

Effectiveness of Covalent Plasma Therapy (CPT) for Combating COVID-19 Diseases: A Rapid of Case Series

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ABSTRACT

To study the effectiveness of Covalent Plasma therapy (CPT) for combating COVID-19 diseases we have carried out a rapid of case series studies. Various academic publication related to convalescent plasma therapy for covid 19 are studied, number of participants their result after convalescent plasma therapy and amount of antibodies level has been studied. How transfusion of convalescent plasma therapy helps to cure Covid 19 patients studies is various series as A, B, C, D, E and F. Most of the studies show convalescent plasma therapy could be one of the approach to treat COVID-19 patients, until the vaccine and other better intervention come into action.

Keywords

Corona Virus; COVID-19; Combating Covid-19; Convalescent Plasma Therapy; SARS-CoV-2.

Introduction

In December 2019, severe acute respiratory syndrome coronavirus-2, a novel corona virus, initiated an outbreak of pneumonia from Wuhan in China, which rapidly spread worldwide. The clinical characteristics of the disease range from asymptomatic cases or mild symptoms, which include nonspecific symptoms such as fever, cough, sore throat, headache, and nasal congestion to severe cases such as pneumonia, respiratory failure demanding mechanical ventilation to multi-organ failure, sepsis, and death [1].

As the transmission rate is quite alarming, we require an effective therapeutic strategy to treat symptomatic patients and adopt the preventive measures in order to contain the infection and prevent community transmission. Corona virus disease 2019 (COVID-19) pandemic is a public health emergency of international concern. Global institutions and companies have begun to develop vaccines for the prevention of COVID-19 however it has not been successfully implemented in practice. Some countries have started plasma therapy to combat COVID-19.

Plasma therapy is the method of treatment under which plasma, found in the blood of a person who had recovered earlier from the same disease, is transfused into the blood of the new patient. It is

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not a universally accepted method of treating COVID-19 patients and is being used as a test case in many countries. Here, we review the current scenario of convalescent plasma therapy (CPT) used globally after the outbreak of the virus in 2019. This qualitative analysis will discuss how plasma therapy helping to combat for COVID-19. **Material and methods**

This research is a qualitative analysis where systematic literature review of records related to effectiveness of Convalescent Plasma therapy (CPT) for combating COVID-19 diseases studied. Inclusion and exclusion criteria is taken, based on the relevant of topic. Pubmed is the key source for database however google scholar and other scholar academic sites were used for data extraction and synthesis.

Out of fifty plus related articles about plasma therapy and its effectiveness to fight with COVID19, ten specific articles were included for inclusion criteria. Among ten articles also only four more specific studies are selected for qualitative analysis. Extracted data and statistics are used for interpretation and

understanding effectiveness of convalescent plasma therapy to fight against Covid19. Comparative studies of antibodies before and after the plasma transfusion is the key guideline that gives the

effectiveness of the plasma therapy to combat covid 19.

Various tables labelled table are used to study different parameters in the study.

A figure 1.1 summarizes the treatment and major laboratory findings of patient A. This patient had persistent positive results for throat tests. Transfusion of convalescent plasma was given on 10th, 13th, and 16th March, respectively. Representative chest CT images on 29th February and 4th March suggest the absorption of patchy scattered GGOs in the right lung (indicated by white arrows). Repeated throat swab test indicates clearance of residual SARS-CoV-2. CT, computed tomography; GGO, ground glass opacity; PCR, polymerase chain reaction result [6].

A figure 1.2 the patient manifested as consolidation involving multiple subsegmental lobes. The patient received convalescent plasma on 5th and 9th March. The dynamic evolution of consolidation was presented by chest CT on 22nd February, 5th, 11th, and 18th March, respectively. CT, computed tomography; PCR, polymerase chain reaction result [6].

