# A Slow Beat and a Dizzying Feat: Covid-19 Related Bradyarrhythmia

**Abstract:**
Coronavirus disease (COVID-19) was formerly thought to be a respiratory ailment, however it has since been discovered to have an impact on practically all organ systems. Bradycardia is a recently identified COVID-19 ramification with uncertain prognostic significance. To the best of our knowledge, very few case reports have been reported on marked bradycardia as a complication of Covid-19 infection. Studies have revealed a higher risk of mortality in individuals with underlying cardiovascular disease as well as an increase in the prevalence of arrhythmias, cardiomyopathies, myocarditis, and acute coronary syndromes in infected patients. We report a case of a 72 year old male patient who exhibited persistent bradycardia following COVID-19 infection resulting in significant dizziness as a symptom. Clinicians should be aware of the mechanism by which COVID-19 affects the cardiovascular system and the drug side effects that are used in the treatment strategy for this fatal virus, even if the pathophysiology of bradycardia in COVID-19 may be multifactorial. A thorough review examining bradyarrhythmia and relative bradycardia in COVID-19-infected patients has not yet been published.

**Keywords:** Covis-19, Bradycardia, Arrythmias, Bradyarrythmias, Covidinfection .

**Introduction :**
In the wake of the global COVID-19 pandemic, medical professionals have been faced with an ever-evolving landscape of symptoms and complications associated with the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus [1] . While respiratory distress and pneumonia have been at the forefront of clinical attention, it has become increasingly evident that COVID-19 can affect multiple organ systems, leading to a wide array of clinical manifestations [7-10]. One such manifestation that has emerged as an intriguing and potentially life-threatening complication is bradycardia, a condition characterized by an abnormally slow heart rate. We describe a case of a 72-year-old man who experienced persistent bradycardia after contracting COVID and displayed symptoms of lightheadedness.

**Case presentation:**
A 72-year-old male with a past medical history of hypertension, was brought to the Emergency Department (ED) due to dizziness that had persisted for three hours. Upon arrival, he tested positive for COVID-19 using a rapid antigen test. The dizziness was described as occurring exclusively during walking and was not associated with changes in position or any other specific triggers.He denied experiencing chest pain, shortness of breath, palpitations, cough, headache, head injury, loss of consciousness, or any recent sick contacts or travel history. His home medications included amlodipine 5 mg PO daily, hydrochlorothiazide (HCTZ) 25 mg PO daily, and Lipitor 20 mg PO daily, all prescribed for the management of hypertension.On physical examination he appeared alert and oriented. Blood pressure was 134/59, pulse was 38,O2 saturation in room air was 98%,temp was 98 degree fahrenheit. Electrocardiogram showed marked sinus bradycardia

