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I hope this letter finds you in good health and high spirits. It is my distinct pleasure to address you as the Editor-in-Chief of Integrative Omics and Applied Biotechnology (IIOAB) Journal, a multidisciplinary scientific journal that has always placed a profound emphasis on nurturing the involvement of young scientists and championing the significance of an interdisciplinary approach.

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As we move forward, I encourage each and every one of you to continue supporting our mission. Whether you are a seasoned researcher, a young scientist embarking on your career, or a reader with a thirst for knowledge, your involvement in our journal is invaluable. By working together and embracing interdisciplinary perspectives, we can address the most pressing challenges facing humanity, from climate change and public health to technological advancements and social issues.

I would like to extend my gratitude to our authors, reviewers, editorial board members, and readers for their unwavering support. Your dedication is what makes IIOAB Journal the thriving scientific community it is today. Together, we will continue to explore the frontiers of knowledge and pioneer new approaches to solving the world's most complex problems.

Thank you for being a part of our journey, and for your commitment to advancing science through the pages of IIOAB Journal.



Yours sincerely,

*Vasco Azevedo*

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## REVIEW

A MINI REVIEW ON SPORTS GENETICS RESEARCHES IN INDIA:  
WHERE WE STAND NOW

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## ABSTRACT



Human genome consists of more than 20,000 genes. The genetic variants of each individual's genes propose characteristic sport capabilities. Genetic polymorphisms are strongly linked to physical performance in humans. Studies related to analysing the association between genetic variations and good athletic capability is of great interest. Athletic performance is highly related to sports training, anthropometric measures, and so on which are influenced by various relevant genes. In this review, we have focused on research papers based on genetic studies related to sports in order to get insight into the factors and underlying genes responsible for the best performance in Indian athletes.

## INTRODUCTION

**KEY WORDS**  
Genetics, Sports,  
Athletes, India,  
polymorphisms, ACL

Both genetic and environmental factors play an important role to be a good performer in athletes which is considered as a complex multifactorial trait [1]. The idea that genetics are strongly linked to human physical performance is believed among various researchers. If a player has participated in sports at a national or international level, he/she is considered an athlete [2]. De Moor et al (2007) [3] proposed that the athletic trait was inherited for approximately 66%. Researchers have identified certain genes related to sports performance, especially power, endurance and speed and are consistently increasing for in the past 2 decades [4, 5]. So far, greater than 200 gene polymorphisms have been discovered responsible for good performance in athletes [1, 6]. India is the second most highly populated country in the world and is generally diverse in nature. It is indeed important to perform genetic related studies in Indian athletes to better understand and recognize talented players to represent the country in games and make champions.

## CRITERIA ADOPTED FOR REVIEW OF LITERATURE

The literature search was performed in PubMed database by using the words "SPORTS" AND "GENETICS" AND "INDIA". The search ultimately resulted in 140 articles. However, the final relevant research papers included 7 records. The search also included the analysis of sub references to include any missed articles. Combining this, it totally resulted in 9 research papers. These articles focused on ACE gene polymorphisms, VEGFA polymorphisms, COL1A1 gene polymorphisms, and oxidative stress and genetic stability.

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## GENETIC STUDIES RELATED TO SPORTS ON INDIAN PLAYERS

Sharma et al. (2012) [7] reported the occurrence of genomic instability in professional sports persons due to the comprehensive exercises and intense training that are carried out during practices resulting in disruption of the intracellular oxidant-antioxidant balance and destruction of macromolecules. Thus, the players are imposed with high risk related to cancer and various other diseases. Gandhi et al. 2019 [18] also found the elevated levels of genetic damage and oxidative stress in *Kho-Kho* players which might be due to the continuous physical exercises for sports events. Sharma et al (2012) [7] investigated the extent of genomic damage in judo players and revealed that the DNA and chromosomal damage were more prevalent in judo players when compared to controls. Gandhi and Kumar (2007) [8] analysed whether chromosomal damage occur in wrestlers due to extreme exercises and found statistically significant numbers of micronuclei

Das et al. (2019) [9] studied the genetic variants with respect to dopaminergic pathways and various other genes in persons involved in gambling sport (teer). They demonstrated the contribution of *GDNF* gene in the development and survival of dopaminergic neurons and also *CNTNAP2* in psychological disorders. Shukla et al. (2020) [10] studied the relationship between the polymorphism specified as *COL1A1* Sp1 + 1245 G > T of Sp1-transcription factor binding site and ACL (anterior cruciate ligament) injury risk in North-Indian athletes. However, they found no significant differences in the studied genotypic distribution of GT/TT and T-allele frequency distribution. Kothari et al. (2012) [11] found no association between ACE gene and athletic performance. However, they found over representation of I allele in the studied athletes.