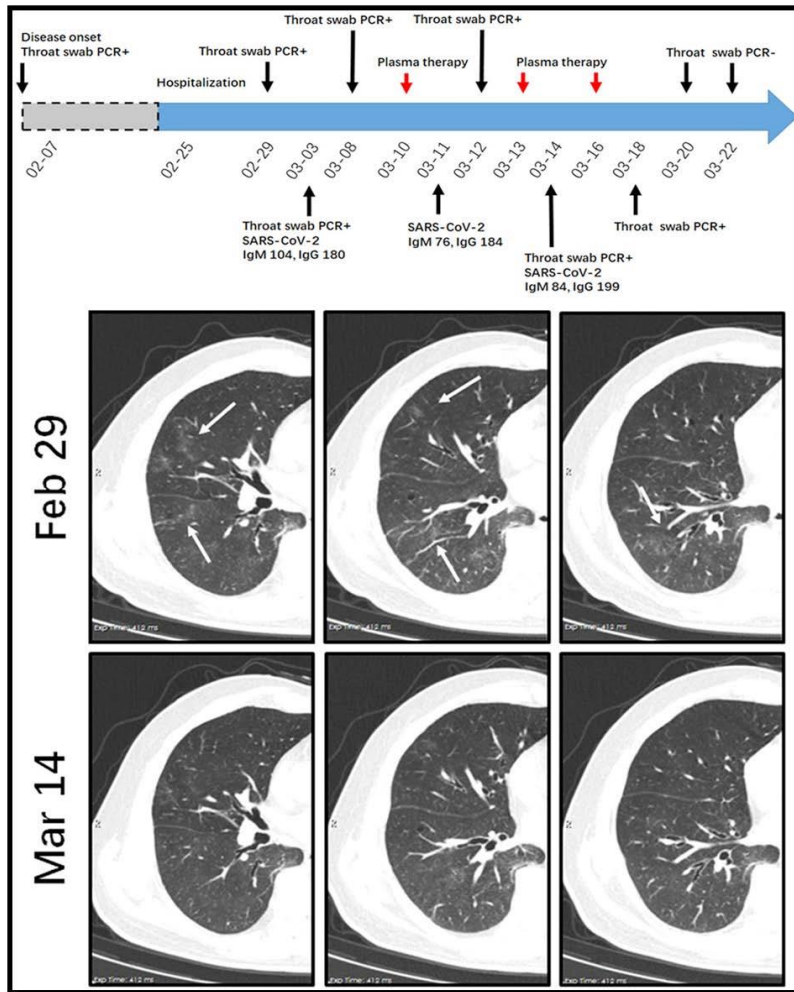


Figure 1.1 Source: Journal Of Medical Virology 2020 (Patient A).

