

The COVID 19 Pandemic and Psychosis: The unusual Insight

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ABSTRACT

Background: COVID, believed to have emerged in Wuhan, China in Nov,19 and swiftly spread like wildfire across the continents. It wasn't much of a fantasy that it would become a headache for governments all over the world and would have a devastating impact on every sector alike, ravaging economies, especially medicine and healthcare. It was declared as a global pandemic in March, 2020. Predominantly thought of causing only pulmonary complications, it was soon revealed to be causing multiple neuropsychiatric complications in a few cases. Although it was with limited evidence, it was significant enough much like its counterparts SARS COV 1 and MERS. Neurological Problems ranged from a spectrum of anxiety to delusions, to even psychosis in some patients. However, the origin and pathogenesis of a COVID induced psychosis is still very much of a question mark. Since, many of the patient's diagnosis could be traced back to their family roots or some kind of substance abuse. In this review, the aim is to assess various associations which could be leading patients to developing new onset psychosis and the possible complications arising out of COVID 19 pandemic.

Objective: The purpose of this review article is to analyse the multiple case reports and their data interpretation reported throughout the world during COVID pandemic and give a summarized view.

Methodology: Various articles were searched individually containing significant key words that are in relevance to the mental illnesses comprising words like COVID, psychosis, schizophrenia, pandemic, mental illness across various platforms that is PubMed, Google scholar, BMJ, Medline, Frontiers, sage journals and various news articles and were summed up so as in an attempt to come to a conclusion which could lead to a certain possible etiology and the risk factors involved.

Key words: COVID, Psychosis, Psychiatry, Pandemic, Mental illness, Hallucinations, Delusions, Stress, Isolation, steroids

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INTRODUCTION

COVID has affected 256,966,237 people all around the world, out of which 5,151,643 died, according to data of WHO as of 22 November, 2021 [1] and many more of them scarred for life ending up with some sort of undiagnosed medical illness with no appropriate aid in sight. In the case of countries like India, where mental health is not a topic for discussion, it's not difficult to imagine the adversity people faced, along with the social stigma that came along with Covid-19. For the major part

of Southeast Asia, it will never be too farfetched to say poverty is a major driving force. The mandatory national lockdown that enforced educational institutions, industries and all and every businesses except food and healthcare to be shut, left many homeless and debt ridden, or battling multiple unprecedented issues. It's not much of a surprise the kind of distress it must have caused. A year and half into the pandemic, we are still dealing with consequences that came along. The devastating second wave that swept across the nation leaving insurmountable trauma to innumerable families and many more individuals, who are nothing but just a number in the ever increasing death toll.

Viral infections are very frequent occurring in nature, some of the notorious ones can cause significant impact on CNS, leading to neuropsychiatric complications that can affect the cognitive, affective and behavioral domains [2]. Coronavirus can be classified as one such virus.

Literature gives evidence of a relationship between

infection and psychotic states which could be traced back many centuries, in the 17th and 18th century it was recognised that specifically, mostly respiratory infections, are temporally associated with acute psychosis. Most notably, hundreds of cases of acute post-influenza psychosis were reported during and after the 1918–19 Spanish influenza pandemic termed as 'psychosis of influenza'.

In bio-scientific terms, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a single stranded, enveloped, RNA virus. It belongs to a family of the human coronavirus (HCoV) that mainly targets the lower respiratory tract and causes respiratory distress in the affected individuals [3]. In the last decade, two outbreaks have been reported by beta coronaviruses, namely, SARS-CoV-1 and MERS-CoV, occurred in 2002 and 2012 respectively. Although it had caused global anxiety, both events were contained without having much widespread concern [4].

COVID 19, shows a very similar pattern to its predecessors MERS and SARS COV 1, supposedly causing central nervous system manifestations which are evidently being seen through the symptoms such as ageusia; loss of taste and anosmia; loss of smell followed after or with generic symptoms of a common viral infection such as muscle aches, headache, congestion or runny nose, fatigue, sore throat, fever and cough [5] and many more that are being studied with its evolving state.

