# Eyelid Myokymia as a presumed manifestation of Coronavirus Disease 2019 (COVID-19)

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**Research Article**

**Keywords:** COVID-19, eyelid myokymia, corona virus, blepharospasm

**Posted Date:** February 15th, 2021

**DOI:** https://doi.org/10.21203/rs.3.rs-203200/v1



**Version of Record:** A version of this preprint was published at SN Comprehensive Clinical Medicine on January 10th, 2022. See the published version at https://doi.org/10.1007/s42399-021-01094-w.

## Abstract

# Purpose

To report the eyelid myokymia in patients recovered from COVID-19 disease.

# Methods

A cohort of 15 patients who developed eyelid myokymia during or immediate post-recovery of systemic disease were evaluated. Demographic, clinical characteristics, effect of age, and hospitalization on the disease course were studied. The disease course was evaluated every month for 3 months period.

# Results

All, except 2, patients had complete resolution of lid myokymia within 3 months of onset. Mean ± SD myokymia recovery time was 44.1 ± 20.9 Days. Gender had no impact on the duration of disease. Age and duration of hospitalization had a strong positive correlation with myokymia recovery time ($r = 0.8$, $p = 0.001$ and $r = 0.8$, $p = 0.01$).

# Conclusion

Eyelid myokymia may involve COVID-19 patients during or immediately after systemic recovery. While myokymia recovers gradually in all these patients; older age and longer duration of hospitalization are associated with slower recovery.

## Introduction

Coronavirus disease 2019 (COVID-19) is the spectrum of clinical manifestations caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is a member of Coronaviridae family.[1] The rapid transmission of the virus has caused a global pandemic with 91.8 million cases and 1.97 million deaths globally.[2] While respiratory disease caused by this virus has been most emphasized; the virus may also affect other body systems and function.

Ocular manifestations of SARS-CoV-2 have been described by several investigators. While ocular surface disease is the most common ophthalmic manifestation of this virus; retinal vascular changes, neuro-ophthalmological complication, and uveal inflammation are also seen in a small number of patients.[3-5]

Eyelid myokymia is the most common type of facial myokymias seen in otherwise healthy individuals. It is a self-limiting benign condition seen involuntary, fine, continuous, undulating contractions of

orbicularis oculi muscles and may be associated with anxiety, depression, heavy caffeine intake and drugs.[6-8]

Nevertheless, there are no reports in literature at this time, to the best of our knowledge, about the eyelid myokymia in COVID-19 patients. The objective of our study was to describe features of lid myokymia developed during or immediately after the recovery from systemic disease.

# Methods

In this multicenter study, a cohort of patients who developed eyelid twitching during or after COVID-19 infection was recruited. Inclusion criteria were (1) New-onset eyelid twitching during or after active COVID-19 infection (2) age between 18 and 70 years, (3) Documented evidence of recovery from COVID-19 infection,

We excluded patients who had (1) History of eyelid twitching within past 1 year, (2) history of ocular surgery or trauma within the past one year, (3) family history of essential blepharospasm or hemifacial spasm, (4) history of any ocular disease including glaucoma, uveitis or ocular surface disorders, and (5) history of head/ face trauma or any known neurological disease.

All, time intervals were calculated from the date of discharge from hospital or documented recovery of systemic infection.

Each patient was evaluated at baseline and every month for 3 months. Comprehensive ophthalmic and neurological assessments including complete cranial nerve assessments were performed at each visit.

Eyelid myokymia was defined as episodic or persistent fine, spontaneous undulating contraction involving any of upper or lower lids. The rate of occurrence was reported by the patient and graded as (1) most of the time, (2) half of the time, (3) sometimes or (4) none of the time. Resolution of lid myokymia was defined as the patient-reported complete absence of lid twitch for 2 weeks. Myokymia recovery time was the interval between the systemic disease recovery and complete resolution of myokymia

**Data analysis;**

Microsoft Excel was used for data collection and handling while Statistical analysis was performed using statistical software (SPSS software Version 21; SPSS, Inc., Chicago, IL, USA). Data were presented as mean ±SD for quantitative variables and as counts (percentages) for categorical variables. Shapiro–Wilk test was used to analyze the normal distribution of data. The effect of gender and hospital admission on ocular recovery interval was tested. The relationship between length of hospital stay and ocular recovery time was analyzed using Pearson (*r*) correlation. P values of $< 0.05$ were considered as statistically significant.