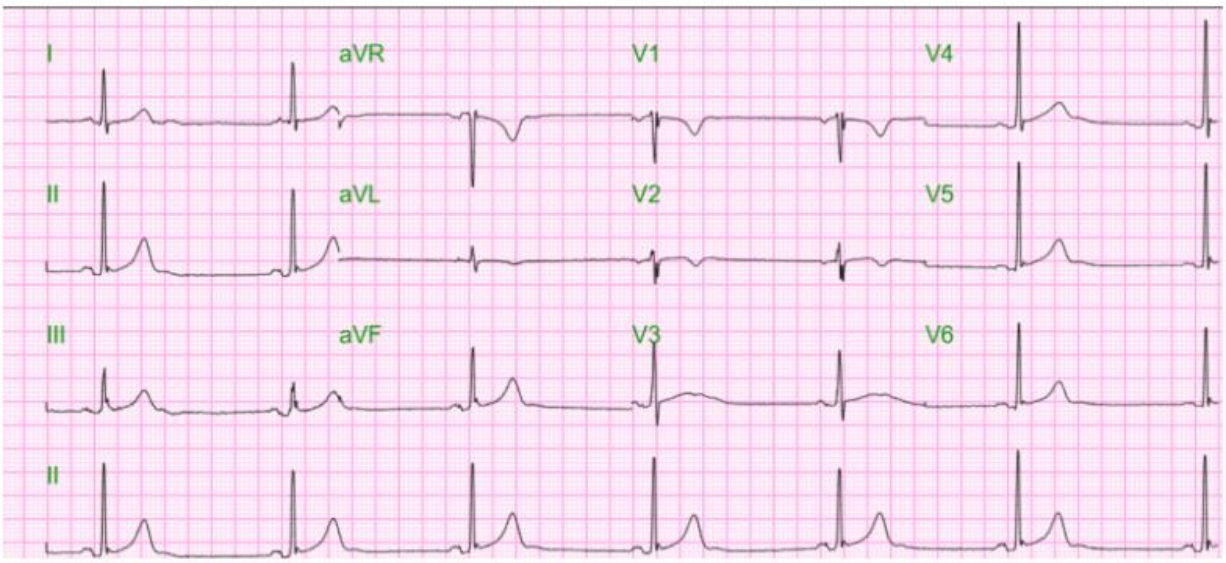


Fig. 1. Electrocardiogram showed marked sinus bradycardia

His labs on admission are illustrated in table 1.

**Table 1**. *Patient laboratory findings* on admission

| Investigation | Value | Reference range |
|---|---|---|
| Hemoglobin | 13.6 | 11.0 - 15.0 g/dL |
| Hematocrit | 39.8 | 35-46% |
| White Blood Cell | 9.5 | 3.8 - 5.3 10x6/uL |
| Platelets | 174 | 130 - 400 10x3/uL |
| Glucose | 117 | 80 - 115 mg/dL |
| Blood Urea Nitrogen | 12.9 | 9.8 - 20.1 mg/dL |

| | | |
|---|---|---|
| Creatinine | 0.87 | 0.57 - 1.11 mg/dL |
| Sodium | 131 | 136 - 145 mmol/L |
| Potassium | 4.4 | 3.5 - 5.1 mmol/L |
| Chloride | 96 | 98 - 107 mmol/L |
| Bicarbonate | 26 | 23 - 31 mmol/L |
| Calcium | 9.0 | 8.8 - 10.0 mg/dL |
| Albumin | 3.9 | 3.2 - 4.6 g/dL |
| Magnesium | 2.2 | 1.6 - 2.6 mg/dL |
| Brain natriuretic peptide (BNP) | 18 | 10.0 - 100.0 pg/mL |
| COVID PCR | Positive | Negative |
| High sensitivity Troponin I | <5.0 | 0.0 - 17.0 ng/L |
| Prothrombin time | 13.1 | 9.8 - 13.4 sec |
| international normalised ratio (INR) | 1.15 | 0.85 - 1.15 |
| Partial thromboplastin time (PTT) | 28.1 | 24.9 - 35.9 sec |
| Thyroid Stimulating Hormone | 2.560 | 0.465 - 4.680 uIU/mL |

| | | |
|---|---|---|
| T4 | 1.13 | 0.78 - 2.19 ng/dL |
| Urine toxicology | Negative | Negative |

Table 2. Investigation report

| Investigation | Value | Reference Value |
|---|---|---|
| Lactate Dehydrogenase (LDH) | 235 | 140-271 U/L U/L |
| Pro-calcitonin | 0.03 | 0.00 - 0.08 ng/mL |
| Erythrocyte Sedimentation Rate | 19 | 0 - 20 mm/hr |
| C-REACTIVE PROTEIN | 7.6 | <=0.1 mg/L |
| D-Dimer | 339 | <=500 ng/mL DDU |
| | | |