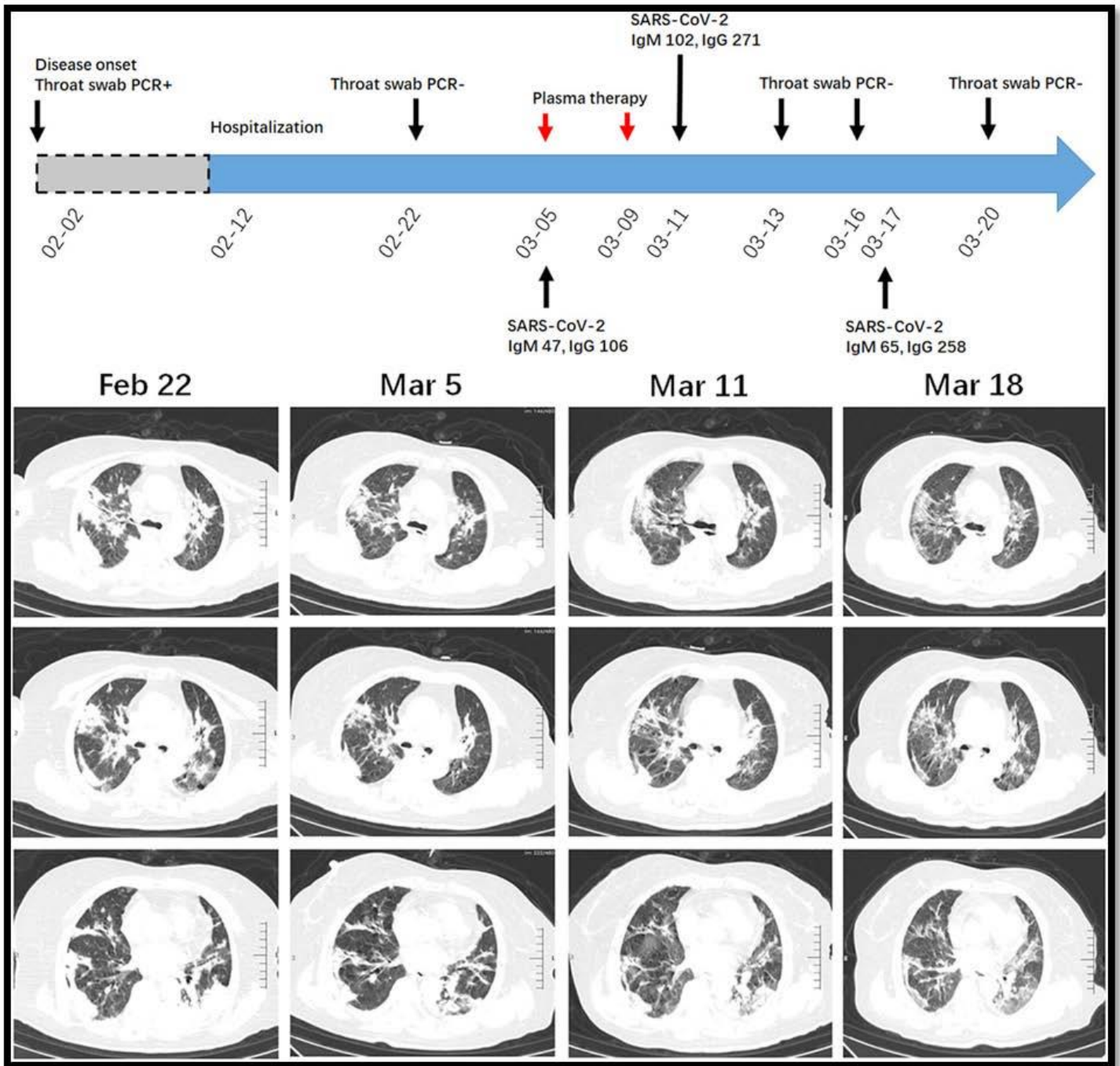


Figure 1.2. Source: Journal of Medical Virology 2020 (Patient B).

A diagram (Figure 1.3) the treatment and major laboratory findings of patient #c. Chest CT on 21st February showed consolidation, multiple GGOs, reticular opacities with fibrosis streak. The patient received three cycles of convalescent plasma therapy and this intervention led to the alleviation of symptoms, as well as a gradually radiologic improvement. A septal line appeared in left down lobe after indicated treatment. CT, computed tomography; GGO, ground glass opacity; PCR, polymerase chain reaction result [6].

A figure 1.4 shows the treatment and major laboratory findings of patient #D. The 63-year-old female patient concurrent with Sjögren syndrome had multiple GGOs with partial consolidation and fibrosis streak at admission. After indicated treatment, she presented as GGOs with partial consolidation. Transfusion of convalescent plasma was done on 10th March, and repeated chest CT showed a slight decrease in the density of GGOs. CT, computed tomography; GGO, ground glass opacity; PCR, polymerase chain reaction result [6].