# Results

A total of 15 patients, 9 (60%) males, were included. Mean± SD age was 48.3 ± 7.9 (range 38 t0 62) years. There was no difference in age between males and females (P=0.81). Ten (66.7%) patients, 3 females and 7 males, had a history of hospital admission for management of COVID 19 disease. Mean duration of hospital stay was 6.7± 2.98 days (Range 3.0 to 13) while females had a shorter hospital stay 7.4±3.21 days vs 5.0±1.7 days (P=0.41). Five (33.3%) patients had a history of conjunctivitis during active systemic disease. All patients experienced lid myokymia during or immediately after the systemic disease recovery. None of them had any neurological signs/ symptoms during or before the current study. Interval between systemic disease recovery baseline ocular examination was 13.1 ± 4.5 days (range 7 to 21). Patient demographics and clinical characteristics are shown in table 1.

**Table 1:** Patient demographics, clinical characteristics and myokymia recovery time

| Patient | Age/Sex | Hospitalized /days | Ocular Examination | Conjunctivitis | Recovery time Days |
|---|---|---|---|---|---|
| 1 | 38/M | Yes/ 3 | 19 | Yes | 31 |
| 2 | 44/F | Yes/ 4 | 17 | Yes | 60 |
| 3 | 41/F | No/0 | 11 | Yes | 21 |
| 4 | 42/F | No/0 | 10 | Yes | 33 |
| 5 | 62/M | Yes/13 | 10 | No | Didn't recover* |
| 6 | 61/F | Yes/7 | 15 | No | Didn't recover* |
| 7 | 46/M | Yes/6 | 21 | No | 49 |
| 8 | 47/M | Yes/5 | 11 | No | 42 |
| 9 | 53/M | Yes/8 | 8 | No | 88 |
| 10 | 55/M | Yes/9 | 7 | No | 62 |
| 11 | 57/M | Yes/8 | 18 | No | 67 |
| 12 | 51/M | No/0 | 15 | No | 43 |
| 13 | 40/F | No/0 | 16 | Yes | 18 |
| 14 | 49/F | Yes/4 | 10 | No | 40 |
| 15 | 39/M | No/0 | 8 | No | 19 |

*Did not recover till the end point of current study

At baseline, most patients had been experiencing lid myokymia half of the time or most of the time. At one-month follow-up, most patients had been experiencing myokymia sometimes while 11 patients (73%) had complete resolution at two months follow-up. Thirteen patients (86.7%) had complete resolution at 3 months follow up. Figure 1 shows the disease course in the current study.

Complete recovery of lid myokymia was observed in 13 (87%) patients at three months post COVID-19 recovery. The interval between systemic disease recovery and complete resolution of lid myokymia was 44.1± 20.84 days. Two patients (1 male), did not report any improvement or deterioration of twitch at three months. Magnetic resonance imaging of the brain in those patients was unremarkable. Myokymia recovery interval was independent of the history of conjunctivitis (P=0.45) and gender (P=0.2). There was a strong positive correlation between age and myokymia recovery time ($r$= 0.8, P=0.001). Length of hospitalization also had a positive correlation with myokymia recovery time ($r$= 0.8, P= 0.01). Myokymia recovery time was independent of gender (t=1.5, df=11, P=0.2). Figure 2 shows the impact of age and duration of hospitalization on ocular recovery time.

# Discussion

Common ocular complications/ manifestations of COVID-19 include dry eye, non-specific conjunctivitis, and retinal vascular changes. The exact incidence of these complications is yet to be determined. However, ocular surface disorders including conjunctivitis and dry eye are most frequently reported in COVID-19 patients.[5,9,10,3] Non-specific conjunctivitis, including conjunctival hyperemia, lacrimation, follicular conjunctivitis, ocular pain have been reported in 5 to 31% of patients.[11-14] While ocular surface diseases ranging from conjunctivitis to keratopathy was seen in up to 60% of critically ill patients.[15,16] Other relatively common ocular manifestations of SARS-CoV-2 include keratoconjunctivitis, epithelial defects subepithelial infiltrates and pseudodendrites.[17,18,10]

