

# **Asymptomatic COVID-19 infection induced first episode psychosis - A case series.**

## **ABSTRACT**

**Aims:** We presented 3 similar cases of 1<sup>st</sup> episode psychosis that occurred after Corona Virus Disease -2019 (COVID-19) infection which we treated at our institute, to provide more evidence to the existing literature and to describe whether even an asymptomatic COVID-19 can induce psychosis in previously healthy individuals and tried to elaborate the probable etiology and nature of the psychotic symptoms.

**Presentation of the Cases:** All the 3 cases had COVID-19 infection, few days before their psychotic symptoms started for the 1<sup>st</sup> time. They didn't have any history of regular substance or medication use that are known to induce psychosis or any psychiatric disease previously, without any abnormality in physical examinations and laboratory investigations. All the cases had history of stress which were not overwhelming (except the 3<sup>rd</sup> case) and were mostly related to COVID-19 infection and pandemic associated social and financial stress. 1<sup>st</sup> case (54 years, married male) developed delusion of persecution, delusion of reference, 2<sup>nd</sup> and 3<sup>rd</sup> person auditory hallucinations, 2<sup>nd</sup> case (61 years, widower male) developed delusion of persecution, 2<sup>nd</sup> person auditory hallucination (commanding type), disinhibited behaviour (disrobing in public) and the 3<sup>rd</sup> case (32 years, unmarried male) developed delusion of persecution and misidentification (Intermetamorphosis). All of them responded well to commonly used antipsychotics within 4 weeks that prompted a diagnosis of Acute and Transient Psychotic disorder.

**Discussion:** This study points out that even an asymptomatic COVID-19 can induce psychosis for the first time in life, where the etiology most probably is the direct effect of the virus itself on brain or the COVID-19 and pandemic related stress which is supported by the fact that factors like substance use or medication use or any comorbidity that can induce psychosis were also absent. The nature of psychosis are commonly persecutory delusion and auditory hallucination with one case having Intermetamorphosis phenomenon which is a rare finding and perhaps a novel finding in post-COVID-19 Psychosis.

**Conclusion:** All COVID-19 infected individuals should be screened early for any symptoms that raise the suspicion of psychosis. Large studies are needed to ascertain the etiology of post-COVID-19 psychosis.

*Keywords: COVID-19; psychosis; first episode psychosis; asymptomatic COVID-19; delusion; hallucination; delusional misidentification; intermetamorphosis*

## **1. INTRODUCTION**

Corona virus disease -2019 (COVID-19) [1] is not only responsible for millions of deaths but also associated with neuropsychiatric sequelae at an alarmingly high prevalence of around 34% [2], which are mostly anxiety disorders, depression and post traumatic disorders [3], but a retrospective study by Taquet M et al on COVID-19 survivors indicated that post-COVID-19 psychosis (1.4%) is also not much behind.

The number of studies investigating psychotic disorders that occurred after or concurrently with documented COVID-19 infection without any prior history or definitive cause, except which can be attributable to COVID-19 are still less in number and are mostly case reports [4] with few case series [5].

A longitudinal study showed 45% increase in new onset psychosis during 2020 in comparison to 2019, but the link between COVID-19 and psychosis could not be well established as the RTPCR for COVID-19 were mostly negative in those cases [6]. Also, studies mostly showed psychosis is more likely among severe COVID-19 survivors who had been hospitalized but chances are less among non-hospitalized patients [2,7] and none of the studies clearly focused on the fact that whether an asymptomatic COVID-19 infection can also cause psychosis.

On the other hand, the fact that furthers the need for more researches on COVID-19 related psychosis is, new strains like Omicron (B.1.1.529) and its variants which are regarded as variants of concerns (VOC) [8] spreading rapidly throughout the countries that may cause huge psychiatric disease burden and significant morbidity.

Here we presented a case series consisting of 3 cases of COVID-19 infection, each of them presented at our institute's post-COVID-19 mental health clinic as 1<sup>st</sup> episode psychosis after asymptomatic COVID-19 infection without having any prior history or family history of psychotic disorders.