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Prabhakar et al. (2018) [12] investigated the genetic association of *COL1A1* gene polymorphisms such as rs1800012 and rs1107946 with ACL injuries in which they found no significant differences in the genotypes or allele distribution between the ACL defective patients and control groups for both the polymorphisms rs1800012 ( $p=0.516$ ) and rs 1107946 ( $p=0.971$  for GT and  $p=0.823$  for TT). In another study, Shukla et al. (2020) [13] analyzed the link between *VEGFA* (Vascular endothelial growth factor) promoter polymorphisms and ACL tears. They identified the elevated frequencies of the A allele (rs699947) and I allele (rs35569394) in ACL group. **Table 1** shows the genetic studies related to sports in Indian sports players.

**Table 1:** Summary on Indian sports genetics studies carried out between 2011 and 2021

| Sports                  | Study centre | Cases/Control | Findings   | Ref  |
|-------------------------|--------------|---------------|--|------|
| Hockey, Baseball        | Punjab       | 36/20         | Athletes are at high risk for various age-related diseases and cancer due to genomic instability                             | [7]  |
| Kho-Kho                 | Punjab       | 18/10         | Oxidative stress and genomic instability   | [18] |
| Athletes ACL vs Non-ACL | Gwalior      | 90/76         | A allele (rs699947), I allele (rs35569394) - significantly overrepresented in ACL cases<br>rs1800012- Insignificant with ACL | [13] |
| Various sports          | Chandigarh   | 52/52         | Insignificant association of <i>COL1A1</i> with ACL  | [12] |
| Athletes                | Mumbai       | 147/131       | No significant association; Overrepresentation of I allele of ACE  | [11] |
| Judo                    | Punjab       | 17/10         | Increased chromosomal and DNA damage   | [7]  |
| Wrestlers               |              | 15/10         | Cytogenetic damage   | [8]  |

## DISCUSSION

Genetics helps to determine a person's athletic abilities. A wide range of studies have shown varied connections between particular gene variants and athletic abilities in different sports and ethnic groups and genders [5]. *ACE* is one of the two genes that have been widely studied in combination with athletic ability [14]. An excess of the I allele is shown to be linked with some characteristics of endurance performance [15, 16].

Many researchers have demonstrated the oxidative stress and oxidation of cellular biomolecules by ROS affecting genomic stability in various professional sports players [17]. Time, intensity, frequency and features of exercises are known to show impact on oxidative stress and the oxidation of cellular macromolecules (including DNA) and cellular dysfunction, and can acquire with age, physical aspects and enhance disease risk [18]. Even though oxygen uptake during intense physical activity and during aerobic and anaerobic training is necessary in order to sustain stamina and endurance, it can, probably, lead to oxidative stress due to a disruption in intracellular homeostasis of the pro-oxidant system, as well as an increase in the formation of reactive oxygen/nitrogen species (ROS/RNS). Oxidative stress causes oxidation of cellular components viz. lipids, proteins and nucleic acids due to which continuous exercising leads to DNA damage [19]. Knowledge about genetic variants and their influence on many areas of training, competitive performance and injury prevention may surely enrich the periodization scheme, shorten injury time and successfully rehabilitate sports among athletes [20]. The associations of *COL1A1* gene polymorphisms with ACL tear were carried out on several populations namely Poland, South Africa, and Sweden by various researchers. Posthumas and his co-researchers observed under-representation of TT-genotype in their analysis of *COL1A1* gene in ACL injured sportspersons in South African population [21]. Similarly, Stepien Slodkowska et al. (2013) [22] identified 11245G/T polymorphisms in rs1800012 SNP in *COL1A1* gene in Poland population. Ficek et al. (2013) [23] found no significant association of *COL1A1* gene polymorphisms but observed over-representation of G-T haplotypes (-1997G+1245T) in Poland population. Similarly, no significant association of *COL1A1* gene polymorphisms with ACL tear was seen in Indian athletes. SNPs within genes coding for collagen matrix remodelling in singularity, linkage analysis, and gene-gene interactions are intriguing targets for further research in sports injuries in general and ACL injuries specifically. It has been found that the rate of ACL injury related to multifactorial aetiology to be 86% among Indian athletes [24].

