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Mini Review

Spike in Mental Health issues among students due to COVID19 Pandemic

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Abstract

Background

The outbreak of COVID-19 has led to a global public health and economic crisis, especially in developing countries. The COVID-19 pandemic is associated with highly significant levels of psychological distress that, in many cases, would meet the threshold for clinical relevance. While psychological support is being provided to patients and healthcare workers, the general public specifically the young adolescent student's mental health requires significant attention as well. Such widespread outbreaks are associated with adverse mental health consequences. Keeping this in mind, existing literature on the COVID-19 outbreak pertinent to mental health was studied and published articles were classified according to their overall themes and summarized. Preliminary evidence suggests that symptoms of anxiety (18.92% to 71%), depression (9% to 78.7%), symptoms of PTSD (2.7% to 16.3%) and stress (14.46% to 88%) are common psychological conditions associated to the COVID-19 pandemic, and may be associated with disturbed sleep. A number of individual and structural variables moderate this risk. This review highlighted the possible causes of mental health issues among the students during the COVID-19 pandemic, the effects of COVID-19 on psychological outcomes of the students and its associated risk factors. Student mental health in higher education has been an increasing concern. The COVID-19 pandemic situation has brought this vulnerable population into renewed focus.

Methods

A search was conducted on PubMed, Medline, Embase, Scopus and Web of Science with various relevant terms. A manual search on Google Scholar was performed to identify additional relevant studies. The articles were selected on predetermined eligibility criteria.

Results

Relatively high rates of symptoms of anxiety (18.92% to 71%), depression (9% to 78.7%), post-traumatic stress disorder (2.7% to 16.3%) and stress (14.46% to 88%) are reported among the students during the COVID-19 pandemic in China, Italy, US, Turkey, Nepal, Bangladesh, Poland, Slovenia, Czechia, Ukraine, Russia, Germany, Israel, Columbia, UAE, Taiwan, Egypt, Czech republic, Netherlands, Greece, Saudi Arabia, Jordan. Risk factors associated with distress measures include female gender, presence of chronic/psychiatric illnesses and frequent exposure to social media/news concerning COVID-19.

Conclusions

During the COVID-19 struggle, providing sound mental health services for individuals is very important to maintain the mental health. Mitigating the hazardous effects of COVID-19 on mental health is an international public health priority. Due to the COVID pandemic situation and onerous measures such as lockdown the COVID-19 pandemic brings negative impacts on higher education. The findings of our study highlight the urgent requirement to develop interventions and preventive strategies to address the mental health of college students. There is a need for more representative research from other affected countries, particularly in vulnerable populations.

Keywords: COVID-19 • Anxiety • Depression • Stress • Public health • Infection • Pandemic • Coronavirus • Mental health • College student • School Student • PTSD • Post Traumatic Stress Disorder

Introduction

We humans are well known to be captive to fear, worry and stress. These are considered to be normal responses perceived to real threat. So it is normal and understandable that people are experiencing fear in the context of the COVID-19 pandemic [1]. Mental health in this context becomes one of the most important aspects. Mental health is considered as an integral part of health. WHO defines health as "Health is a state of complete physical, mental and social well-being and not merely an absence of disease or infirmity". Mental health can be defined as a state of balance between the individual and the surrounding worlds state of harmony between one self and others ,a coexistence between the realities of the self and that of other people and that of the environment[2]. The current ongoing Pandemic has forced the countries to go into strict lockdowns. These lockdowns have caused all the educational institutes, be it schools, colleges or other institutes to be closed for very long duration. In the new realities of working from home, temporary unemployment, home-schooling of children, and lack of physical contact with other family members, friends and colleagues, it is important that we look after our mental, as well as our physical health [3]. Many of us are facing challenges that can be stressful, overwhelming, and cause strong emotions in adults and children [4]. From a psychopathological viewpoint, the current pandemic is a relatively new form of stressor or trauma for mental health professionals [5]. It has been compared with natural disasters, such as earthquakes or tsunamis [6]

Though the mental health and psychological consequences can be evident in any group of people, there are a few groups where these consequences can be significantly evident. These groups can be people who have been directly or indirect exposed to the virus; people who have certain mental or psychological stressors already present; people directly or indirectly associated to health infrastructure; even people who routinely follow news via different modes are also equally exposed to these consequences.

