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Research Article

Daily Response of Vital Signs to COVID-19 Infection: A Case Study of an Unvaccinated 70-Year-Old Male with Type II Diabetes Treated with Monoclonal Antibodies and Selected Supplements

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Abstract

In much of the current scientific literature on COVID-19, potential treatments are studied singly or in combination with two or three other items. Treatment options for unvaccinated individuals at high risk for COVID-related complications and mortality have improved but may still be limited for remote locations. A case study of an unvaccinated older male with co-morbidities at higher risk for COVID-19 related mortality is used to illustrate possible solutions to some of the issues. His vital signs, including O_2 saturation, breathing rate, heart rate variability, night skin temperature, and resting heart rate, were monitored for 30 days before and after COVID-19 infection, providing more individual details than available in most studies to date. Supplements may have limited his vulnerability to COVID-19 while monoclonal antibodies led to rapid improvement in multiple vital signs. Tests for COVID-19 may not detect the earliest stages of COVID infection as fever levels increased before the patient tested positive for COVID-19.

Keywords: COVID-19, Monoclonal antibodies, Vitamin D, Quercetin, Resveratrol, Zinc, Combination therapies, Vaccine resistance

Statement of the Problem

Although its exact origins remain unclear, the COVID-19 virus appears to have originated in the city of Wuhan, China in the late fall of 2019. By January 2020 it had reached the United States and many other nations. Since then, millions of infected persons have perished (over one million in the USA) while some survivors have experienced long-term COVID symptoms, up to at least two years [1,2]. Adverse psychological outcomes have been common [3]. Due to vaccine hesitancy or medical restrictions, some potential victims of COVID-19 may not have been vaccinated. Vaccine hesitancy is not without legitimate concern; the Open VAERS website [*https://www.openvaers.com*] lists over 1.5 million adverse event reports as of June 2023, including over 35,000 deaths, over 200,000 hospitalizations, and nearly 67,000 permanent disabilities. Young men may be at higher risk for myocarditis after COVID vaccination [4]. There may be other unintended consequences of vaccination [5]. Some have proposed that vaccination may result in autoimmune disease, cancer growth, and autoimmune myocarditis, as well as reduced immunity to COVID [6]. Natural immunity from mild COVID infection may be more protective against severe reinfection than vaccination [7,8]. Vaccine immunity may wane over time, especially against

new variants [9]; some have claimed that "all-cause mortality" may be higher among the vaccinated than those not [10]. In some data, vaccination rates have not correlated with infection rates [11]. Data seem to support less need for vaccination of children against COVID [12]. Five trillion dollars were spent to fight COVID in the USA, including vaccine development [13], but the effectiveness of societal lockdowns remains questionable [14]. Older individuals, including men, African Americans, persons with high BMI or other comorbidities, including diabetes, heart problems, or cancer appear to be at much higher mortality risk if they become infected with COVID-19. A final basis for vaccine hesitancy is the alarming rate of retractions of scientific articles on COVID vaccines and other treatments [15]. However, the question remains - how to treat unvaccinated individuals at high mortality risk from COVID-19? Furthermore, how could they be treated at lower cost? Not all nations may be able to afford higher cost treatments for all their vulnerable citizens.

Literature Review

Several reports have highlighted the potential role of nutrition in preventing COVID infection or reducing its severity [16-20]. *Ashok, et al*., [16] have recommended specific fruits and vegetables for consumption to obtain nutrients for improving immune response. *Ali* [21] has stated that "preventive health measures that can reduce the risk of infection, progression and severity of COVID-19 are desperately needed". Improved nutrition might enhance vaccine effectiveness in older persons [17]. Our focus will be on over-the-counter supplements or medicines due to their relatively low cost and greater availability than for prescription medications. Even if some nutritional supplements might assist a human body's resistance to colds or flu, it might not be certain that those supplements would be helpful for dealing with the novel COVID-19 virus. Ideally, a supplement would reduce one's chances of being infected with the COVID-19 virus (presumably by enhancing the body's own immune system prior to infection), reduce the ability of that virus to replicate and establish itself inside the human body, limit its damage to the human body's cells and organs, limit the body's inflammatory overreaction to the virus, preventing the cytokine storm that often leads to fatal cell and organ damage, especially to the heart and lungs, and lastly, minimize the damage, if it occurs, to the heart, lungs, and other critical organs. Of course, not all substances will help with all those ideal goals, so each substance must be evaluated for the conditions under which it would be most helpful, if at all. Evidence for a substance might range from mere theoretical speculation to results from double-blind randomized trials with low bias and high quality. It is also possible that a deficiency of a substance might be a risk with respect to different stages of COVID-19 infection, but that more of the same substance above deficiency levels might not provide greater benefits against COVID-19. The value of substances may also vary with a person's comorbidities. Perhaps some substances might work to offset the disadvantages of diabetes (or other co-morbidities) as well as dealing with COVID-19. Furthermore, we must remain alert to potential interactions between substances with each other or with prescription drugs.

