51	23.5%

MODERATE TYPE OF COVID-19 PNEUMONIA WITH ARDS**Severe Covid-19 Pneumonia with ARDS**

The majority of patients were Male 19/51 (37.25 %) above 50 years as compared to female 04/51 (7.8 %)

Out of 51 patients, 38 patients were above 50 years with comorbidities like Diabetes, Hypertension, COPD, Cardiac anomalies, etc.

Total 37 out of 51 patients were recovered completely and discharged after RT-PCR turns out to be negative, while 14 cases were referred to Higher Centre (Level 3) for advanced treatment.

Not even single death is reported in ICU at our institution.

Table 3: Severity of ARDS on the basis of CT score

Duration	Number of CT scan (ICU)	ARDS Mild	CT SS	Moderate	Severe	CTSS
July 2020	03	02	8-10	01	11-15	- >15
August 2020	16	07	8-10	03	11-15	06 >15
September 2020	32	19	8-10	07	11-15	06 >15

DISCUSSION:

Our study on covid-19 ARDS revealed low static disease pattern with high D-dimer concentration.

ARDS is characterized by loss of aerated pulmonary tissue, increased vascular permeability in lungs associated with inflammation.

The diagnosis of ARDS is based on evidence of moderate to severe grades of hypoxemia and multiple Bilateral patchy ground glass opacities /consolidations involving multiple lobes of lungs on HRCT Chest scans within 24-48 hours period.

Early studies suggested that widespread pulmonary vascular thrombosis were seen as consistent findings of ARDS.

We observed high ventilatory ratio, a marker of dead space in our study of covid-19 related ARDS.

On the basis of main findings of our study, we observed the patients admitted in ICU due to Covid-19, ARDS are associated with high grade of morbidity and mortality, caused by development of respiratory failure and resulting into pulmonary fibrosis as a post-covid-19 sequelae. (7)

The incidences of ARDS were seen more in advanced age, with comorbidities and severe grade of covid-19 pneumonia associated delay in sign and symptoms onset and ICU admission, resulting low oxygen saturation, such type of patients are treated with using high flow nasal oxygen. (8)

The co-factors like immuno-suppression, lower steroid dose, and positive fluid balance were added in resulting with poor outcome.

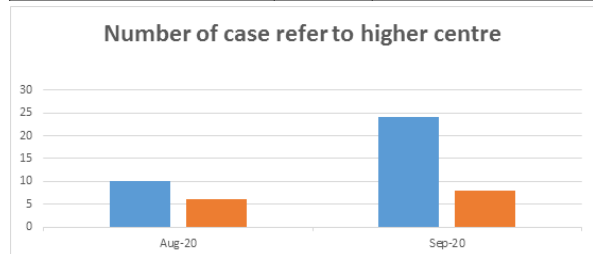
The MOD score is a validity scoring system which is quantifying estimation of multi organ dysfunction and is made up of six components (respiratory, CVS, Neurological, Renal, Hematological and Hepatic), each of which is scored from 0-4, giving a maximum score of 24.

The mean maximal MOD score in our patients was only 5, with maximum component of respiratory which indicates SARS-Cov-2 Pneumonia related ARDS mainly causes Respiratory failure.

A restricted fluid regime with treatment of ARDS with prone positioning may result in better outcomes in ARDS. (9).

Table 4: Number of case refer to higher center

Total Number of ARDS	Recovered	Referred to higher center
July 2020	03	-
August 2020	10	06
September 2020	24	08

**CONCLUSION –**

On Comparing our data from previous data proves that Covid-19 ARDS requiring ICU admission have significant morbidity and mortality due to respiratory failure.

This disease mainly affects respiratory system resulting severe grade of Pneumonia developing ARDS and requires admission in ICU for oxygen therapy and ventilation support to prevent multiple organ failure.

Active diuresis and administration of higher doses of steroid may be associated with better outcome.

Covid-19 ARDS is a predictable serious complications of covid-19 pneumonia that requires early detection and prompt comprehensive treatment.

Conflict of interest –

The authors declare that they have no conflict of interest.

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