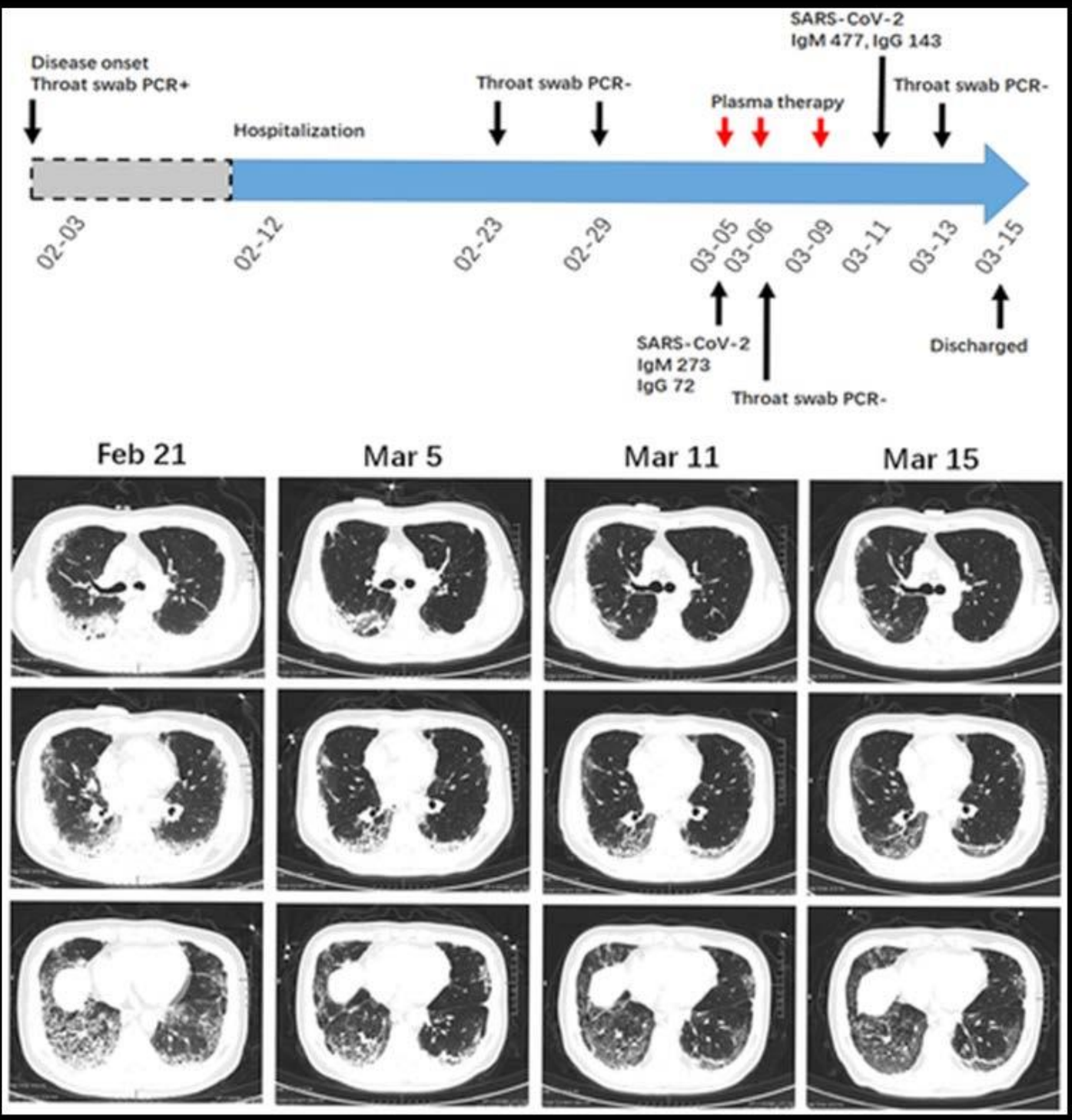


Figure 1.3. Source: Journal of Medical Virology 2020 (Patient C).

