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Dawn to sunset fasting and the fatigue manifestations of Post COVID-19 syndrome: A Case control study

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ABSTRACT

A growing number of individuals previously infected with the SARS-CoV-2 have reported persistent symptoms which are called post-COVID syndrome. It is a widely prevailing problem in which chronic fatigue is primarily the most common reported symptom in up to 72% cases. Therefore, solutions should be made to help post COVID-19 syndrome patients overcome this major problem. Dawn to sunset fasting plays an important role in human health and it has many beneficial effects on fatigue, mood, and wellbeing. Thus, our study aims to investigate the effect of dawn to sunset fasting on fatigue manifestation among post COVID-19 cases compared to the control. A case control study was carried out in which two groups were assigned and evaluated by the Piper fatigue scale during dawn to sunset fasting. The results showed that fatigue manifestation, during dawn to sunset fasting, was less severe among cases versus control. Only 6% of post COVID-19 cases had severe fatigue symptoms compared to 21.5% of control. It was concluded that fasting may be a good solution for cases suffering from post-COVID-19 syndrome to regain their health and reduce their daily sense of chronic fatigue that will improve their quality of life. Further research needs to be carried out on a large scale.

Keywords: Dawn to sunset fasting, post COVID-19 syndrome, fatigue manifestation, piper fatigue scale.

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INTRODUCTION

Since November 2022, A notable number of COVID-19 patients have been suffered from long term post COVID-19 fatigue syndrome, with signs and symptoms resembling chronic fatigue syndrome (CFS). Research revealed that within two years following the acute phase of infection, post-COVID symptoms affected 59.7% of hospitalized patients and 67.5% of those who were not hospitalized. Fatigue, pain, and memory loss emerged as the most common symptoms 2 years after SARS-CoV-2 infection in both groups (Fernández-de-Las-Peñas et al., 2022). The cluster of these persistent symptoms was then given the term post-COVID disorders syndrome (PCDS).

Post-COVID disorders syndrome encompasses a range of ongoing symptoms that a patient may develop after suffering from COVID-19 infection. This condition typically presented with a mix of symptoms, mainly fatigue, sleep disturbances as well as other features such as joint pains, anxiety, hair loss, dyspnea, chest pain, low mood, cognitive dysfunction, thromboembolism, and chronic kidney disease (Barrea et al., 2022). Fatigue is the most frequently reported symptom affecting up to 72% of cases, followed by chest dyspnea up to 40% of cases, then mental problems, chest pain, gustatory and olfactory dysfunction. Most patients with PCDS have underlying co-morbid condition such as diabetes mellitus and hypertension (Pavli et al., 2021).

The post COVID-19 syndrome pathophysiology is multifaceted and involves direct viral damage, persistent viraemia due to weak or absent antibody response and the possibility of relapse or reinfection. Also, inflammatory and immunological sequels, in fact, the SARS-Cov-2 infection can prompt a rapid activation of the innate immune cells leading to elevated levels of pro-inflammatory chemokines and cytokines. In individuals with obesity, the immune response is further amplified, constituting the most severe cases in this population (El-Meidany et al., 2023; Lan et al., 2020; Wu et al., 2020).

Intermittent fasting such as dawn to sunset fasting or time restricted fasting has been shown to offer many different health benefits such as reducing inflammation, enhancing insulin sensitivity and simulation cellular repair response. These positive effects are associated with improved immune function and may play a supportive role in managing post-COVID-19 syndrome (Moothadeth et al., 2020).

Fasting has been shown to boost autophagy, which is a lysosome-dependent cellular process that is very important for both innate and adaptive immunity. Studies have demonstrated that fasting dawn to sunset for one month was associated with more than seventy-fold increase in autophagy compared to levels measured a week after the completion of the duration of that study. This surge in autophagy was accompanied by a reduction in oxidative stress and inflammatory biomarkers in individuals with metabolic syndrome. (Dikic and Elazar, 2018).

Moreover, fasting had been shown to significantly decrease the total leukocytes, granulocytes, monocytes, and lymphocytes after completing three weeks of dawn to sunset compared with baseline levels (Faris et al., 2012). Fasting also enhances insulin signaling, helps regulate blood pressure, and improves lipid profile with a notable significant increase in high-density lipoprotein levels. These effects contribute to reduced inflammation via a decrease in adipose tissue and weight in the absence of strict regulation of caloric intake or food quality (Tahapary et al., 2020). Fasting has also been linked to a beneficial change in the gut microbiome and upregulation of the genes that play an essential role in immune defense (Yeoh et al., 2021).