Covid Symptoms

All of the authors of this paper have witnessed the severe symptoms of COVID-19 infection for themselves or for friends or family members, including mortality. In many cases, victims have been unable to work, even remotely, due to the extreme fatigue experienced (up to two weeks), as well as high fevers and other symptoms. Severe symptoms have lasted up to two weeks for some while long-term symptoms have remained for up to several months. Some of our friends have died from or with COVID-19. In summary, COVID-19 infection is not to be taken lightly. However, many victims have not had access to day-by-day readings of their vital signs.

Methodology

A 70-year-old male with type 2 diabetes and type O blood [22,23] had avoided COVID-19 infection until October 2021 and served as the patient and research participant for this study (and is senior author). Older age [24] and a type 2 diabetes diagnosis placed him at higher risk from COVID infection [25]. The patient did not suffer from obesity (BMI 22) obesity being related to a poor immune response to infections [20] nor from hypertension or cardiovascular disease. He had undergone prostate surgery for cancer in 2015. However, on 2 October 2021 his wife fell and broke her femur, necessitating surgery and a week of hospitalization, followed by seven weeks of care at a rehabilitation center in the midwestern USA. A terminal case of COVID occurred at the rehabilitation center in a room immediately adjacent to his wife's, and his wife became infected. The patient's wife first tested positive for COVID-19 on October 14; the patient tested positive for COVID-19 on October 19 and 21 after testing negative on October 16 and 18. After his wife tested positive, the patient was only allowed to visit her if wearing a disposable gown and a face mask; the patient also had to depart the rehabilitation center via a back door rather than through the front entrance. The patient's positive test results were reported to his county's health department who placed him under a 10-day quarantine, which prevented him from visiting his wife at the rehabilitation center, other than leaving items at the front desk to be taken to her. His wife never felt any symptoms from COVID-19; the patient only felt like he had a mild cold - without a positive test for COVID-19, he would not have sought treatment. However, in addition to more frequent COVID-19 testing (freely available at several nearby locations) the patient responded to the risk with a regime of supplements thought to help him avoid infection or at least reduce any impact of infection, while knowing that his physician had told him that if he did become infected, he could apply for treatment with monoclonal antibodies due to his high risk of mortality due to his age and type 2 diabetes. In essence, plan A was a combination of increased testing for infection and increased nutritional supplements while plan B was the antibody treatment. He did become infected and elected to take the monoclonal antibody treatment as soon as it was available.

Smart watches can be used to collect data from patients at risk for COVID *Banks, et al.,* (2021) [26]. Data from the patient's smart watch were recorded from October 13 to November 15, as present-

ed in Table 1. Data were analyzed using SPSS [27]. The patient was teaching a basic statistics class at Highland Community College that fall, and this became the second research project in which the class was involved, the first previously published in this journal [28] (Table 1).

Table 1: Case Study Health Indicators Over Time During a Confirmed COVID-19 Infection.