Shukla et al. (2020) [10] proposed that the genetic link to ACL injuries and subsequent healing capacity might be helpful in identifying 'high risk' athletes related to ACL tears and configuring their trainings sessions for the purpose of continuing their "sporting career". *ACE* gene polymorphism is identified to be related to athletic abilities [25]. The functional polymorphism rs.5186 exists with absence (deletion; D allele; corresponding to good performance in sprint of power based sports), rather than the presence (insertion, I allele; related to excellence in endurance sports) of 287bp Alu repeat element in intron 16 (Thompson and Macleod, 2006). Researchers found that it is difficult to predict the connection between *ACE* genotype and sporting supremacy among sportspersons who take part in multiple sports rather than a single discipline [11].

## CONCLUSION

Very few genetic studies related to sports have been conducted in India. It is clear that among Indian athletes, the polymorphism COL1A1 Sp1 +1245 G> T SNP is not related to ACL. Studies should be focused on Indian athletes who are involved in single sport to get insight into the association between ACE and sporting capacity. Since oxidative stress due to continuous exercises can lead to severe diseases, conducting such studies in Indian athletes will allow preventing those diseases. Also, the studies are based on few sports only which should be extended on various other sports. Identification of polymorphisms in various other genes such as ACTN3, NOS3, UCP2, UCP3, and many is much more important for correlating different physiological parameters with sport performance. Also, majority of the studies were conducted in Northern region of India and is also gender biased. Thus, studies should combine sport players from all the parts of India including women to conclude the association of genes and its polymorphisms which would certainly help identification of talented players to give the best performance in sports.

### CONFLICT OF INTEREST

Author declares no conflict of interest.

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None.

### FINANCIAL DISCLOSURE

None.