According to all the benefits of fasting mentioned previously, the goal of this study is to investigate the role of dawn to sunset fasting on the chronic fatigue symptoms associated with the PCDS among people who suffer from post-COVID disorders syndrome.

MATERIALS AND METHODS

A case control study was done on 50 post COVID-19 cases and 65 control The study sample size was calculated after carrying out a pilot study that was done on 15 cases because the study was new to the literature at that time using Epi-info software. Participants who were prescreened based on an initial medical history assessment to assess whether their symptoms aligned with those associated with symptoms of post COVID-19 syndrome or not. Accordingly, the study participants were selected as cases by which the study sample of participants were assigned into two groups case group and control group.

The cases were reported retrospectively concerning the acute phase of the COVID-19 infection. Symptoms varied in severity and were classified as asymptomatic, mild, moderate, severe, or critical. Cases also suffered from post COVID-19 syndrome fulfilling the criteria of the WHO for post COVID-19 syndrome (World Health Organization (WHO), 2021). The definition states that post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of COVID-19. The condition is characterized by symptoms that last for at least two months that cannot be attributed to alternative diagnosis. Common symptoms include fatigue, cognitive dysfunction, and shortness of breath which generally interfere with daily functioning. Symptoms may newly appear after recovery from an acute COVID-19 episode or persist from the initial illness and may also fluctuate or relapse over time (World Health Organization (WHO), 2021). While the control group were individuals who don't have post COVID-19 syndrome matched for age and gender.

Those who were described as case group and control group were mailed a survey that included all items of the designed questionnaire. The completed surveys were scored using the Piper fatigue scale (PFS). The PFS was included in our survey, it is a 22-item scale that measures four subscales: behavior (6 items), affective meaning (5 items), sensory (5 items) and cognition/mood (6 items).

These 22 items were used to calculate the four subscale scores and the total fatigue scores. To score the PFS, the items within each subscale were summed and then divided by the number of items on that subscale. This provided the scores of each subscale that remains on the same "0" to "10" numerical scale. The total fatigue score was calculated by adding 22-item scores together then we divided them by 22 in order to keep the score on the same numeric "0" to "10" scale. The respondent should answer at least 75% - 80% of the items in each subscale. Each item has eleven response categories on a 0 to 10 and each subscale is scored individually, then poled together for an overall score, the participant showing higher scores reflecting more fatigue (Piper et al., 1998). The severity score was categorized as 0 is none, 1-3 is mild, 4-6 is moderate, and 7-10 is severe (Ostlund et al., 2007).

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RESULTS AND DISCUSSION

Table 1 shows the Piper fatigue scale score during fasting among both post COVID-19 cases and control. The table illustrates that dawn to sunset fasting negatively affects the fatigue symptoms among post COVID-19 cases compared to control.

The majority of post COVID-19cases had a mild behavior subscale score of PFS (56%) during fasting and about 40% of cases had a moderate behavioral score, while the minority (4%) had a severe behavioral score during fasting. Similarly, 56.92% of control had mild behavior score followed by those with moderate behavioral score then, 15.3% of control had severe behavioral score during fasting with no statistically significant difference between two groups.

The effect of dawn to sunset fasting on the affective meaning subscale score, there was no statistically significant difference regarding the affective meaning score between post COVID-19 cases and control, although the severity was less among cases (4%) versus control (15.38%). Otherwise, both cases and control were having the highest percentage is mild affective meaning score (62 %, 44.6% respectively) followed by moderate (34%, 40% respectively), then severe score.

Regarding the effect of dawn to sunset fasting on the sensory subscale score, a statistically significant difference was found between post COVID-19 cases and control. By which half of cases, had a moderate sensory score compared to 47.7% of control, while 34 % of cases had mild score compared to 18.4% of control, then only 16% of cases had severe sensory score during fasting compared to larger percentage (33.9%) among control.

The cognitive/mood subscale score between two groups showed no statistically significant difference although among post COVID-19 cases, the majority had mild cognitive/mood score followed by moderate then severe score during dawn to sunset fasting. On the other hand, the control were mainly having moderate cognitive/mood subscale score during fasting followed by mild then severe score. The cases had less percentage of those suffering from severe symptoms of cognitive\mood score during fasting than control (12%, 26.15% respectively).