Date	O_2 SAT	Resting Heart Rate	Breathing Rate	Heart Rate Variability	Night Skin Temperature
October 13	No data	70	14	19	-0.1
October 14 Wife tested (+)	No data	72	13	18	-0.3
October15	No data	72	13	20	-0.5
October 16 Tested (-)	96/94	72	12	28	1.7
October 17	94/92	68	13	26	1.8
October 18 Tested (-)	94/94	72	12	19	2
October 19 Tested (+)	94/94	74	14	15	1.2
October 20	92/93	75	16	9	1.8
October 21	93/92	77	14	18	1.8
Tested (+)					
October 22 Antibodies Infusion (*)	94/92	76	17	20	1.5
October 23	96/92	75	17	18	1.5
October 24	97/93	73	14	20	1
October 25	98/94	71	13	21	0.5
October 26	97/94	69	14	25	0
October 27	98/93	69	14	20	-1
October 28	98/95	69	13	20	0
October 29 Tested (-)	98/94	70	14	18	-1.1
October 30	96/94	72	15	18	0.1
October 31	98/94	73	14	15	-0.3
November 1	96/94	75	15	13	0.9
November 2	98/95	73	13	20	-0.2
November 3	96/94	73	13	18	0.7
November 4	98/95	73	13	15	-0.2
November 5	98/94	73	13	16	-0.2
November 6	96/94	72	13	14	-0.4
November 7	97/93	71	13	20	0.3
November 8	95/93	72	14	18	0.6
November 9	97/95	71	14	18	0.8
November 10	97/94	73	13	15	0
November 11	98/94	70	14	17	1.1
November 12	98/95	70	13	17	0.2
November 13	96/94	72	14	14	0
November 14	95/93	74	13	13	1.2
November 15	95/95	71	15	25	-1.6
Mean	96.23/93.74	72.12	13.79	18.24	0.44
Median	96.00/94.00	72	14	18	0.25
SD	1.71/0.93	2.1	1.17	3.91	0.92
1.5 SD	93.67/92.35	75.27	15.55	12.38	1.82

Note*: (*) Antibodies infused were casirivimab and imdevimab, 1200 units each, manufactured by Regeneron Pharmaceuticals. See: U.S. Food and Drug Administration. Letter of Authorization for Monoclonal Antibodies Casirivimab and Imdevimab. November 21, 2020. Washington, DC.

During this period (and before to a lesser extent) the patient was taking 2000 to 6000 IU of vitamin D [17,18,20,21,29-36], 1000-3000 IU of Vitamin C [17,36-40], 100-200mg of zinc tablets [41], four resveratrol tablets [42-44] daily that each included 200 mg red wine extract (30% polyphenols), 200mg red wine powder, 200mg Japanese knotweed extract, and 100 mg grape seed extract [45]; 2000mg, vitamin C [17,36-40]; 45mcg of vitamin K_2 [46,47]; multivitamins that included a total of 2400mcg of vitamin A [17,20,48-51], 150mg of vitamin C, 800 IU of vitamin D, 27mg of vitamin E [17,36,52], 10mg of vitamin B-6 [17,53], 800mcg of folic acid [53], 30mcg of vitamin B-12 [35,53], 1200mcg of biotin [54,55], 20mg of pantothenic acid [55], 12mg of choline, 300mcg of iodine, 10mg of zinc [17,54,55], 220mcg of selenium [17,37,56-58], and 80mcg of inositol [59]; 1000mg of magnesium [35,60], 2grams of beet root, 600mg of alpha lipoic acid [61-63], 200mg grapeseed extract [45] with 800mg of grapefruit powder, 1500mg quercetin [64-69], and 60-200mg of Coenzyme Q-10 [70-73]. The patient was taking 1500 units of metformin for diabetes as well as 25 units of insulin per day; the patient took 325mg of aspirin [74-81] two or three times during the first week to relieve general discomfort.

Hypotheses

The general research question was how the dependent variables would vary over time from before COVID infection, during infection, and post infection. The general hypothesis was that levels would become worse during infection and recover, often leading to a quadratic effect. Small declines in health outcomes before and during COVID infection might suggest that there was an early onset of COVID infection before detection. Larger declines in health outcomes would suggest that COVID infection had a more substantial impact during detectable infection. Improvements from infection to post infection health outcomes would indicate the degree of recovery. Changes from pre infection to post infection would reflect if recovery was partial or more complete.