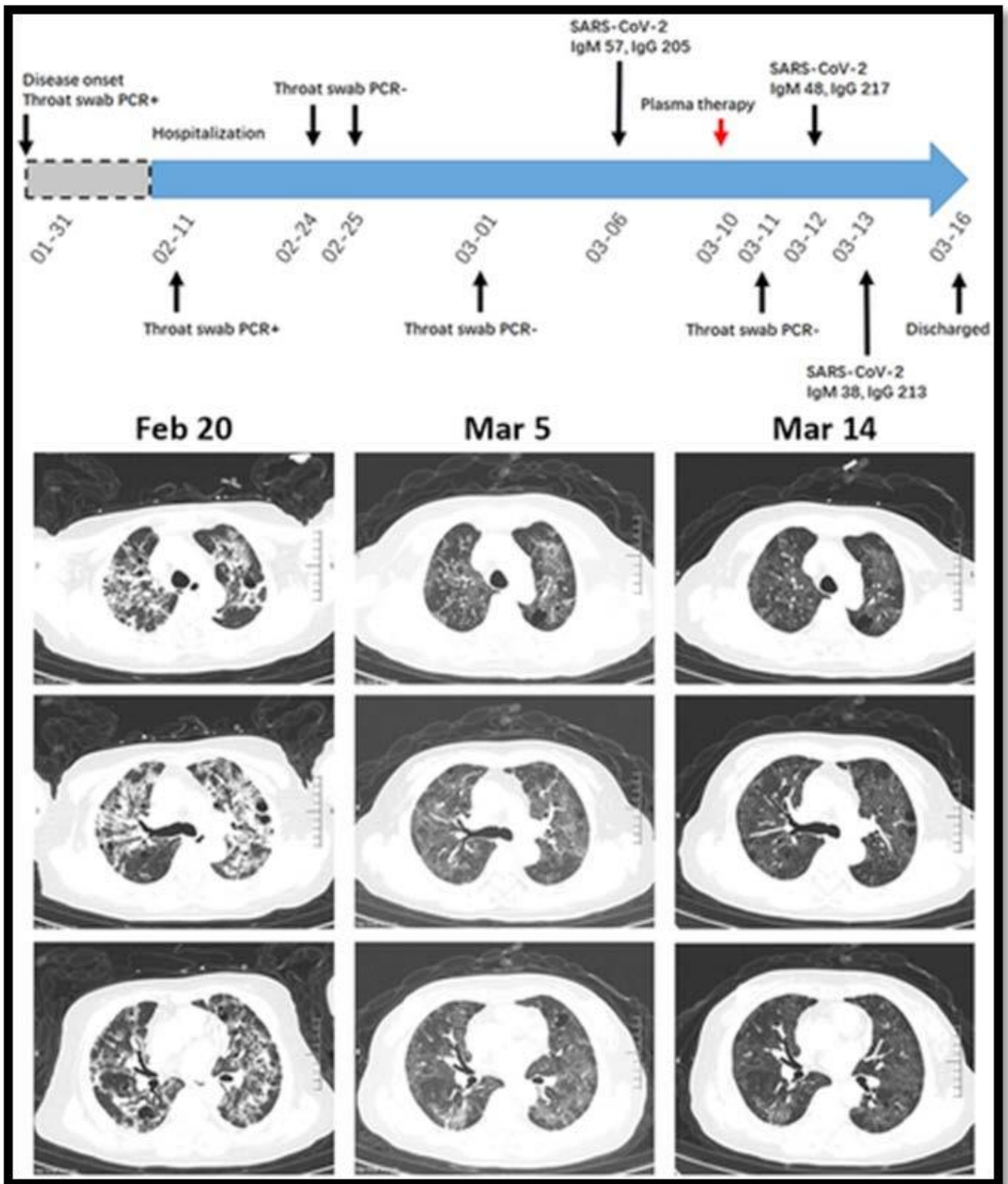


Figure 1.4. Source: Journal of Medical Virology 2020 (Patient D).

Figure 1.5. Source: Journal Of Korean Medical Science (Patient E).