The total fatigue score was statistically significant when comparing between post COVID-19 cases and control, by which 42% of cases had mild fatigue during fasting, and 52% had moderate fatigue score during fasting, leaving only 6% (3 cases) who had severe fatigue score during fasting. On the other hand, among control 41.5% had mild fatigue score during fasting, 36.9% had moderate fatigue score, and 21.5% (14 cases) had severe fatigue score during dawn to sunset fasting.

Table 2 shows the history of previous COVID-19 infection among cases and control, by which 52% of post COVID-19 cases tested positive for COVID -19 infection, and 42% of post COVID-19 cases tested negative for COVID-19 but having typical clinical signs and symptoms of COVID-19. On the other hand, most control (80%) tested negative for COVID-19 but with typical clinical signs and symptoms of COVID-19, and about 12.3% were tested positive for COVID-19 with typical symptoms and signs of COVID-19, leaving only 7.7% tested negative for COVID-19 and didn't have any previous sign or symptoms of this viral infection.

None of the control group who had COVID-19 clinical signs and symptoms without positive test suffered from post COVID-19 syndrome, while 100% of cases had this syndrome. Among those who had COVID-19 clinical signs and symptoms with\without positive test, half of post COVID-19 cases (50%) had the COVID-19 infection twice, and 34% of post COVID-19 cases had COVID-19 infection once in their life, while only 16% had the infection more than twice. Regarding the number of previous COVID-19 infections among control, 55.3% had COVID-19

infection twice, and 18.4% had this infection once and also the same percentage more than twice with a statistically significant difference between two groups.

Table 3 shows the distribution of the studied sample of post COVID-19 cases and control according to their sociodemographic characteristics. The majority of post COVID-19 cases (48%) aged between 31-40 years old, followed by those aged from 20-30 years old, then those from 41-50 years old and finally those aged 51 or more years old. Also, the majority of control aged between 31-40 years old (40%). The majority of both cases (78%) and control (87.7%) were females.

The majority of cases (89.5%) and control (80%) were residing in Egypt and only 10% of post COVID-19 cases and 20% of control were from other countries (Qatar, Saudi Arabia, Kuwait, and Jordin).

The majority of cases (89.5%) and control (80%) were residing in Egypt and only 10% of post COVID-19 cases and 20% of control were from other countries (Qatar, Saudi Arabia, Kuwait, and Jordin).

Discussion

Post COVID-19 syndrome is a condition that develops at least three months following probable or confirmed SARS-CoV-2 infection which persists for at least two months and cannot be explained by an alternative diagnosis. These symptoms may fluctuate or relapse or persist since the initial infection, or might also be new onset after recovery from the acute illness (Chamsi et al., 2023; World Health Organization (WHO), 2021).

The post COVID-19 cases who had COVID-19 signs and symptoms including fever, sore throat, fatigue, body aches, cough, shortness of breath, congestion or runny nose, headache, diarrhea, nausea or vomiting but with negative COVID-19 test can be explained according to the CDC statement that a negative COVID-19 test means that the test didn't detect the virus, but this doesn't rule out the that the patient is having a COVID-19 infection. Another possibility for this is that the patient may have COVID-19 but tested before the virus was detected (Centers for Disease Control Prevention (CDC), 2024).

Based on the systemic review and meta-analysis done in July 2024, the global prevalence of post COVID-19 syndrome worldwide was 41.79%, accordingly, the number of control recruited in our study were more than that of cases. The prevalence of post COVID-19 syndrome in the systemic review was more among females than males 78% and 22% respectively. In our study the prevalence was also more among females than males 52.77%, 47.23% respectively (Abd Razak et al., 2024). Our findings showed that the majority of post COVID-19 cases were aged 31-40 years old. This is concomitant with a study done in 2024, the mean age in adults with post COVID-19 symptoms were 34 years old (Sugiyama et al., 2024). Post COVID-19 condition among adults in US was found to affect 1 in 5 COVID-19 survivors aged 18–64 years and one in four survivors aged 65 years or more experienced at least one incident condition that might be attributable to previous COVID-19 (Bull-Otterson et al., 2022).

In our study, the post COVID-19 cases and control had once or more numbers of previous covid 19 infections, this might be explained by that as long as the virus evolves, new variants appear with the ability to evade the existing immunity. This can increase the risk of reinfection which can occur as early as several weeks after a previous infection (Markkanen, 2017).

Although most of the post COVID-19 cases in our study had twice previous infection with COVID-19 but at a lower percentage than control, this might be explained by a previous study that concluded that the risk of new-onset long COVID after a second SARS-CoV-2 infection is lower than that after a first infection for persons aged 16 years old or more. However, there remains some risk of new-onset long COVID after a second infection, with around 1 in 40 of those aged16 years old or more compared to 1 in 165 of those aged less than16 years old reporting long COVID after a second infection (Bosworth et al., 2023).