## REFERENCES

- [1] Guth LM, Roth SM. [2013] Genetic influence on athletic performance. *Curr Opin Pediatr.* 25(6):653-658.
- [2] Macarthur DG, North KN. [2005] Genes and human elite athletic performance. *Hum Genet.*, 116: 331-339.
- [3] De Moor MH, Spector TD, Cherkas LF, et al. [2007] Genome-wide linkage scan for athlete status in 700 British female DZ twin pairs. *Twin Res Hum Genet.*, 10: 812-820.
- [4] Puthuchery Z, Skipworth JRA, Rawal J, et al. [2011] The ACE gene and human performance. *Sport Med.* 2011;41(6):433-48
- [5] Ma F, Yang Y, Li X, et al. [2013] The association of sport performance with ACE and ACTN3 genetic polymorphisms: a systematic review and meta-analysis. *PLoS One.* 8(1):e54685.
- [6] Davids K, Baker J. [2007] Genes, environment and sport performance: why the nature-nurture dualism is no longer relevant. *Sports Med.*37(11):961-980.
- [7] Sharma R, Shailey, Gandhi G. [2012] Pre-cancerous (DNA and chromosomal) lesions in professional sports. *J Cancer Res Ther*8(4):578-585.
- [8] Gandhi G, Kumar P. [2007] The capillary blood "in-vivo" micronucleus test: Wrestlers exercising at "Akharas." *Journal of Exercise Science and Physiotherapy.* 3(2): 129-135.
- [9] Das A, Pagliaroli L, Vereczkei A, et al. [2019] Association of GDNF and CNTNAP2 gene variants with gambling. *J Behav Addict.* 8(3):471-478.
- [10] Shukla M, Gupta R, Pandey V, et al. [2020] COL1A1 + 1245 G > T Sp1 Binding Site Polymorphism is Not Associated with ACL Injury Risks Among Indian Athletes. *Indian J Orthop.* 54(5):647-654.
- [11] Kothari ST, Chheda P, Chatterjee L, et al. [2012] Molecular analysis of genetic variation in angiotensin I-converting enzyme identifies no association with sporting ability: First report from Indian population. *Indian J Hum Genet.* 18(1):62-65.
- [12] Prabhakar S, John R, Dhillon MS, et al. [2018] Are COL1A1 gene polymorphisms associated with anterior cruciate ligament tear in the Indian population? Results of a preliminary case-control study. *Muscles, Ligaments and Tendons Journal.* 8(1):15-22.
- [13] Shukla M, Gupta R, Pandey V, et al. [2020] VEGFA Promoter Polymorphisms rs699947 and rs35569394 Are Associated With the Risk of Anterior Cruciate Ligament Ruptures Among Indian Athletes: A Cross-sectional Study. *Orthop J Sports Med.* 8(12):2325967120964472.
- [14] Montgomery HE, Marshall R, Hemingway H, et al. [1998] Human gene for physical performance. *Nature.* 393:221-222.
- [15] Bray MS, Hagberg JM, Pérusse L, et al. [2009] The human gene map for performance and health-related fitness phenotypes: the 2006–2007 update. *Med Sci Sports Exerc.* 41:35-73.
- [16] Ahmetov II, Rogozkin VA. [2009] Genes, athlete status and training - An overview. *Med Sport Sci.* 54:43-71.
- [17] Mergener M, Martins MR, Antunes MV. [2009] Oxidative stress and DNA damage in older adults that do exercises regularly. *Clin. Biochem.* 42:1648-1653.
- [18] Gandhi G, Sharma R, Kaur G. [2019] Traditional Indian sports - A case-control study on Kho Kho players investigating genomic instability and oxidative stress as a function of metabolic genotypes. *Heliyon.* 5(6):e01928.
- [19] Okamura K, Doi T, Hamada K, et al. [1997] Effect of repeated exercise on urinary 8-hydroxy-deoxyguanosine excretion in humans. *Free Radic Res.* 26(6):507-514.
- [20] Rambaud AJM, Semay B, Samozino P, et al. [2017] Criteria for Return to Sport after Anterior Cruciate Ligament reconstruction with lower reinjury risk (CR\*STAL study): Protocol for a prospective observational study in France. *BMJ Open.* 7(6):e015087.
- [21] Posthumus M, September AV, Keegan M, et al. [2009] Genetic risk factors for anterior cruciate ligament ruptures: COL1A1 gene variant. *Br J Sports Med.* 43(5):352-356.
- [22] Stepien-Słodkowska M, Ficek K, Eider J, et al. [2013] The +1245g/t polymorphisms in the collagen type I alpha 1 (col1a1) gene in polish skiers with anterior cruciate ligament injury. *Biol Sport.* 30(1):57-60.
- [23] Ficek K, Cieszczyk P, Kaczmarczyk M, et al. [2013] Gene variants within the COL1A1 gene are associated with reduced anterior cruciate ligament injury in professional soccer players. *J Sci Med Sport.* 16(5):396-400.
- [24] John R, Prabhakar S, Dhillon MS, et al. [2016] Association of ACL tears and single nucleotide polymorphisms in the collagen 12 A1 gene in the Indian population - a preliminary case-control study. *Muscles Ligaments Tendons J.* 6(2):253-257.
- [25] Gayagay G, Yu B, Hambly B, et al. [1998] Elite endurance athletes and the ACE I allele--the role of genes in athletic performance. *Hum Genet.* 103(1):48-50.