In terms of definition, Psychosis is a state in which the patient stays out of touch with reality and a lack of insight. The manual for psychiatry illnesses DSM-V doesn't provide a solid or proper definition for psychosis. Rather, it allows for psychotic disorders, to be defined as abnormalities in one of the five domains as mentioned below:

- ✓ Delusions.
- ✓ Hallucinations.
- ✓ Disorganized speech (frequent derailment/incoherence).
- ✓ Disorganized behavior (disoriented/catatonic).
- ✓ Negative symptoms [6].

The specific DSM-5 criterion for brief psychotic disorder includes:

- ✓ Patients must have one or more of the above mentioned symptoms that are delusions, hallucinations and disorganized speech .Out of which, one or more of the first three symptoms should be present.
- ✓ The time span of an episode should be at least one day but less than a month, with ultimately a return to their premorbid functioning
- ✓ The disturbance couldn't have been aptly attributed to a major depressive/bipolar Disorder with their psychotic features or by any other psychotic

disorder (eg, schizophrenia or catatonia), nor resulting as physiologic effects of a substance use or medication or some medical morbidity [7].

Pathophysiology

The various factors involved in Pathophysiology of a COVID pandemic related psychosis still remain a mystery with a multitude of hypotheses floating around. COVID 19 is a neurotropic virus, which means it has a particular affinity to neurons. Most of the theories focus in favor of its meddling and exploiting the ACE2 receptors. The spike protein on SARS-CoV-2 binds to the ACE2 receptors and the enzyme TMPRSS2, which assists the virion entrance into the cell, following which the virion proceeds to release its RNA, some part of which is translated to proteins and the RNA are assembled into a new virion in the Golgi [8]. Exposure to SARS-CoV-2 induces inflammation by meddling with these receptors, which are found over glial cells and neurons in the brain leading to neuro inflammation [9]. These cells were found to be a potential target for COVID 19 and eventually lead to development of neuropsychiatric and behavioral symptoms. The movement of the COVID-19 virus to the brain via the cribriform plate close to the olfactory bulb can be an additional pathway [10].

Immune based triggers have usually been incriminated in the past behind the pathogenesis for a great number of psychiatric illnesses, as in case of schizophrenia, depression, and implicated in neuropsychiatric manifestations of HIV infection and other viruses as well [11] This is one such aspect which could play an important factor, namely 'cytokine storm', a hyper inflammatory response in the central nervous system, infiltrating immune cells [12]. To summarize, mechanisms include dissemination into the CNS via blood, relocating from the ethmoidal bone into olfactory bulb, from immune mediated channels, and through the glial cells and neurons expressing angiotensin converting enzyme 2 receptors that lines our blood-brain barrier [13].

Development of a new onset psychosis comes more as of a late manifestation. There are a myriad of limited studies and case reports that have shown the association between SARS-COV1/ MERS-COV outbreak and psychosis. So, a possible similar pattern in relevance to Covid19 is very much plausible.

However, it is very likely to be influenced by various risk factors including environment, medications and biological roles. In relevance to countries like India, there has been a great deal of collective triggers. Beginning from shutting down of the educational institutions, industries, work from home, refraining from socializing and public gatherings, and the whole stigma around it, loss of jobs and a failing healthcare system trying to cope up with the aftermath of a devastating pandemic. Frequent mention and constant fear mongering of it all over the news, television and social media had a great impact on the quality of life of people and brief psychotic episodes were mostly set off by stress and anxiety in even rather asymptomatic individuals. Abuse of High

dose corticosteroids has been implicated as a significant causative factor in psychotic presentations. However, a definitive biological association cannot be asserted without much evidence based data.