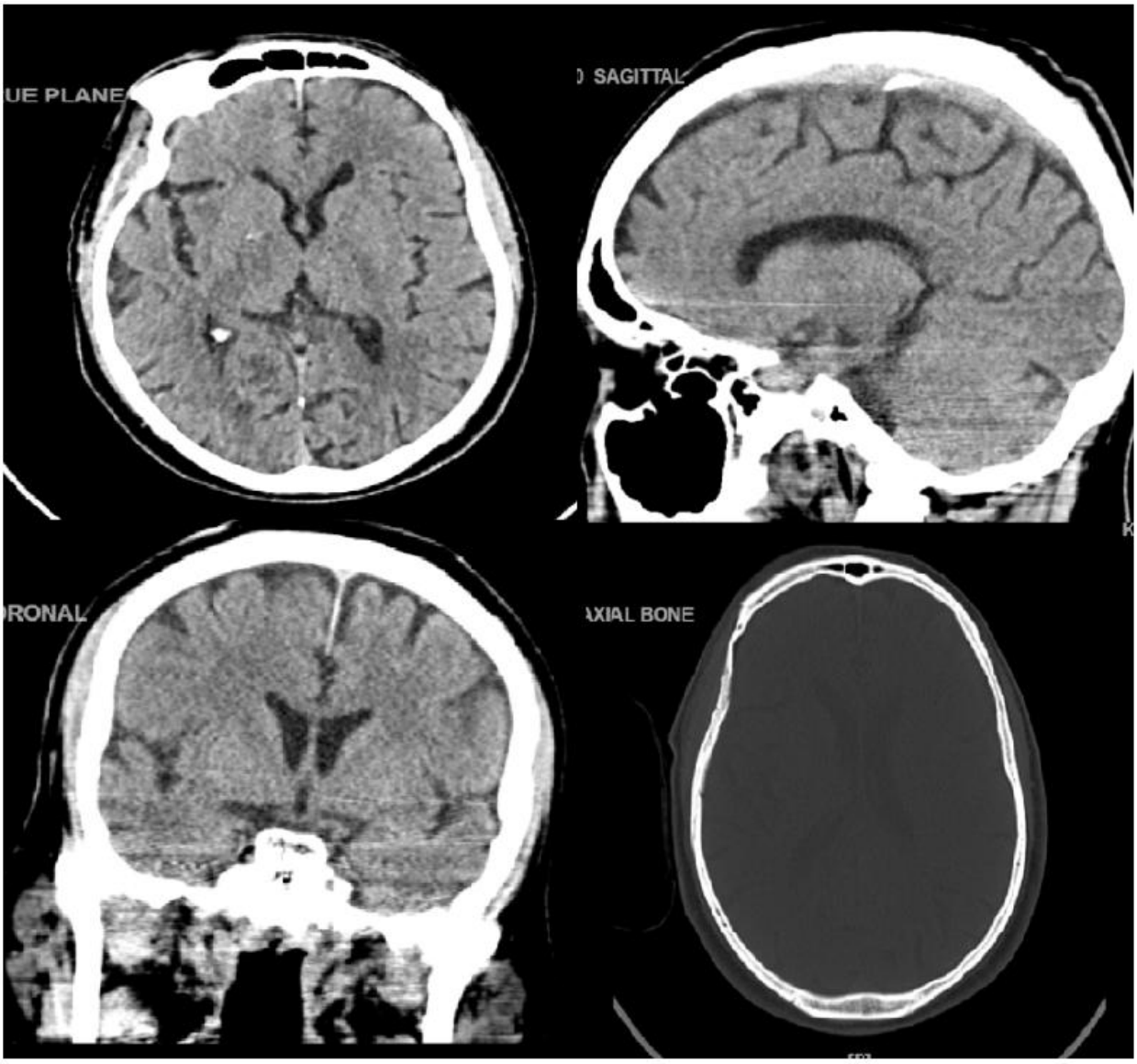


Fig. 2. Computed Tomography report

Computed Tomography of the head was performed showing Mild diffuse cerebral atrophy without any acute hemorrhages, acute infarction, or mass effect is identified.