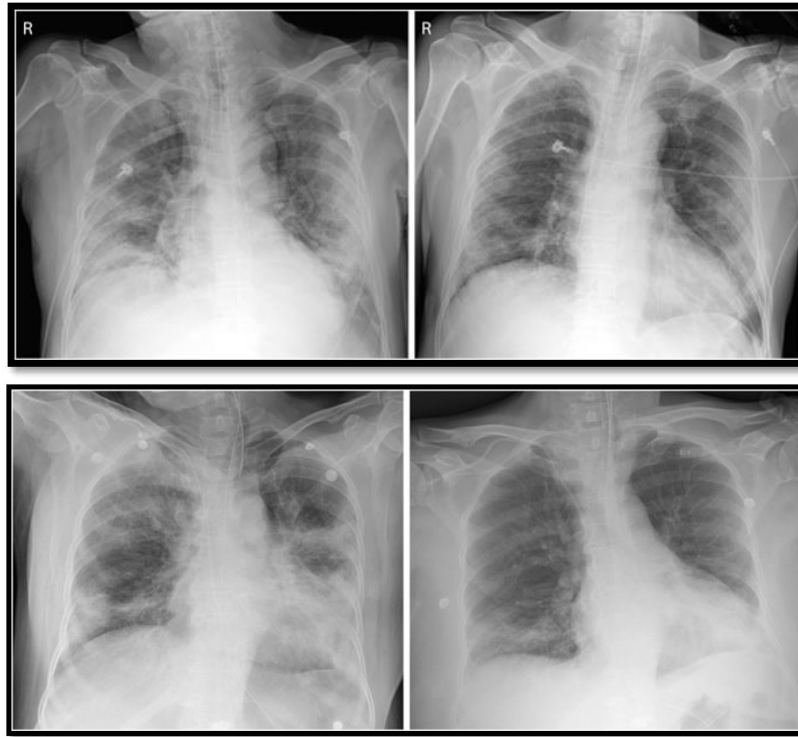


Figure 1.6. Source: Journal Of Korean Medical Science (Patient F).

No of articles	Authors/Publication	Number of patients	Country	Patients symptoms	Therapy applying.
Series1	Chenguang Shen ¹ , Zhaoqin Wang ¹ , Fang Zhao ¹	5	China	acute respiratory distress syndrome (ARDS) who met the following criteria: severe pneumonia with rapid progression and continuously high viral load despite antiviral treatment	All 5 were treated with convalescent plasma transfusion.
2	No authors listed (journal is referenced)	103 participants with laboratoryconfirmed COVID-19	Wuhan china	severe (respiratory distress and/or hypoxemia) or life-threatening (shock, organ failure, or requiring mechanical ventilation)	Convalescent plasma in addition to standard treatment (n = 52) vs standard treatment alone (control) (n = 51),
3	Mingxiang Ye MD, PhD Dian Fu MD Yi Ren MD Faxiang Wang MD Dong Wang MD, PhD Fang Zhang MD Xinyi Xia MD	19	China	A cluster of pneumonia patients manifesting as fever, cough, and dyspnea with unknown etiology.	at least one cycle of ABOcompatible convalescent plasma transfusion (200 mL for each cycle). Each transfusion was administered over a 30-minute period.
4	Jin Young Ahn, ^{1*} Yujin Sohn, ^{1*} Su Hwan Lee, ¹ Yunsuk Cho, ¹ Jong Hoon Hyun, ¹ Yae Jee Baek, ¹ Su Jin Jeong, ¹ Jung Ho Kim, ¹ Nam Su Ku, ¹ Joon-Sup Yeom, ¹ Juhye Roh, ² Mi Young Ahn, ³ Bum Sik Chin, ⁴ Young Sam Kim, ¹ Hyukmin Lee, ² Dongeun Yong, ² Hyun Ok Kim, ² Sinyoung Kim, ² and Jun Yong Choi	Korea	2	Patient (E) Fever and cough. Patient (F) medical history of hypertension developed fever and myalgia. <i>.(Jin Young Ahn, et al 2020)</i>	Plasma transfusion.