Clinical presentation

A few cases reported from a number of countries revealed association of COVID 19 and brief psychotic episodes, most of them resolving with the help of medications or on its own. The patients had presented with no prior family history or did any kind of substance abuse. Symptoms included delusions, being prejudice, reference and persecutory, attention disturbances and disorientation, hallucinations (auditory/visual). Here, we discuss a number of case reports that linked the psychotic episodes to COVID affected individuals.

Case report 1[14]

Desai et al describe a case of 55 year-old female patient, having no prior history of any known psychiatric illness treated for COVID 19 with oxygen, steroids and was briefly on remdesivir therapy before presenting to emergency medicine department with a brief psychotic episode, where she was experiencing auditory hallucinations and delusions of religious themes. She reportedly was hearing the voice of God for saving the earth. Also, COVID-19 was consistently a centre of focus to those hallucinations/delusions. She was successfully treated with lorazepam, valproate and antipsychotics such as haloperidol. The conclusion being, there could be multiple variables like psychosocial stress, underlying bipolar disorder, steroid therapy which cannot be ruled

out, COVID 19 infection did enhance the likelihood of a psychotic episode in such individuals.

Case report 2[15]

Cameron et al reports a case of a 58 year old male with no hallmark symptoms of COVID and presenting with acute psychosis, with a positive RTPCR report. Patient was markedly confused and hallucinating. He gave a history of substance abuse in the past including opioids and cocaine. No obvious abnormality could be seen in scans and no amount of alcohol in the bloodstream was there. Urine was negative for any kind of substance use. Patient was initially treated for hepatic encephalopathy with chronic hepatitis C in view of a USG abdomen suggesting ascites and cirrhosis, but despite the medications continued to show erratic behavior for which he was shifted to inpatient psychiatric care. Eventually diagnosed with acute psychosis and was treated with lorazepam and haloperidol following which he made improvements. The possible explanation for encephalitis and altered sensorium may occur as a result of inflammatory response and cerebral edema [16], which has its roots in neuro inflammation.

Case report 3 [17]

Chandra et al give an account about a 34 year old rural woman, married and having two children presenting with a history of 2 days of feeling being too anxious and dreaded getting infected and death of her family. Being an extremely religious woman, she was stressed over the cancelled rituals and visits to local temples during the lockdown and was thoroughly convinced that she would

Table 1: Details of psychosis.

Study	Design	No. of cases	COVID 19 Infection	Age/ Sex	Details of psychosis	Past/ Relevant medical history
1	Chandra et al [17]	2	No	34/F	Acute polymorphic psychosis, induced by stress. Convinced that she was cursed by deity for not following religious rituals.	H/O 1 brief psychotic episode in father K/C/O Anxiety
			No	24/F	Acute polymorphic psychosis (postpartum onset), induced by pressure from the family for male child. Also worried that she might infect the baby by nursing.	Nil
2	Saral Desai et al [13]	1	Yes	55/F	Brief psychotic episode Auditory hallucinations Hearing God commands Constant agitation	F/H/O bipolar disorder type one in a distant cousin
3	Cheng et al [21]	1	Yes	58/M	Acute psychosis	H/O Hepatitis C and substance in past Tt with hydroxychloroquine for COVID
4	Parker et al [22]	1	Yes	-	Psychosis secondary to COVID 19	Nil
5	Correa Palacio et al [23]	1	Yes	43/M	Psychosis secondary to COVID 19	Treated with steroids H/o cocaine abuse
6	Smith et al [24]	1	Yes	36/F	Persecutory delusions (Health care professional)	Nil
7	Alba et al [25]	1	Yes	40/M	Thoughts about angels and demons possessed Diagnosed as brief psychotic episode	Nil
8	Varatharaj et al [20]	10	Yes	-	New onset psychosis	Nil with most of them
9	Oca Rivas et al [26]	1	No	60/M	Obsessive delusions about infecting family (Medical Professional)	Nil
10	Al Busaidi et al [27]	1	Yes	45/M	Suspicious Jumps out of the window on God's command Brief psychotic disorder	H/o ICU Stay on mechanical ventilation Treated with steroids
11	Lim et al [28]	1	Yes	55/F	Persecutory delusions and hallucinations Lasted for 40 days	Nil
12	Zulkifli et al [29]	1	No	31/M	Extreme stress induced psychosis	Nil