## CASE REPORTS

## CASE SERIES: MYOFASCIAL PAIN SYNDROME (MFPS) IN LONG COVID

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## ABSTRACT

We present a case series on patients presenting post “long SARS - COVID 19” infection of a rarely encountered manifestation; the myofascial pain syndrome (MFPS) at a major tertiary referral medical college hospital in Vijayapur. We recorded the clinical presentations of patients coming with long COVID to Al Ameen Medical College and Hospital from January 2021 to December 2021. Patients above 18 years of age presenting with long COVID and new onset and long-standing musculoskeletal pain who had worsening episodes of pain were included. The patients for this case series were selected based on those who had typical specific trigger points diagnostic of MFPS. We attempt to analyse the relationship between MFPS and SARS-CoV-2. We hypothesise that coronavirus-induced hypoxic muscle dysfunctions and psychological stress could trigger nociceptive receptors.

## INTRODUCTION

Long COVID is a modern terminology with a unique history being testament to the times we live in. Long COVID is a “patient-created term” which was first used in May 2020 as a hashtag on Twitter by Elisa Perego, an archaeologist at the University College, London [1,2]. Long COVID is a long-term sequelae appearing or persisting after the typical convalescence period of COVID-19. It is also described with different terminologies as the post-COVID-19 syndrome, post-COVID-19 condition [3,4] post-acute sequelae of COVID-19 (PASC), or chronic COVID syndrome (CCS)[5-7]. Long COVID can affect any organ system, with sequelae in the form of respiratory system, nervous system and neurocognitive disorders, mental health disorders, metabolic disorders, cardiovascular disorders, gastrointestinal disorders, malaise, fatigue, musculoskeletal manifestations and anemia[8].

Worldwide, studies are few due to the novelty of the COVID-19 disease and Indian studies are extremely scarce on this topic. Studies on populations who experience long-term symptoms is unknown and variable. In the survey by the UK Office for National Statistics it is estimated that about 14% of people who tested positive for SARS-CoV-2 experienced one or more symptoms for longer than 3 months [9]. A study from University of Oxford of 273,618 survivors of COVID-19, mainly from the United States, showed that about 37% experienced one or more symptoms between 3 and 6 months after diagnosis [10].

We present a case series on patients presenting post “long SARS - COVID-19” infection of a rarely encountered manifestation; the myofascial pain syndrome (MFPS) at a major tertiary referral medical college hospital in Vijayapur. We recorded the clinical presentations of patients coming with long COVID to Al Ameen Medical College and Hospital from January 2021 to December 2021. Patients above 18 years of age presenting with long COVID-19 and new onset and long-standing musculoskeletal pain who had worsening episodes of pain were included. The patients for this case series were selected based on those who had typical specific trigger points diagnostic of MFPS. We attempt to analyze the relationship between MFPS and SARS-CoV-2. We hypothesize that coronavirus-induced hypoxic muscle dysfunctions and psychological stress could trigger nociceptive receptors.

## CASE SERIES

We present a case series of 5 cases where patients diagnosed with SARS-CoV-2 developed myofascial pain syndrome.

## Case 1:

64 -year-old female patient was diagnosed with SARS-CoV-2 in April 2021 with RT- PCR test and was hospitalized for 10 days. Past medical history was significant for bronchial asthma, psoriasis and hypertension. She was on amlodipine and inhaled rotahalers for management of asthma. She was treated with high-dose oxygen therapy with CPAP for 3 days followed by 7 days of high flow oxygen, along with medical management including remdesivir and steroids. 1 month after discharge, patient presented with myalgia, described as tightness in her neck and shoulder with tingling sensation radiating down to bilateral arms. She was advised cervical collar and pain medications with physiotherapy. After 1 week follow-up she was not relieved of her symptoms. Physical examination revealed palpable taut tender muscle bands in the trapezius bilaterally especially eliciting typical pain on deep palpation. She was referred to a rheumatologist for treatment with dry needling and physiotherapy with good self-reported immediate relief

**KEY WORDS**  
Long COVID, COVID-19,  
musculoskeletal  
complications, myofascial  
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of 40%. On follow-up 4 weeks later, patient's numerical pain rating scale (NPRS) was a 2/10 and seemed to have had a significant improvement and reduction in her self-reported pain by 80%.