Table 1: Demographic studies.

Patient characteristics	Patients characteristics after treatment	Remarks
series 1	Patients received transfusion with convalescent plasma with a SARS-CoV-2-specific antibody (IgG) binding titer greater than 1:1000 (end point dilution titer, by enzyme-linked immunosorbent assay [ELISA]) and a neutralization titer greater than 40 (end point dilution titer) that had been obtained from 5 patients who recovered from COVID-19. Convalescent plasma was administered between 10 and 22 days after admission	
Series2	Primary outcome was time to clinical improvement within 28 days, defined as patient discharged alive or reduction of 2 points on a 6-point disease severity scale (ranging from 1 [discharge] to 6 [death]). Secondary outcomes included 28-day mortality, time to discharge, and the rate of viral polymerase chain reaction (PCR) results turned from positive at baseline to negative at up to 72 hours	
Series 3	The primary outcome was the improvement in symptoms and chest CT in the following days after the indicated intervention.	
Series 4	Patient(E)The patient underwent a tracheostomy, is successfully weaned from the mechanical ventilator.(<i>Jin Young Ahn,etal2020</i>) Patient (F)he patient is successfully extubated and discharged from the hospital on day 24. SARS-CoV-2 was negative after day 20. .(<i>Jin Young Ahn,etal2020</i>)	

Table 2: Patients characteristics after treatment.

Series no	Change in pulmonary function	Number of patients	Remarks
1	Of the 5 patients, 3 have been discharged from the hospital (length of stay: 53, 51, and 55 days), and 2 are in stable condition at 37 days after transfusion.	5	The limited sample size and study design preclude a definitive statement about the potential effectiveness of this treatment, and these observations require evaluation in clinical trials.
2	patients in the convalescent plasma group experienced adverse events within hours after transfusion that improved with supportive care.	2	
3	Patient aged (A) 69, serum anti-SARS-CoV-2 it is said that antibody were comparable to those before plasma therapy. After careful evaluation, the patient was considered as cured and was ready to discharge from the hospital (<i>mingxiang et al ,2020</i>) . Patient aged (B)75, After two cycles of convalescent plasma intervention, the density of consolidation was gradually reduced and turned into scattered GGOs with the subpleural line. Three independent throat swab tests were all negative for SARS-CoV-2. The patient was considered cured and was under further clinical monitoring(<i>mingxiang et al ,2020</i>). Patient aged© 56 (with extensive lung lesions before transfusion has given cycles of plasma therapy . As expected, serum IgM and IgG titers increased after plasma transfusion. Repeated chest CT examination on showed a complete resolution of the consolidation and gradual resolution of GGOs around the reticular vacuole. Arterial blood gas analysis on after plasma transfusion indicated a PO ₂ /FiO ₂ ratio of 330. The patient was cured and has discharged from the hospital(<i>mingxiang et al ,2020</i>) . A patient 63-year-old (D)woman with 10 years history of Sjögren syndrome after plasam transfusion the density of GGOs tended to reduce, while the distribution pattern was not changed. The serological examination showed that the patient was positive for anti-SARS-CoV-2 IgM and IgG and the patient had a negative throat swab result (<i>mingxiang et al ,2020</i>)	19 (out of 19 participants 4 participants result is tabulated as, patient A,B,C,D and E)	The mechanism of action in this setting was not fully understood. Researchers speculated that the anti-SARS-CoV-2 IgM and IgG directly neutralizes the virus, and the anti-inflammatory contents may prevent cytokine storms. For the latter hypothesis, there is great debate of using corticosteroids
4	Patient (E) A chest X-ray revealed further resolution of both lung infiltrates. (SARS-CoV-2 was quantified by detection of the RNA-dependent RNA polymerase region of the ORF1b gene on rRT-PCR. Patient (F) the density of bilateral infiltration on chest X-ray much improved with increased PaO ₂ /FiO ₂ to 230..(<i>Jin Young Ahn,etal2020</i>)		

Table 3: Changes of pulmonary function character.