Methods

Groups. Results for October13 to 18 (3-6 cases) were classified as a pre-COVID baseline. Results for October 19 to 24 (6 cases) were classified as during-COVID. Results between October 25 and November 15 (22 cases) were classified as post-COVID treatment. Because patients may become contagious 2-3 days before onset of symptoms [82], it is possible the patient was contagious as early as October 18.

Measures. Oxygen saturation levels were measured on a oximeter at the patient's home and as measured by the patient's smart watch, as averaged over each day. Resting heart rate was measured by the smartwatch as averaged over each day. Breathing rate, heart rate variability, and night skin temperature (above/below 98.6 degrees) were also measured by the patient's smartwatch, averaged over the day. Complete data are reported in Table 1 and correlations among the vital signs are presented in Table 2, showing interrelationships among the different vital signs (Table 2).

Table 2: Vital Signs Correlations.

	O_2, Home	O_2, Fitbit	Resting Heart Rate	Breathing Rate	Heart Rate Variability	Night-time Skin Temperature
O_2, Home	xxxxxxxxx	0.542**	-.490**	-.336+	0.109	-.621***
O_2, Fitbit	.515**	xxxxxxxxx	-.355*	-.422*	-0.033	-.540**
Resting Heart Rate	-.438*	-.321+	xxxxxxxxxx	.415*	-.491**	.424*
Breathing Rate	-0.27	-0.3	0.241	xxxxxxxxxx	-0.207	0.133
Heart Rate Variability	0.073	-0.052	-.496**	-0.164	xxxxxxxxxxx	-0.049
Night-time Skin Temperature	-.652***	-.529**	.360*	0.073	-0.022	xxxxxxxxxx

Note*: Correlations above the diagonal are Pearson zero-order correlations; below the line are Spearman rho correlations.

Analysis. Levels of the dependent measures were compared across three groups using one way analysis of variance, a more conservative approach than using repeated measures. Post hoc tests were conducted with LSD comparisons. Tests for quadratic trends were conducted as part of the analysis of variance. Cohen's d and Hedge's g were calculated as noted in Table 3.

Table 3: Analysis of Variance of Vital Signs Comparing Across Three Times with Test for Quadratic Trends and Post Hoc Comparisons with Effect Sizes.

Vital Signs	Mean/SD Pre-COVID (A)	Mean/SD COVID (B)	Post-COVID (C)	One way ANOVA/ Welh Test sig. level	Test of Quadratic Trend	Post Hoc Comparisons (LSD) (effect sizes, d and g)
O_2, Home	94.67/1.15	94.33/1.86	96.95/1.13	F (2,28) = 12.07*** p = .028	F (1,28) = 4.98*	AB (.22/.20) AC** (2.00/2.01) BC*** (1.70/2.01)
O_2, Fitbit	93.33/1.15	92.67/0.82	94.09/0.68	F (2, 28) = 8.95** p = .044	F (1,28) = 7.40*	AB (.77/.71) AC (.80/1.04) BC*** (1.89/2.00)
Resting Heart Rate	71.00/1.67	75.00/1.41	71.64/1.68	F (2,31) = 11.65*** p = .001	F (1,31) = 23.02***	AB*** (2.59/2.59) AC (.38/.38) BC*** (2.17/2.06)
Breathing Rate	12.83/0.75	15.33/1.51	13.63/0.73	F (2,31) = 12.46*** p = .019	F (1,31) = 24.60***	AB*** (2.10/2.10) AC+ (1.08/1.09) BC*** (1.43/1.82)
Heart Rate Variability	21.67/4.23	16.67/4.18	17.73/3.35	F (2,31) = 3.42* p = .144	F (1,31) = 3.14+	AB* (1.19/1.19) AC* (1.03/1.11) BC (.28/.30)
Night Skin Temperature	0.77/1.18	1.47/0.32	0.06/0.702	F (2,31) = 8.75** p < .001	F (1,31) = 8.74**	AB (.81/.81) AC+ (.73/.87) BC*** (2.58/2.18)

Note*: Effect sizes were Cohen's d and Hedge's g, the latter more useful when group sizes are not equal. Effect sizes were calculated from the website *https://www.socscistatistics.com/effectsize/default3.aspx*.