Methods

A search was conducted on PubMed, Medline, Embase, Scopus and Web of Science. A manual search on Google Scholar was performed to identify additional relevant studies. The search terms that were used were: (COVID-19 OR SARS-CoV-2 OR Severe acute respiratory syndrome coronavirus 2 OR 2019nCoV OR HCoV-19) AND (Mental health OR Psychological health OR Depression OR Anxiety OR PTSD OR Post-traumatic stress disorder) AND (College students OR Students OR School Students). Studies were eligible for inclusion if they: 1) followed cross-sectional study design; 2) assessed the mental health status of the School or College students or both during the COVID-19 pandemic and its associated risk factors; 3) utilised standardised and validated scales for measurement. 4) Were conducted between nov 2019 to dec 2020. Studies were excluded if they: 1) were not written in English 2) focused on any other subgroups of the population (e.g., healthcare workers, or pregnant women) or general population 3) were not peer-reviewed 4) did not have full-text availability.

Result

A total of 653 publications were identified. After exclusion for not having a standardized/appropriate measure, being review papers, not being full texts along with screening of duplicated copies, 22 studies were taken into consideration (as per inclusion criteria). The sample size of the 22 studies ranged from 195 to 8079 participants, with a total of 36647 participants. A

majority of study participants were over 18 years old. Female participants (n = 21962) made up 59.93% of the total sample (1 study did not mention total percent of females, hence excluded from total sample here). All studies followed a cross-sectional study design. The 22 studies were conducted in eight different countries, including China (n = 7), Italy (n = 1), US (n = 6), Turkey (n = 2), Nepal (n = 1), Bangladesh (n=3),Poland (n=1), Slovenia (n=1), Czechia (n=1), Ukraine (n=1),Russia (n=1), Germany (n=1), Turkey (n=2), Israel (n=1), Columbia (n=1), UAE (n=1),Taiwan (n=1),Egypt (n=1),Czech (n=1), Netherlands (n=1),Greece (n=1),Saudi Arabia (n=1) and Jordan (n=1). The primary outcomes chosen in the included studies varied across studies. 18 studies included measures of depressive symptoms while 19 studies included measures of anxiety. Symptoms of PTSD were evaluated in 4 studies. It was also observed that 7 studies contained general measures of stress.

Discussion

Violence against children.

The World Health Organization (WHO) (2020) identifies six types of violence against children: 1) physical maltreatment and neglect, 2) bullying, 3) youth violence, 4) intimate partner violence, 5) sexual violence, and 6) emotional and psychological violence. McKay, Metzl, and Piemonte (2020) draw from the United States' Gun Violence Archive and argue that stay-at-home orders have reduced gun violence in public settings or schools (but increased injuries at home)[7]. A study by Jones et al. (2020) analysed interviews with adolescents in Bangladesh, Ethiopia, Jordan and the State of Palestine, and their participants talked about an increase in community violence, as well as an increase in police brutality[8]. Similar study by Parkes et al. (2020) made identical claims regarding adolescents in Uganda[9]. All these studies gives us an preliminary idea about the rise in cases if violence among children. UNICEF also stated that the COVID-19 pandemic is having a devastating impact across the world. Even if the efforts to contain the coronavirus are vital to the health of the world's population, they are also exposing children to increased risk of violence – including maltreatment, gender-based violence and sexual exploitation. 20% of college students, according to a study said that their mental health has significantly worsened. There is sufficient evidence in the literature which has established this bidirectional nature of mental health issues and domestic violence. Experimental research in non-human animals has documented that stress causes alterations in body and brain measures. In contrast, the requisite evidence for causation in human children is weaker. Hence, we can say to an extent that with the increase in cases of violence against children due to the pandemic situation, there would have been a proportional or at least a significant detoriation in mental health status of the adolescents and children.