Series	Result of SARS-CoV-2 RNA before transfusion	Result of SARS-CoV-2 RNA after transfusion	Remarks

Series 1	Positive	Viral load decrease and negative after 12 days of transfusion.	Of the 5 patients, 3 have been discharged from the hospital (length of stay: 53, 51, and 55 days), and 2 are in stable condition at 37 days after transfusion.
Series 2 and 3	Patient (A) The serum anti-SARS-CoV-2 antibody titers on 3rd March were 104 and 180 for IgM and IgG, respectively. Patient (B) Before the treatment, serum anti-SARS-CoV-2 antibodies titers for IgM and IgG were 47 and 106, respectively. Patient (C) the anti-SARS-CoV-2 IgM and IgG titers were 273 and 72, respectively. Patient (D) no particular data available about antibodies before plasma transfusion.	In patient (A) serum anti-SARS-CoV-2 antibody titers on 11th and 14th March were comparable to those before plasma therapy. Patient (B) a twofold increase in IgM and IgG titer than before plasma transfusion. In patient (C) it has mentioned that As expected, serum IgM and IgG titers increased after plasma transfusion however value has not been noted. Regarding patient D it has been said that the patient was positive for anti-SARS-CoV-2 IgM and IgG and the patient had a negative throat swab result.	the patient was considered as cured and was ready to discharge from the hospital.
Series 4	COVID-19 positive.	Convalescent plasma was administered after 22 days from the onset of symptoms in patient (E) and 7 days in patient (F), respectively. Because these are not in the early phase of the disease, it is difficult to determine clearly that the decrease in the viral load shown in both cases is due to convalescent plasma or natural pathology of COVID-19. (Jin Young Ahn, et al 2020)	

Table 4: Results of SARS-CoV-2 RNA load in A-F observed (patients) before and after convalescent plasma transfusion.

Chest X-rays in figure 1.5 of patient E taken before and after convalescent plasma infusion. Taken on day 7, just before the convalescent plasma infusion (left). Taken on day 13 shows marked improvement of bilateral infiltrations (right). The images are published under agreement of the patient [7].

Chest X-rays in figure 1.6 of patient F taken before and after convalescent plasma infusion. Taken on day 2, before the convalescent plasma infusion (left). Taken on day 6 shows marked improvement of bilateral infiltrations (right). The images are published under agreement of the patient [7].

Discussion

This rapid case series studies shows all participants A to F (six covid -19) patients who recovered from virus and discharged from hospital was under plasma transfusion. This literature review study highlights convalescent plasma therapy as an effective and specific treatment for COVID-19. In this research Series of cases has been studied which was observation report of clinician. One common parameter amongst all research article is plasma therapy an intervention measures to neutralise covid-19 on different patient.

In research different series of studies has shown how plasma therapy play role in order to treat COVID19. Most series of data suggest it is efficient to use plasma of the patient who is previously infected with Covid-19 and recover, however it has not clearly seen that how accurate and what amount of antibodies is administrated. In all research it was not discuss how many antibodies were produced in the patient bodies which is the limitation of the studies.

The key strength of this research is data, x-ray photos and graph (which are fully referenced) which suggest the incident of patient condition before and after covid19.

Conclusion

Convalescent Plasma therapy for combating COVID-19 diseases could be an effective measures, as many of the patient to whom convalescent plasma was injected recovered. However there are limitation on research as study is designed on small number of population. In addition number of antibodies administered to individual patient was not same (standardized). Further research and investigation is necessary to conclude the accuracy and success rate of plasma therapy.

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Conflict of interest

We all authors in collaboration declare that we don't have any conflict of interests.

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