Results

Overall tests. One-way analyses of variance yielded statistically significant results for all six health outcome variables while the Welch test yielded five significant results. Five of the quadratic trends were statistically significant, while a sixth was not significant (p<.10). From Table 1, it can be seen that all of the six measured health outcomes improved at least somewhat within three days of medical treatment (infusion of monoclonal antibodies). Early shifts in health outcomes (pre-COVID to during COVID infection). The largest deteriorations for health outcomes occurred for resting heart rate and breathing rate with smaller changes for both measures of oxygen saturation, heart rate variability, and night skin temperature. The changes were small enough for night skin temperature yet lower post infection to suggest that an increased night skin temperature might have been a leading indicator of an oncoming COVID infection. Recovery from COVID (during COVID to after COVID infection). Except for heart rate variability, all health outcomes featured very substantial (effect sizes of 1.43 to 2.58) and statistically significant (p<.001) improvements after monoclonal antibodies treatment of the patient. Heart rate variability improved but only slightly, possibly a factor in long COVID (slower heart tissue recovery) and remained significantly (p<.05) well below (effect size of at least 1.03) initial levels even after treatment. While both measures of O_2 levels improved upon pre-COVID levels as well as COVID levels, resting heart rate, breathing rate, and night skin temperature did not return completely to pre-COVID levels, even after treatment (Table 3).

There are many potentially useful drugs, supplements, or treatments that were not used by the patient that might have been useful or were used but without apparent effect: nicotine, ivermectin, remdesivir, chloroquine, nasal disinfection, green and black teas, catechins, prednisone, kampo, rosemary, molnupiravir, ranolazine, Paxlovid, antihistamines, trimetazidine, thiamine, riboflavin, L-carnitine tartrate, niacin, pantothenic acid, iodine, nitric oxide, Glutathione (GSH), myo-inositol, iron, probiotics; papaya, chamomile, bitter orange, hawthorn, echinacea, golden poppy, Siberian ginseng, tea tree oil, lemon balm, holy basil, panax ginseng, purple passionflower, dexamethasone, Asian knotweed, golden root, sage, elderberry, cat's claw, valeric acid [19]; inhaled corticosteroids, nitazoxanide, mometasone, ciclesonide, doxycycline, albendazole, theophylline, fluvoxamine, Pepcid, albendazole, copper, turmeric/curcumin, various antibiotics, tocilizumab, N-Acetylcysteine (NAC),

pantoprazole, Eliquis, beet root, iodine, choline, metformin, insulin, hyperbaric oxygen, favipiravir, colchicine, anticoagulant therapy, clopidogrel, budesonide, hydrogen peroxide nasal rinse, povidone-iodine nasal rinse, ozone blood therapy, omega-3 fatty acids (docosahexaenoic acid), and melatonin, among others. The possible effects for these items with respect to COVID can be found using Google Scholar or medical indices.

Discussion

The origins of COVID remain controversial. One of our neighbors contracted a virus-like illness in late November 2019 after visiting with a Chinese student who had just flown into our hometown from Wuhan, China. Was it an early case of COVID - or were there other infectious agents circulating in Wuhan at the time? Many facilities checked temperatures of persons entering as a way to detect infections, but the results here suggest that higher body temperatures may indeed be a leading indicator of a COVID infection not yet detected officially but if a pre-COVID body temperature is lower than average, a rise in temperature may not show up as abnormal, allowing COVID infected persons to enter facilities with undetected infection. A variety of nutritional supplements may reduce the severity of infection by promoting the human immune system and by reducing inflammation, but more research needs to be done to determine which supplements are best, at which times before or during a COVID infection. Monoclonal antibody treatments appear effective and may be enhanced for those on effective supplements, even for high-risk individuals. In the future, physicians and medical researchers might be able to assess a patient's condition more clearly and rapidly if they were provided access to personal vital signs detection devices, as can be found on many current smart watches. Those with cancer may need particular attention [83-85].

Acknowledgement

None.

Conflict of Interest

None.

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