#### Case 2:

A 45-year-old male patient was diagnosed with SARS-CoV-2 by RT-PCR test in July 2021. He was hospitalised for 5 days. Past medical history was significant for autoimmune thyroiditis on treatment with thyroxine 25mcg. 3 months post COVID-19, patient started experiencing left knee pain interfering with regular walking and driving. There was no postural instability. Physical examination revealed palpable taut tender muscle bands and multiple trigger points in the tendons of the hamstring muscles. MRI knee revealed findings of chondromalacia patella. Patient opted for conservative treatment. He was treated with physiotherapy and anti-inflammatory painkillers. Patient was followed 1 month post SARS-CoV-2 diagnosis at which time he continued to have pain with reduction of 20%. Patient was subsequently followed up in clinic 3 months later with some improvement. The NPRS at this follow-up visit was 4/10. On physical exam, palpable taut musclebands were still identified. Patient still refused interventional management in the form of trigger point injections.

#### Case 3:

35 year old female patient was diagnosed with SARS-CoV-2 in April 2021 with RT-PCR test and hospitalized for 6 days. Past medical history was significant for hyper IgE syndrome and allergic rhinitis. She was on symptomatic treatment for exacerbations. 2.5 months post COVID, patient started experiencing right elbow pain interfering with regular movements of the elbow. There was no neurological deficit. Physical examination revealed trigger points in the tendons of the triceps muscle. 4 months later she developed another trigger point at the base of the left thumb in the tendons of the Extensor pollicislongus. Patient opted for conservative treatment. She was treated with elbow and wrist guards and anti-inflammatory painkillers. Patient was followed 1 month post SARS-CoV-2 diagnosis at which time he continued to have pain with reduction of 60%. Patient was subsequently followed up in clinic 3 months later with some improvement. The NPRS at this follow-up visit was 5/10.

#### Case 4:

60-year-old female presented with SARS-COV-2 in November 2021 with history of chronic sciatica. She was treated with high-dose oxygen therapy with CPAP for 3 days followed by 7 days of high flow oxygen, along with medical management including remdesivir and steroids. 1 week after discharge she started experiencing back pain with trigger points in the trapezius. She was treated conservatively. 12 days later she continued to be symptomatic. Patient continued conservative management. Patient was subsequently followed up 3 months later with some improvement self reported as pain reduction of 40%. The NPRS at this follow-up visit was 6/10. On physical examination trigger points were less painful. Patient still refused interventional management in the form of trigger point injections.

#### Case 5:

68-year-old female patient was diagnosed with SARS-CoV-2 in September 2021 with RT-PCR test and was hospitalized for 7 days. Past medical history was significant for diabetes, hypertension and coronary artery disease(CAD). She was on antiplatelets, statins, antidiabetic and antihypertensive medications. She was treated with high-dose oxygen therapy with CPAP for 2 days followed by 6 days of high flow oxygen, along with medical management including remdesivir and steroids. 20 after discharge, patient presented with severe disabling pain on movement of the right shoulder. She was reassessed for CAD and pain medications were prescribed along with physiotherapy. Physical examination revealed palpable tender muscle bands in the right deltoid eliciting typical pain on deep palpation. After 1 month follow-up she was not relieved of her symptoms. She opted for continuing conservative treatment with relief of 40% at 2 months. Patient's numerical pain rating scale (NPRS) was a 4/10. She was lost to follow-up.

All the 5 patients were given the option to undergo conventional care versus interventional therapy. This syndrome has a specific treatment as compared to other musculoskeletal presentations. However, only one patient opted for dry needling treatment which is the treatment of choice for myofascial pain. The rest of the patients opted for conservative treatment. The major cause of refusal of intervention treatments seemed to be the non-availability of the same at the centre/ city and the other factor was cost of treatment. This being a novel presentation, time frame of follow up was not defined and instead tailored on a case-to-case basis. At the time of publication cases 1-4 were on regular follow up and case 5 was lost to follow up.

## DISCUSSION

### Defining Long COVID

#### *World Health Organization clinical case definition*

The World Health Organization (WHO) clinical case definition of October 2021, describes it as a post-COVID-19 condition described in patients with a history of probable or confirmed SARS-CoV-2 infection, usually 3

months from the onset, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, and cognitive dysfunction, and generally have an impact on everyday functioning. Symptoms might be new onset following initial recovery from an acute COVID -19 episode or persist from the initial illness. Symptoms can fluctuate or relapse over time.