Social Isolation

Various studies have shown that extended period of loneliness can deteriorate many mental and physical outcomes over time, causing problems like depression, musculoskeletal disorders, and even some chronic diseases. Pandemics and health emergencies, including SARS, Swine Flu, and influenza, have been associated with problematic coping behaviours, anxiety, suicide attempts and mental health disorders, including post-traumatic stress and depressive disorders, with quarantines, social isolation and limitations on freedom as possible contributing factors. According to a study, 38% of all the students said having trouble focussing on studies and/or work.It has also been seen that social isolation can modulate gene expression across various species, from Drosophila to mammals. In Drosophila, adult male flies exposed to social isolation for 4 days show robust changes in the expression of 90 genes mostly related to immune response. It is quiet consistent with the finding that social isolation modulates immune response and induce inflammation. Prolonged isolation of postnatal rats resulted in differential miRNAs expression in the anterodorsal bed nucleus of the stria terminalis (adBNS), a region involved in anxiety responses. All these prove that prolonged social isolation caused by the lockdowns in this pandemic situation is quite a concern as this will trigger more cases of anxiety and depression. A study has in fact proved that significant amount of college going students had significant levels of anxiety and depression. Approximately 18.9% of the total study subjects suffered from significant anxiety level whereas 9.20% of the total study subjects suffered from significant depression levels.

Deterioration of economic status

Many studies reported that mental health problems are associated with occupation income and economic condition. Study of Liang and colleagues found that participants working as an employee in a local enterprise had an elevated risk of poor mental health outcomes compared to other occupational groups. Many factories were shut down during the lockdown period so the majority of the workers returned to their hometowns because of uncertainty and a lack of income, which put a lot of pressure on the marginal families. A study stated 48% of college students have experienced financial setback due to COVID-19. This economic stress in one way or other puts a huge stress on the minds of the students too. The National Crime Records Bureau of India informed that a total of 11,716 businesspersons died by suicide in 2020. This amounts to a jump of over 29% of the figure reported for the section in 2019 or the pre-Covid times. During lockdown many farmers faces enormous socio-economic challenges which lead them to the part of suicide. Suicides by the earning members of the family in fact put tremendous pressure on the female counterparts as well as sons and daughters even if they are student. There is a sharp decrease in economic activities ranging from decline in restaurant and hotel bookings, air travels, fuel consumption, retail sector and even media industry. Data analysis revealed that top 15 Economics of the world are badly hit by this covid-19 outbreak. This economic crunch will have an effect on donation programmes of internally displaced people (40.3 million), Refugees (25.9 millions) and Asylum seekers (3.5 millions). These data and information shows that occupational loss, which leads to economic instability leads to mental health issues during Covid-19 period.

Genetic linkage of susceptibility to Anxiety and Depression

Genetic factors have an important role in the susceptibility to depression. A meta-analysis of two studies on major depressive disorder (MDD) estimated the heritability at 37%. In the National Comorbidity Survey Replication, 59% of the subjects with a lifetime diagnosis of MDD also fulfilled the criteria for a lifetime anxiety disorder diagnosis. A genome-wide association study (GWAS) including almost half a million participants from the UK Bio bank study revealed the existence of genetic variants associated with loneliness and regular participation in social activities.Interestingly, the expression of 8 genes was linked to susceptibility to loneliness: GPX1, C1QTNF4, C17orf58, MTCH2, BPTF, RP11-159N11.4, CRHR1-IT1, and PLEKHM1. All these studies indicate that there will be a few numbers of students who are comparatively more susceptible compared to other groups. We can say that these individuals have a lesser threshold of developing significant levels of anxiety and depression and hence are more susceptible.

Other factors

Research shows that people who follow COVID-19 news the most, experience more anxiety. Most of the news relating to COVID-19 is generally either related to number of infections, number of deaths or other distressing information. This kind of news is associated to rise in anxiety levels, especially when someone is constantly exposed to them. On the other hand, Misinformation and fabricated reports about COVID-19 can exacerbate depressive symptoms in the general population. Another study shows that people who spent too much time thinking about the COVID-19 outbreak (≥3 hours) were more likely to develop anxiety symptoms. On the other hand, the latest and most accurate information, such as the number of people who have improved and the progress of medications and vaccines, can reduce anxiety levels.It shows too much spent on COVID-19 related news and social media has an effect on mental health. The results of epidemiological studies show that women are at a higher risk of depression. Women are more vulnerable to stress and post-traumatic stress disorder than men. In recent studies, the prevalence of anxiety and depression and stress during COVID-19 pandemic is shown to be higher in women than in men. According to recent studies, during the COVID-19 pandemic, there is an association between education levels, and anxiety and depression levels. During the COVID-19 pandemic, people with higher levels of education were found to have greater levels of anxiety, depression, and stress. According to a study which was conducted in China, the higher prevalence of mental symptoms among people with higher levels of education is probably due to this group's high self-awareness in relation to their own health.