be cursed by the deity for the same reason. Her father had experienced a brief psychotic disorder in the past. All her cognitive functions were intact. She was given a diagnosis of Acute Polymorphic Psychosis and was significantly improved with the doses of Risperidone and clonazepam. Although being negative for COVID 19 and no other symptom in sight, the above patient showed delusion apparently triggered by the COVID pandemic as a whole by exaggerating the risk factors in an already vulnerable population.

There are miscellaneous reports identified with inconsistent findings varied along with different geographical, racial, personality differences.. A case report from Los Angeles describes a patient who came with neck stiffness, possibly a sign of meningitis and came out to be positive for COVID-19, despite revealing no respiratory symptoms on initial presentation [18]. She became disoriented and had hallucinations, though CSF results were inconclusive and didn't point out the cause as COVID.

While another woman in Japan presenting with fever, and fatigue followed soon after by meningitis revealed a negative nasopharyngeal swab but CSF confirmed the presence of coronavirus [19].

A nationwide study done by Varatharaj et al United Kingdom in collaboration identified a total of 153 confirmed cases, out of which 10 were suggestive of having a new onset psychosis [20].

It's difficult to attribute the psychotic episodes to a single cause, but the association seems to be there. However, not significant enough until there are more calculated studies rather than isolated incidents. Many of these patients did not necessarily fit into the criteria since many of them had a predisposing condition which could be easily blamed or, the treatment. For instance, in the previous SARS pandemic, many patients who received large doses of corticosteroids consequently dealt with hallucinations and manic disorders, subsiding soon after the medications ceased [21].

Treatment guidelines are not specified per se, limited mostly to symptomatic and providing supportive treatment to alleviate the symptoms, via appropriate antipsychotics and anxiolytics wherever needed.

DISCUSSION

COVID 19 is a continuously evolving virus with complex modes of propagating. It has left in ruins the greatest of economies, creating havoc with the rapid transmission and high infectivity rates. In order to contain the spread, the world came to a halt with numerous lockdowns re-enforced, social distancing measures enforced and mandatory mask application. This forced millions of people into an endless spiral of poverty and in isolation which came with its own set of problems either in the form of exacerbated pre-existing mental disorders or with the emergence of conditions like new onset psychosis, distributing across the varied age

groups. It affected the quality of life of people one way or another. Patients presenting with brief psychotic episodes were eliciting delusions, hallucinations and disorientated speech and behaviors and were briefly put on medications to aid them with. Almost all of them resolved, leaving no existing morbidity to the affected individuals. The literature on its ever evolving clinical presentation and pathophysiology still remains in a great deal of ambiguity.

CONCLUSION

While most cases presented with very similar and redundant patterns. It's still challenging enough to determine a firm causal association between the COVID 19 pandemic and psychosis. As the studies that have been done come with their own set of limitations, hence It warrants detailed and further extensive studies to corroborate the already reported findings, keeping the influencing factors like geographical, economical, psychosocial variables in mind. Both the symptomatic and asymptomatic population is at risk because of the multitude of risk factors at play. At present, the treatment we have established appears greatly symptom based and supportive as in case of neurological complications. More research should be done so as to know how corona virus propagates and mitigates through the blood brain barrier to cause a variety of symptoms and its isolation from the CSF. Role of corticosteroids must be investigated with thorough studies to distinguish from a steroid induced psychosis. It will also be a sound decision to screen through the family histories before ascertaining the diagnosis.

CONFLICT OF INTEREST

The authors are responsible for the content and have no conflicts of interest.

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