#### **British definition**

The British National Institute for Health and Care Excellence (NICE) divides COVID-19 into three clinical case definitions:

- acute COVID-19 for signs and symptoms during the first 4 weeks after infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the first, and
- long COVID for new or ongoing symptoms 4 weeks or more after the start of acute COVID-19, which is divided into the other two:
  - ongoing symptomatic COVID-19 for effects from 4 to 12 weeks after onset, and
  - post-COVID-19 syndrome for effects that persist 12 or more weeks after onset [11]

#### **U.S. definition**

In February 2021, the U.S. National Institutes of Health (NIH) Director Francis Collins, stated that long COVID symptoms for individuals who "don't recover fully over a period of a few weeks", be collectively referred to as Post-Acute Sequelae of SARS-CoV-2 infection (PASC). The NIH describes long COVID symptoms of fatigue, shortness of breath, "brain fog", sleep disorders, intermittent fevers, gastrointestinal symptoms, anxiety, and depression. Symptoms can persist for months and can range from mild to incapacitating, with new symptoms arising well after the time of infection [12]

The Centers for Disease Control and Prevention (CDC) term Post-COVID conditions qualifies long COVID as symptoms 4 or more weeks after first infection [13].

#### **Defining Myofascial pain syndrome (MFPS)**

It is a chronic pain syndrome wherein trigger points in sensitive taut areas in muscles, cause pain in the muscle belly itself or at a distant location [14]. The trigger point is the distinguishing feature of MFPS. It is a small, localized area of muscle contraction that is extremely tender on palpation. Diagnosis is mainly clinical based on palpating the trigger point. Repetitive strain, postural dysfunction, psychological stress and trauma are postulated causes [15]. An initiating event increases acetylcholine release which enhances depolarization at post-junctional membrane of the muscle fiber causing a muscle contraction. When this recurs, there is a continuous contracture of sarcomeres which form a trigger point. Repetitive stimulation creates hypoxia within the muscle fibres, which in turn sensitizes of nociceptors [16,17]. This can also have intermediate and long-term effects on fatigue, respiratory function and carditis. The pain-related symptoms including myalgia and arthralgias account for 36% of cases [18].

Conservative management is medical using multi-modal analgesics like NSAIDs, COX-2 inhibitors, opioids and anaesthetic patches. In severe cases, muscle relaxants and antidepressants such as Benzodiazepines and Tricyclic antidepressants, respectively can also be considered [19]. Tizanidine specifically is considered a first line agent whereas TCAs may be used if other treatment options fail due to the high side effect profile [20]. Botulinum type A toxin may also be used; however, data is inadequate [21]. Non-invasive therapies like electrical stimulation (transcutaneous electric nerve stimulation), ultrasound, laser and magnet therapies have been used but have moderate evidence for short and long-term relief [22]. Invasive therapies are inactivating the trigger point with a trigger point injection, with or without local anaesthetic [23]. Inserting a needle in the trigger point causes a local twitch response, often with reproduction of pain, followed by a relaxation of taut muscle band and alleviation of pain.

## **CONCLUSION**

Varied presentations are seen with coronavirus infections after time has elapsed since recovery. An unusual presentation is MFPS in long SARS-CoV-2 as described in these 5 cases. There is no direct relationship that can be demonstrated between SARS-CoV-2 and MFPS due to inadequate literature and novelty of this infection. It is seen in the current literature that myalgia in SARS-CoV-2 infection could be inflammatory cytokine dysregulation response which is one of the hallmarks of COVID -19. Due to immune reactions interactions with nociceptors pain occurs in SARS-CoV-2. SARS-CoV-2 could induce changes in nociceptor excitability that would be expected to promote pain, induce neuropathies, and possibly worsen existing pain conditions. This can result in prolonged pain, morbidity and the resultant 'long COVID syndrome'. Most patients report immediate moderate relief with conservative management and physiotherapy. Due to lack of infrastructure, dry needling procedure needed patients to travel out of town which was not opted for by the patients due to various reasons. However, it is one of the triggers for development of a chronic pain syndrome. Further large-scale studies are needed to assess patients with long COVID with MFPS independent of other co-morbidities.