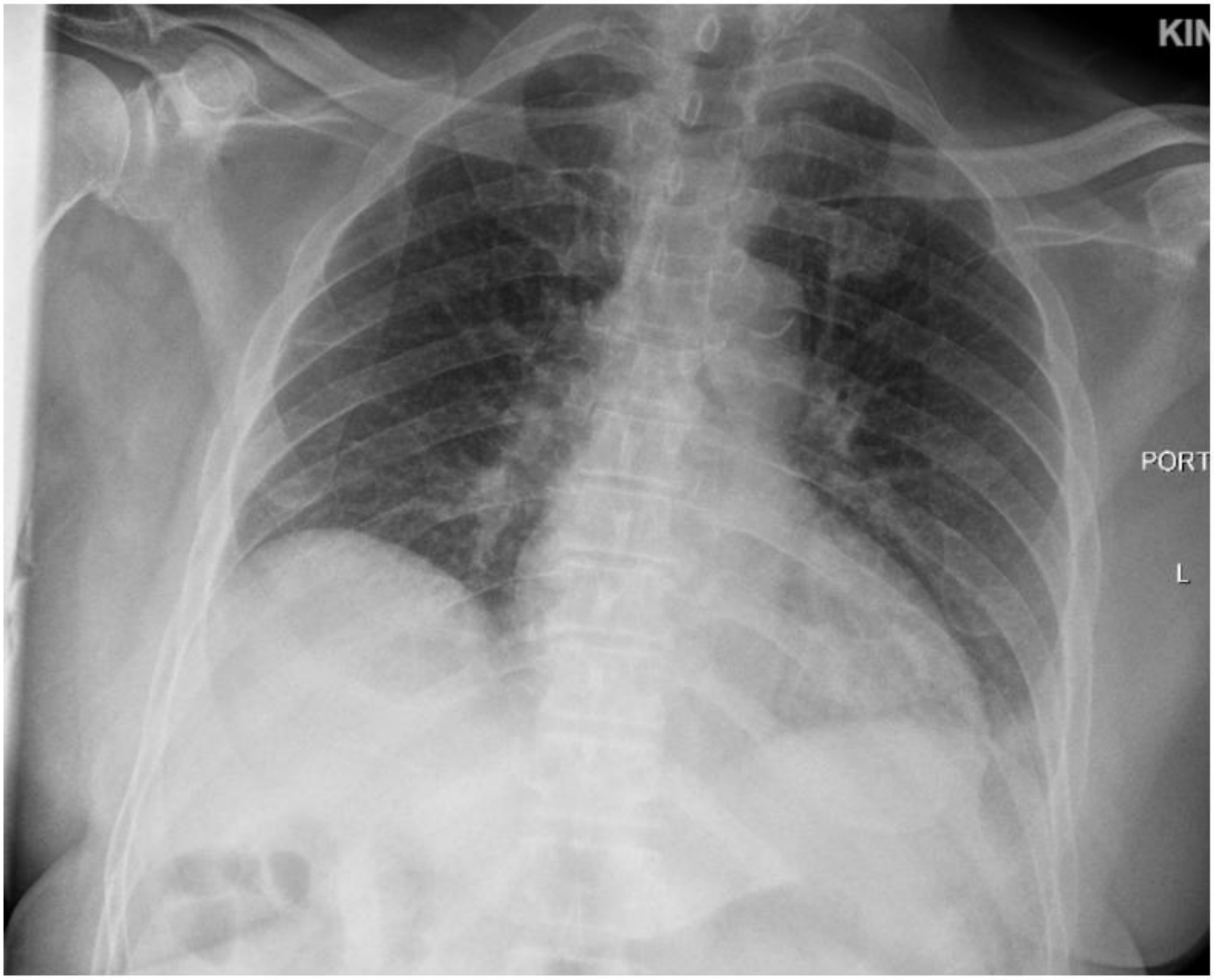


Fig.3. Chest X Ray

Chest X Ray showed Possible mild left-sided pleural effusion and left basilar lung infiltrate or pneumonia.Echocardiogram showed Normal left ventricular systolic function with Ejection fraction of 60-65% with Mild aortic and tricuspid regurgitation.Duplex imaging, color doppler and spectral analysis was performed on bilateral carotid system demonstrating no evidence of hemodynamically significant disease.

Covid markers and other inflammatory markers were measured shown in table 2 .

Table 2. Covid markers and other inflammatory markers

| | Value | Reference range |
|---|---|---|
| D-Dimer | 339 | <=500 ng/mL DDU |

| | | |
|---|---|---|
| C reactive protein | 7.6 | <=0.1 mg/L |
| Erythrocyte Sedimentation Rate | 19 | 0 - 20 mm/hr |
| Procalcitonin | 0.03 | 0.00 - 0.08 ng/mL |
| Lactate Dehydrogenase | 235 | 140-271 U/L U/L |

He was treated with Ceftriaxone 1 gm intravenous daily, Azithromycin 500 mg intravenous daily,IntravenousRemdesivir and Dexamethasone. During hospitalization since admission his heart rate ranged between 46-58. He was discharged with outpatient cardiology follow up.