## **2. PRESENTATION OF THE CASES**

### **2.1 Case 1:**

A 45 years old married man, educated upto 9<sup>th</sup> standard, working as a tailor, living with his wife and son, an occasional smoker, without history any other substance abuse, long-term medication or physical comorbidity, presented with complaints of suspiciousness, fearfulness, hearing of voices even when alone, reduced sleep and occasional agitation for last 8 days, that started 1 week after being diagnosed as COVID-19 positive by RTPCR (Reverse Transcriptase Polymerase Chain Reaction) of nasopharyngeal swab on 03/04/2021, because his wife became symptomatic and had tested positive for COVID-19. He told us that his next-door neighbors and some unknown people wanted to harm him and his son. He was hearing voices that were speaking to him directly as well as discussing about him, which were threatening in nature and about killing him and his son, because they want to end his family and family lineage. The patient was collecting rods and sticks because he wanted to protect himself and his family from any probable attack conspired by those who were persecuting him.

Mental Status examination revealed delusion of persecution, delusion of reference, 2<sup>nd</sup> and 3<sup>rd</sup> person auditory hallucinations, absent judgement and insight. He did not receive any medicine for COVID-19 as he was completely asymptomatic and was in home isolation only.

No abnormality was found on general physical examinations, systemic examinations. Blood and urine biochemistry and MRI of brain (non-contrast) was normal. He was started with Olanzapine 10 mg/ day once a day and was reviewed after 1 week and 2 weeks and his symptoms reduced (BPRS score was 91, 46 and 22 on 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> visit respectively)

Absence of any pre-existing disease, absence of use of medication and alcohol or any other substance abuse, normal biochemical examination of blood, urine and MRI of Brain ruled out organicity. Preserved consciousness and orientation ruled out delirium. Symptom resolution within 4 weeks prompted a provisional diagnosis Acute and Transient Psychotic Disorder (ICD-10).

### **2.2 Case 2:**

A 61 years old, widower, graduate, working as an accountant, with diagnosed hypertension well controlled on medication, without any history of substance use, living with his son and daughter in law, presented with suspiciousness, reduced sleep, hypervigilant look, delusion of persecution ( that his colleagues implanted a computer virus in him, so that they can spy on him), 2<sup>nd</sup> person commanding hallucination ( some evil spirit is commanding him through the computer virus to do things which he doesn't want to do but he will be killed if he doesn't follow the command) and disinhibited behaviour in the form of disrobing in front of others, 3 days after being diagnosed of COVID-19 by RTPCR of nasopharyngeal swab on 3<sup>rd</sup> January 2022, because many of his office colleagues were tested positive. He presented in our OPD after 3 days of his symptoms started.

His physical examination, biochemical parameters of blood and urine and MRI of brain didn't reveal any significant abnormality. He was started with 1 mg / day tablet Risperidone on his first visit, 10 days after the symptoms started, and assessed after 1 week and the dose was increased to 3 mg/ day by increasing 0.5 mg/day, tablet Trihexyphenidyl 2mg /day was started in 2 divided doses, and was again assessed on 2<sup>nd</sup> week. His symptoms resolved completely on 3<sup>rd</sup> visit with BPRS scores being 90, 61 and 21 on 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> visit respectively.

With the presence of above-mentioned clinical features and normal and laboratory investigations, and without having any prior history of psychiatric disorder, substance use and use of medications that can induce psychosis, and the patient being conscious and oriented (that ruled out delirium) the provisional diagnosis of Acute and Transient Psychotic disorder (ICD-10) was made.

### **2.3 Case 3:**

In the 3<sup>rd</sup> case we treated a young man aged 32 years, graduate, unmarried, living in a joint family, without any comorbidity, any medication and without history of any addiction to alcohol or drugs. He was working as sales execute but lost his job after the COVID-19 pandemic started.

He presented with social withdrawal, absent eye contact, occasional agitation and aggressive episodes directed towards family members, reduced sleep, delusion of persecution (occasional refusal to food and water and sniffing them before eating or drinking, as he thought that his family members are trying to poison him), delusional misidentification ( his friend , who died of COVID-19 is not actually dead but has been replaced by his cousin brother, an Internetamorphosis phenomenon) for last 3 to 4 days which started after initial 5 days period of excessive worrying about dying, restlessness, perplexity, reduced sleep after being diagnosed with COVID-19 by RTPCR for Nasopharyngeal swab and death of one of his friends due to COVID-19 on the same day.