According to a study done in 2024 which stated that there is a greater health impact from the initial infection compared to reinfections with closely related variants. Infected adults were less likely to experience reinfection but more likely to report persistent symptoms and long-term health consequences of SARS-CoV-2 infections. This is particularly relevant in the current context where reinfections occur without being officially reported (Golding et al., 2024).

Piper fatigue scale was used previously in many studies to assess the level of fatigue among healthy and diseased individuals. Also, it was used to determine the level of fatigue among persons during dawn to sunset fasting (Ovayolu et al., 2016) that is the reason behind using it as a tool to measure the fatigue symptoms among post COVID-19 cases compared to control. One of the important advantages of Piper fatigue scale is that it assesses the 4 subdomains of fatigue (behavioral, sensory, affective, and cognition/mood) as well as the overall fatigue level with all 22 items (Reeve et al., 2012).

Behavioral subscale measures the degree by which fatigue is causing the individual to be distressed or interfering with the ability to complete work or school activities or interfering with the ability to visit or socialize with friends or ability to engage in sexual activity, or the ability to engage in the kind of activities that usually he\she enjoys doing.

The affective subscale of PFS categorizes whether the fatigue that the individual is experiencing is considered protective or destructive, positive or negative, normal or abnormal, pleasant or unpleasant, agreeable or not. The sensory subscale assesses the effect of fatigue on the feelings whether the individual feels strong or weak, sleepy or awake, lively or listless, refreshed or tired, energetic or unenergetic. The cognitive\mood subscale measures the condition of individual whether he\she is patient or impatient, relaxed or tense, exhilarated to depressed, able to concentrate or not, able to remember or not, able to think clearly or not.

The finding of our study showed that during dawn to sunset fasting the post COVID-19 cases were significantly experiencing less severe fatigue symptoms compared to control based on the total fatigue score. Regarding the 4 subscales, only the sensory subscale was statically significant among cases compared to control. This suggests that post COVID-19 cases may benefit more from dawn to sunset fasting than control who are not suffering from post COVID-19 syndrome. This might be explained by the following mechanisms which highlight the importance of fasting on human health.

Fasting is a non-pharmacological intervention that has been practiced since the 5th century and is well-documented for its role in managing various health conditions. Numerous studies focused on its benefit in cancer prevention (Lee and Longo, 2011), enhancement of the immune system (Ghram et al., 2021) and insulin sensitivity improvement (Teong et al., 2023), and as well as accelerating recovery from disease (Castellano-Tejedor, 2022). Moreover, scientific evidence supports fasting in preventing SARS-CoV-2 infection (Horne et al., 2022; Karagiannis et al., 2022) and aiding the recovery process for patients with COVID-19 (Abunada et al., 2020).

Dawn to sunset fasting is a month-long fast from sunrise to sunset had many beneficial effects due to different underlying mechanisms (Rouhani and Azadbakht, 2014). One of the primary effects is the stimulation of autophagy which is a process with therapeutic potential in addressing spike protein-related pathologies which also supports cellular renewal and maintenance (Halma et al., 2024). Fasting also caused an increase level of nicotinamide adenine dinucleotide (NAD+), a molecule that plays a critical role in enhancing immune cells combating COVID-19, thereby offering potential protection against viral infections, particularly SARS-CoV-2.

Research suggests that coronaviruses like SARS-CoV-2, exploit NAD+ resources during their replication cycle, causing a diminish in cellular NAD+ levels which in turn weaken the immune cells that are important for recognizing and combating the viral infections (Tan and Doig, 2021). However, experimental studies have shown that restoring NAD+ accelerates the recovery from COVID-19 (Jiang et al., 2022). Thus, the fasting-induced increase in NAD+ may serve as a promising approach to strengthen the body's immune defenses and help in managing viral infections, especially COVID-19 (Dongoran et al., 2024).

On the other hand, a few studies demonstrated that dawn to sunset fasting did not significantly influence fatigue or mood or quality of life of the participants when compared to non-fasting group (Nugraha et al., 2017). Another studies showed that participants during dawn to sunset fasting had higher fatigue and anxiety scores and lower vigor scores may be due to sleep disturbances (Khemila et al., 2023). Similarly, previous studies have presented an increase in subjective feelings of fatigue, lethargy and mood alterations during the fasting period (Roky et al., 2004; Zerguini et al., 2007). Reduced sleep duration and quality observed during dawn to sunset fasting are likely associated with these mood related changes (Roky et al., 2004).