**Discussion**

Sars COV-2, the causative agent that began the 2020 pandemic, had detrimental health care burdens on the global population that the healthcare industry is still unearthing. The Ribonucleic acid (RNA) virus that originated in 2019 from Wuhan, China has infected 770,563,467 of the population as of August 2023, including 6,957,216 deaths [World Health Organization (WHO)]. [1] The virus is known to cause a diverse range of symptoms targeting different bodily systems. The main presentation of the virus has been to target the respiratory tract with symptoms ranging from cough, dyspnea, to more severe presentations of hypoxia and pneumonia.

However, there has been a certain subset of the patient population that have exhibited cardiac manifestation after being confirmed with the virus. According to a study done by Huang C et al, myocardial injury occurred in 5 of the first 41 patients diagnosed with COVID-19 in Wuhan, which was evidenced by an increase in high-sensitivity cardiac troponin I (hs-cTnI) levels (>28 pg/ml)[1]. For further evidence, the National Commission of China reported that 11.8% of the infected patient population passed away with elevated levels of cardiac troponin I (cTnI) or cardiac arrest with pre-existing cardiovascular (CVS) comorbidities [1][2]. The cardiac manifestations have been diverse ranging from chest pain, palpitations to myocarditis, myocardial infarction, and decompensated ACS and arrhythmias [3]. The cardiac syndromes have been presented in different age populations, and in patients with different health profiles. Cardiac arrhythmias in association with COVID-19 have been especially difficult to pinpoint in patients due to the transient and often silent nature of the symptom. Only 7% of patients reported in a study conducted by Liu et al. presented with palpitations as a presenting symptom[3]. This has made it difficult to predict the likelihood of cardiac arrhythmias in a patient with COVID-19, therefore making it necessary to further study the pathophysiology of the virus on cardiac pacemaker cells and the complications.

Arrhythmias have been known to originate from dysfunctional cardiac pacemaker cells and conduction systems. With the exception that the virus is taken through the Angiotensin-converting enzyme 2 (ACE2) receptor found abundantly in cardiac pacemaker cells [1], the mechanism of Covid-19 and its association with arrhythmias is still being discovered and much is unknown. However, there has been knowledge of viruses such as parvovirus B19, human herpesvirus 6, adenovirus, and coxsackievirus B3 through myocardial inflammation and myocarditis causing arrhythmogenicity[3]. Myocarditis-inflammation of the myocardium- is often a benign and asymptomatic disease; however, arrhythmias have been associated as a fatal complication. The inflammation leads to electrophysical and structural changes in the pacemaker cells leading to downregulation and upregulation of certain ion channel changes. The result is changes in the repolarization and depolarization of these cells leading to arrhythmias and its subsequent complications. Another mechanism is the resulting inflammation can cause pericardial fibrosis leading to conduction blocks and arrhythmias [2][3]. SARS-COV, which caused an outbreak in 2003, in a case report, demonstrated that out of 121 patients, 105 patients had arrhythmias, with 18 of them being sinus bradycardia [4]. The most recent SARS-COV-2 virus has also been shown to be associated with sinus bradycardia.

The first case of Sars COV-2 associated with Bradycardia was described in a retrospective case report conducted at St. Luke's University in 2020 [5]. The study follows four patients of different genders and half the group had pre-existing CVS comorbidities. All four patients were admitted due to severe hypoxic respiratory infection induced by COVID-19 [5]. The patients developed bradyarrhythmia ranging from day 5-day 18 during their hospital stay(5). The duration of the bradycardia was transient with the arrhythmia resolving between 24 hours to 4 days. The bradycardia resolved during their treatment of COVID-19 which consisted of hydroquinone and azithromycin (exception patient 2) [5]. Although these medications are noted to cause arrhythmias with long term chloroquine use reported to increase depolarization length duration and Purkinje fiber refractory period (2), the researchers believe that the reported bradycardia did not have any association.