Granulomatous anterior uveitis, retinal detachment, retinal vasculitis, retinitis, and retinal degenerations are seen in animal studies.[4,5,10] In a study of 54 COVID-19 patients, dilatation of retinal veins and vascular tortuosity were most common and seen in 27.7% and 12.9% of patients. Other changes included retinal hemorrhages in 9.25% and cotton wool spots in 7.4% of patients.[17] Another study reported hyperreflective foci in the macula of 12 COVID-19 patients using optical coherence tomography. Besides OCT findings, 4 patients had cotton wool spots and retinal microhemorrhages.[18] Concerns about the potential misinterpretation of these results have recently been posed, signifying that hyperreflective areas could merely represent normal retinal vessels.[19,20] Retinal vein occlusion and valsalva retinopathy are rare potential associations of COVID-19.[11] Neuroophthalmological associations of SARS-CoV-2 are rare. A limited number of case reports have described Miller Fisher syndrome, Guillain-Barré syndrome, polyneuritis cranialis, internuclear ophthalmoparesis and oculomotor palsy.[5] Meningitis, encephalomyelitis and encephalopathy may also affect these patients.[10,21]

The primary outcome of the present study was to evaluate the pattern of eyelid myokymia presumably associated with COVID-19 and to the best of our knowledge, it is the first study to reporting eyelid

myokymia as a potential association of SARS-CoV-2 infection. We included all patients who experienced lid twitching during or after recovery from covid-19 infection.

The frequency/rate of myokymia gradually declined over time to total resolution and most patients completely recovered within two months of recovery from systemic disease. Older age and longer hospital stay were associated with prolongation of lid myokymia while the history of conjunctivitis had no impact on the time for recovery of myokymia.

Eyelid myokymia results from doublets or triplets of spontaneous non-synchronous discharges of adjacent motor units at a 30 to 70 Hz rate with inter-discharge intervals of 100-200 ms.[8,22] It is most common of all facial myokymias, typically unilateral with a tendency for lower lid and limited to orbicularis oculi muscle. It is a self-limiting benign condition affecting otherwise healthy individuals at any age and resolves completely over days to months.[23,8,6] Nonetheless stress, anxiety, excessive caffeine intake and administration of topiramate are known associations.[24,7,8] Rarely it may be associated with Guillain-Barre syndrome and multiple sclerosis.[25,26] Mental illness including anxiety and depression are common, affecting roughly $1/4^{th}$ to half of the COVID-19 survivors, immediate post-recovery and may persist for long. The incidence of mental illness was greater in hospitalized patients.[27,28,1,29,30] None of our patients had a recent history of topiramate intake or heavy caffeine consumption. Nonetheless, eyelid myokymia in our cohort of patients is attributable to anxiety or presumably it is a manifestation of SARS-CoV-2 infection itself. Akin to classic eyelid myokymia, there was a gradual recovery of myokymia in our patients. While older age and hospitalization were associated with slower resolution of the disease.