Also, there is strong evidence that fasting can trigger adaptive cellular responses that can contribute to improved glucose regulation, reduced production of free radicals, increase resistance to stress, and suppress inflammatory reactions (de Cabo and Mattson, 2019). Dawn to sunset fasting can improve physical function, and endurance (Moro et al., 2016), as well as support cognitive functions such as working memory, and can reverse neurotoxic effects of obesity, diabetes, and neuroinflammation (Wahl et al., 2017). Dawn to sunset fasting appears to have a significant positive impact psychological well - being and mental health, mood, and regulation of sleep pattern (KhoshniatNikoo et al., 2012; Tootee and Larijani, 2020).

Previous studies have shown that following a16:8 intermittent fasting regimen for three months significantly enhances various aspects of quality of life and reduces fatigue among healthy people. This fasting pattern also led to a notable decrease in Insulin-like Growth Factor-1 (IGF-1) which may help protect against the development and progression of tumors (Anic et al., 2022). Grundler et al., emphasized the potential effect of long-term fasting as an effective intervention in the management and treatment of long COVID (Grundler et al., 2023). According to Halma et al 2024, fasting holds promise as a therapeutic intervention for SARS-CoV-2 spike protein related diseases; with broad implications for human health (Halma et al., 2024).

Figures and Tables

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Table (1): The Piper fatigue scale score during fasting among both post COVID-19 cases and control.

	Cases		Control		
Piper fatigue scale during fasting	No.	9/0	No.	%	P
Behavioral	(n = 50)		(n=65)		
Mild	28	56	37	56.92	
Moderate	20	40	18	27.69	0.093
Severe	2	4	10	15.38	0.093
Affective_meaning					
Mild	31	62	29	44.6	
Moderate	17	34	26	40	0.067
Severe	2	4	10	15.38	
Sensory					
Mild	17	34	12	18.4	
Moderate	25	50	31	47.7	0.045*
Severe	8	16	22	33.9	
Cognitive/ mood					
Mild	24	48	21	32.3	
Moderate	20	40	27	41.5	0.099
Severe	6	12	17	26.15	
Total-fatigue <u>.</u>					
Mild	21	42	27	41.5	
Moderate	26	52	24	36.9	0.047^{*}
Severe	3	6	14	21.5	

χ²: Chi square test

p: p value for comparing between the two studied groups.

^{*}Means statistical significance (p<0.05)

Table (2): The History of previous COVID-19 infection among cases and control.

History of previous COVID-19	Cases		Control		
infection	No.	%	No.	%	_ р
Testing for COVID-19 infection	(n = 50)		(n = 65)		
Positive test with typical clinical signs	26	52	8	12.3	
and symptoms of COVID-19	20	32	o	12.3	
Negative test with typical clinical signs	24	42	52	80	0.000
and symptoms of COVID-19	24	42	32	80	0.000
Negative test with no symptoms or	0	0	5	7.7	
signs of COVID-19	V	O	3	7.7	
Experiencing post COVID-19					
manifestation					
Yes	50	100	0	0	0.000
No	0	0	65	100	0.000
Number of previous COVID					
infections (clinical signs and					
symptoms with\without positive test)					
Once	17	34	12	18.4	
Twice	25	50	36	55.3	0.045*
More than twice	8	16	12	18.4	

^{*} P value < 0.05 χ²: Chi square test

p: p value for comparing between the two studied groups. MC: Monte Carlo

Table (3) The distribution of the studied sample of post COVID-19 cases and control according to their sociodemographic characteristics.

Socio-demographic	Cases (n=50)		Control (n=65)		
characteristics					
	No.	%	No.	%	
Age (years)					
20-30	19	38	8	12.3	
31-40	24	48	26	40	
41-50	6	12	11	16.93	
>51	1	2	20	30.77	
Gender					
Female	39	78.0	57	87.7	
Male	11	22.0	8	12.3	
Place of residence					
Egypt	45	89.5	52	80.0	
Other countries (Qatar, Saudi	5	10.5	13	20	
Arabia, Kuwait, Jordan)					

CONCLUSION

It was concluded that fasting may be a good solution for cases suffering from post-COVID-19 syndrome to regain their health and reduce their daily sense of chronic fatigue that will improve their quality of life. Further research needs to be carried out on a large scale.

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