A significant finding was that all four patients had a body temperature greater than 100F during their bradycardia episode [5]. This finding is significant as it could give indication to the buildup of a cytokine storm induced by the viral inflammation of cardiac pacemaker cells discussed previously. In a study conducted in mice with bradyarrhythmia, there were increased levels of Interleukins (IL)-6, IL-10, IL-12, and tumor necrosis factor alpha (TNF-α) [4][5]. Like the mice, all four patients from the study had elevation of inflammation markers during their bradycardia. There is prior evidence that IL-6, which produces inflammatory markers, can directly act on the sinoatrial (SA) node and cause arrhythmias [3][5].

Since the Sars COV-2 virus is relatively new and much of our knowledge is still in infancy, we can fall back on our knowledge on Sars COV in 2003- a sister virus. Significant sinus bradycardia was seen in 14.9% of SARS-CoV patients, with a prevalence of 9.1%, 9.1%, and 4.4% in the first, second, and third week of hospitalization, respectively [5]. All episodes were seen to be transient, like the patients with Sars COV-2. From our knowledge on the relationship between viruses and the finding in our patients we can conclude that the causation of bradycardia in a COVID-19 patient is multifactorial but can be explained by the inflammation caused by the virus on pacemaker cells and the subsequent structural and conduction changes.

In addition, to the mechanism of the causative agent, we must also consider the medications used to treat the pathogen and its effect on the myocardial conduction system. Many of the drugs used to treat COVID-19, as discussed above, can have arrhythmias as a side effect. One such drug is Remdesivir which is a nucleotide analog that has been widely used in the treatment of COVID-19. It is important to distinguish between COVID-19 bradycardia vs Remdesivir bradycardia. According to a study conducted by WHO, in a study with a COVID 19 patient population of 2603, bradycardia was the most common cardiac adverse effect caused by Remdesivir with it affecting 302 patients, with men being the prominent patient population. Interesting to note, is that the bradycardia in this study was seen in day 3 from illness onset (6). In previous case reports, where Remdesivir use was absent, the bradycardia reported in COVID-19 patients was seen in day 6 and more closely aligns to onset of myocardial inflammation. Remdesivir associated bradycardia is due to its mechanism of action in that it is structurally similar to adenosine and adenosine receptors at the SA node have a negative chronotropic effect on the heart [6][7]. The activation of the adenosine receptor causes suppression of calcium current and activation of potassium current leading to hyperpolarization and subsequent bradycardia [6]. Knowledge of this mechanism is important in distinguishing the origins of bradycardia in a COVID-19 patient and will equip the physician for better treatment plans.

The rarity of Covid-19 related bradycardia reports leads to our diminutive knowledge of the phenomenon. Most of our knowledge is based on the previous history of viral inflammation on myocardial cells and consequent complications. However, epidemiological evidence suggests that COVID-19 infection has a direct correlation to the bradycardia and clinical evidence of the elevation of inflammatory markers suggest that inflammation plays a major role in inciting bradycardia. However, much more information is needed to establish the relationship and explore the mechanism to how conduction damage is caused by the virus. A much bigger sample patient population is needed to ascertain the relationship and the variables such as COVID-19 treatment, previous comorbidities, presenting illness etc. that might worsen or better the bradycardia. Awareness of Covid 19 bradycardia will aid physicians in better patient care and lead to early treatment and prevention, thereby decreasing the amount of long-term complication inflicted by this destructive pathogen.

**Conclusion:**
Close CV surveillance is crucial due to the potential COVID-19 presentation of transient sinus bradycardia. Severe hypoxia, inflammatory injury to cardiac pacemaker cells, and an excessive response to drugs are probable triggers, while the etiology may be complicated. High amounts of pro-inflammatory cytokines may have an immediate effect on the sinoatrial (SA) node, causing bradycardia to develop. This could signal the beginning of a major cytokine storm. When using empiric drugs that have arrhythmogenic effects, it's vital to be more conscious of the possibility of an excessive bradycardia response.

**Ethical Approval:**
As per international standard or university standards written ethical approval has been collected and preserved by the author(s).

**Consent**
As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

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