Complete physical examination, Biochemical parameters of blood and urine including urinary drug screening and MRI of brain did not reveal any abnormality. We started oral olanzapine 5 mg /day on his first visit which was increased to 10 mg /day divided into 2 doses on 2<sup>nd</sup> visit after 1 week and also lorazepam tablet 2mg/ day at night was started due to inadequate sleep. He was again assessed after 2 weeks and his symptoms improved (BPRS scores were 97, 68 and 26 on 1<sup>st</sup> 2<sup>nd</sup> and 3<sup>rd</sup> visit respectively).

From the history, clinical features, laboratory examinations and resolution of symptoms within 4 weeks, in absence of history of any substance abuse, the patient being conscious and oriented throughout, and not having any history of previous psychiatric disorder, we gave a provisional diagnosis of Acute and Transient Psychotic disorder (ICD-10).

## **3. DISCUSSION**

All the 3 cases described above had acute onset of psychosis and didn't have history of any psychiatric disorder, no obvious abnormality in laboratory findings, with only the 2<sup>nd</sup> cases having comorbid hypertension which was well controlled. Also, they didn't have history of use of any

medication like corticosteroid, antiviral or hydroxychloroquine that can induce psychosis [9]. Substance induced psychosis can also be ruled out as none of them had such history with only the 1<sup>st</sup> case identified as an occasional smoker. These findings are similar to some previous findings [10,11] where the 1<sup>st</sup> episode psychosis cannot be attributed to any other etiology except COVID-19.

The most probable etiology of psychoses in these cases is COVID-19 pandemic related psychosocial and COVID-19 related stress, as the stressful situation related to the pandemic were there in all the 3 cases [12], however stress and anxiety of the social and financial crisis due to the pandemic and fear of death were not severe enough except in the 3<sup>rd</sup> case. In some case reports, asymptomatic [13] and mild [11] COVID-19 cases were also followed by psychosis where stress was minimal or absent, and the possible cause were postulated as inflammatory response to COVID-19 [13]. Also, the neurotropism of the virus crossing the blood brain barrier [14,15] may be a possible etiology according to some researchers. But our in our cases, neither the inflammatory markers of these patients were raised, nor the brain neuroimaging had any abnormal finding. Again, facing job related and financial stress for more than two years since the pandemic started and the sudden onset of psychotic symptoms just after asymptomatic COVID-19 infection doesn't fit well, which should alarm the quest for more researches to find out whether only stress or anxiety are the possible etiologies or there are more to it.

Coming to the clinical findings, the primary psychotic symptoms in all the 3 cases were delusions and hallucinations except the 3<sup>rd</sup> case where hallucination was absent, which are a common feature in COVID-19 related psychotic disorders [16]. But we got a very rare finding, and also perhaps a novel finding in post COVID-19 psychosis which is Intermetamorphosis, one of the delusional misidentification syndromes, in the 3<sup>rd</sup> case.

We got excellent response to pharmacotherapies with 2<sup>nd</sup> generation commonly used antipsychotics in our cases, same as other studies [5, 10, 11]. Some studies showed that 1<sup>st</sup> episode of psychosis related to COVID-19 already accounted for cases of suicide [17,18], so it cannot be overemphasize that early diagnosis and treatment of new onset psychosis has several benefits like by improving the outcome through reduced duration of untreated psychosis, improving the treatment response, global functioning and social skills with reduction of burden on the family and society and prevention of disease progression into chronic disease like schizophrenia as well as decreasing the chances of suicide [19, 20].

#### **4. CONCLUSION**

First episode psychosis, though not much common like post-COVID-19 depression and anxiety disorders but can be one of the neuropsychiatric sequelae of COVID-19, which may be induced by even an asymptomatic COVID-19 infection also. It's still uncertain, whether it is the direct effect of the virus itself or the stress and anxiety related to COVID-19 or some other factors plays a role. With prompt diagnosis and treatment with commonly used antipsychotics, the prognosis is good and symptoms mostly resolves early. Individuals who had COVID-19 infection, even those who were asymptomatic, must be screened and followed up for any new onset psychiatric symptoms that warrants development of psychosis. More studies including prospective studies are required to ascertain the severity, nature, long term outcome of post-COVID-19 psychosis and the mechanism by which it can induce psychosis in previously healthy individuals.

#### **CONSENT**

As per international standard or university standard patients' written informed consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

Ethical committee approval was not applicable, as all the histories taken, clinical examinations and investigations done in this study are the parts of the natural treatment process of the patients who sought treatment at our institute's ongoing post-COVID-19 Mental Health Clinic. However, authors declare that this study was done in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

## COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors

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