**CONFLICT OF INTEREST**

Authors declare no conflict of interest.

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**FINANCIAL DISCLOSURE**

None.

**REFERENCES**

- [1] Perego E, Callard F, Stras L et al. [2020] Why the Patient-Made Term 'Long COVID' is needed. *Wellcome Open Res.* 5:224
- [2] Callard F, Perego E, [2021] How and why patients made Long COVID. *Social Science & Medicine.* 268: 113426.
- [3] WHO. 6 October 2021. A clinical case definition of post COVID-19 condition by a Delphi consensus,
- [4] Soriano JB, Murthy S, Marshall JC, et al. [2021] WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis.* S1473-3099(21)00703-9.
- [5] Baig AM. [2021] Chronic COVID syndrome: Need for an appropriate medical terminology for long-COVID and COVID long-haulers. *Journal of Medical Virology.* 93 (5): 2555–2556.
- [6] CDC 13 November 2020. Long-Term Effects of COVID -19". Centers for Disease Control and Prevention.
- [7] National Institute for Health and Care Excellence. 18 December 2020. COVID-19 rapid guideline: managing the long-term effects of COVID-19.
- [8] Al-Aly Z, Xie Y, Bowe B. [2021] High-dimensional characterization of post-acute sequelae of COVID-19. *Nature.* 594 (7862): 259–264.
- [9] Office for National Statistics. 1 April 2021. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 1 April 2021. Accessed on 14 August 2021.
- [10] Taquet M, Derco Q, Luciano S, et al. [2021] Incidence, co-occurrence, and evolution of long-COVID features: A 6-month retrospective cohort study of 273,618 survivors of COVID-19. *PLoS Med.* 18(9):e1003773
- [11] Brodin P. [2021] Immune determinants of COVID-19 disease presentation and severity. *Nature Medicine.* 27 (1): 28-33.
- [12] Wu, KJ. [2021] Nine Pandemic Words That Almost No One Gets Right. *The Atlantic.* (<https://www.theatlantic.com/science/archive/2021/10/covid-vocabulary-pandemic-words/620351/>)
- [13] National Institute for Health and Care Excellence. 18 December 2020. NIH launches new initiative to study "Long COVID.
- [14] Friction JR, Kroening R, Haley D, et al. [1885] Myofascial pain syndrome of the head and neck: a review of clinical characteristics of 164 patients. *Oral Surg Oral Med Oral Pathol.* 60(6): 615-623.
- [15] Simons DG, Travell JG, Simons LS. [1999] *Myofascial Pain and Dysfunction: the Trigger Point Manual.* Frost EAM (Ed.), Williams & Wilkins, MD, USA,
- [16] Giamberardino MA, Affaitati G, Fabrizio A, et al. [2011] Myofascial pain syndromes and their evaluation. *Best Pract. Re. Clin Rheumatol.* 25(2):185-198.
- [17] Coupe C, Midttun A, Hilden J, et al. [2001] Spontaneous needle electromyographic activity in myofascial trigger points in the infraspinatus muscle: a blinded assessment. *J Musculoskelet Pain.* 9(3): 7-16.
- [18] Li LQ, Huang T, Wang YQ, et al. [2020] COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. *J Med Virol.* 92(6):577-583.
- [19] Gerwin RD. [2014] Diagnosis of myofascial pain syndrome. *Phys Med Rehabil Clin N Am.* 25(2): 341-355.
- [20] Malanga GA, Gwynn MW, Smith R, et al. [2002] Tizanidine is effective in the treatment of myofascial pain syndrome. *Pain Physician.* 5(4):422-432.
- [21] Soares A, Andriolo RB, Atallah AN, et al. [2012] Botulinum toxin for myofascial pain syndromes in adults. *Cochrane Database Syst Rev.* 18(4):CD007533.
- [22] Desai MJ, Saini V, Saini S. [2013] Myofascial pain syndrome: a treatment review. *Pain Ther.* 2(1): 21-36.
- [23] Cummings TM, White A. [2001] Needling therapies in the management of myofascial trigger point pain: a systematic review. *Arch Phys Med Rehabil.* 82(7):986-992.