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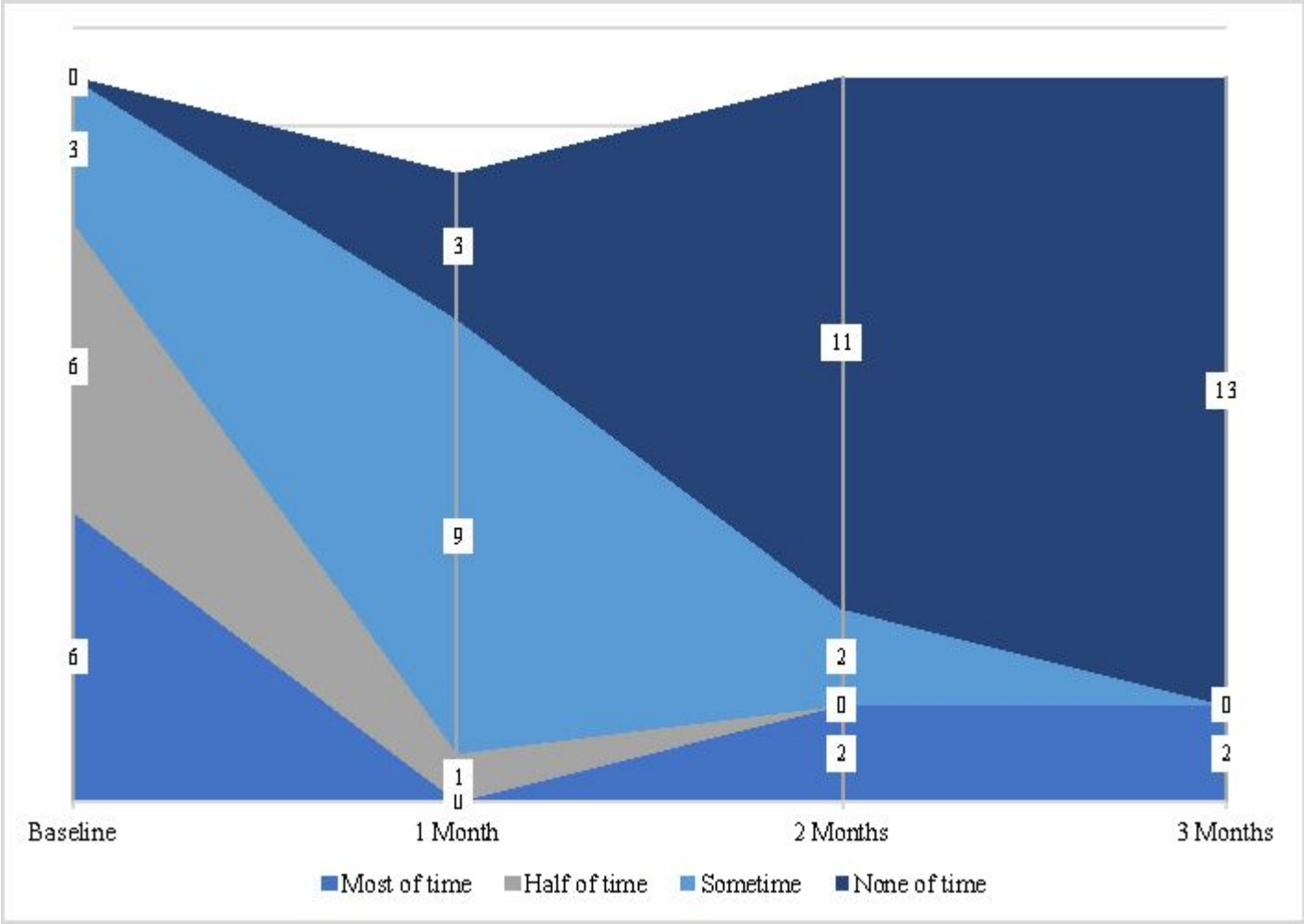
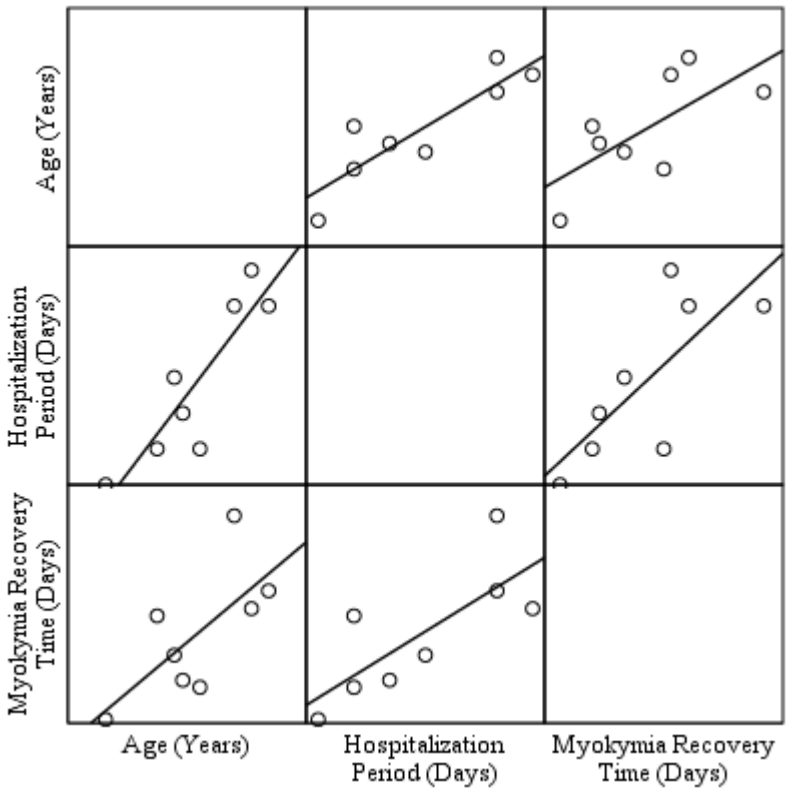
# Figures




## Figure 1

Figure 1 shows the disease course in the current study.




## Figure 2

Figure 2 shows the impact of age and duration of hospitalization on ocular recovery time.