Solution

Mental health professionals recommend promoting healthy behaviours, avoiding exposure to negative news, and using alternative communication methods such as social networks and digital communication platforms to prevent social isolation. Government and Health officials should routinely provide accurate information and provide with updates against myths and misinformation. Optimistic and positive thoughts and attitude toward the COVID-19 spread are considered to be protective factors against depression and anxiety. According to activeminds, 55% of the college students do not know where to go for help for their mental health. So, authorities should take care of this and should consider opening a hotline for such students. In these hard times, where pandemic are having such disastrous effects over every aspects of the society with its multiple waves approaching humans. It is a high time that we, along with the programs for mass vaccine administration and other steps to stop the virus from causing damage, need to think about the mental aspects caused by such long term isolation too. And take appropriate steps to avoid the possible 4th wave which, as stated by Dr. Victor Tseng will consist of issues like psychological trauma, mental illness economic injury and others.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Author's Contributions

• Shubham Goswami: contributed to the overall design, article selection, review, and editing and manuscript preparation.
• Soujanya Chakraborty: article selection, abstract preparation.
• Sudip Pal: contributed to review, editing, and article selection.

Limitations

Certain limitations apply to this review. A significant degree of heterogeneity was noted across studies. The description of the study findings was qualitative and narrative. All included studies followed a cross-sectional study design and, as such, causal inferences could not be made. In addition, all the studies were conducted via online questionnaires independently by the study participants, which raises few concerns, firstly, individual responses in self-assessment vary in objectivity when supervision from a professional psychiatrist/ interviewer is absent, and secondly, people with poor internet accessibility were likely not included in the study, creating a selection bias in the population studied. Another concern is the over-representation of females in most studies.

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The Survey on Adherence Rate of Breathing Exercises and Relationship with Quality of Life in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Objective: Determine the percentage of patients who adhere to breathing exercises (puffy-lip breathing, diaphragmatic breathing) and the relationship between adherence with breathing exercises and quality of life.

Methods: A cross-sectional descriptive study was performed on 100 patients with chronic obstructive pulmonary disease indicated in the general department of the Tay Nguyen Regional General Hospital and District 11 Hospital in 4 months from December 2020 to April 2021.

Results: The percentage of patients who adhered to breathing exercises was determined to be very low, 16%. The relationship between adherence to breathing exercises and quality of life was statistically significant (P=0.000). The average score of quality of life of the group that adhered to breathing exercises was lower than that of the group that did not adhere to breathing exercises (18.50<27.77).

Conclusion: The rate of adherence to breathing exercises in patients with chronic obstructive pulmonary disease is 16%. For patients who adhere to breathing exercises, Chronic Obstructive Pulmonary Disease (COPD) will affect their quality of life less than patients who do not adhere to breathing exercises.

Keywords: Adherence • Breathing exercises • Chronic obstructive pulmonary disease • Quality of life

Introduction

Adherence is 'the extent to which a person's behaviour corresponds to agreed-upon recommendations from a healthcare provider' that is a key determinant of health care outcomes. Includes medication, dietary restriction, and/or appropriate lifestyle change [1]. and non-adherence is the leading cause of treatment failure in chronic diseases. Adherence to treatment in patients with COPD is considered key in the treatment and management of the disease. But according to WHO, the rate of adherence in COPD is relatively low [2]. As a result, the patient's quality of life and respiratory status is reduced. Many studies have shown that breathing exercises have a great role in the management of COPD: improve gas exchange, improve lung function, improve quality of life, save energy [3]. However, in Vietnam, there are currently no authors or studies that refer to the issue of adherence with breathing exercises, so we started conducting the study "The survey on adherence rate of breathing exercises and relationship with quality of life in patients with chronic obstructive pulmonary disease".

Methods

Time and place of study

From December 2020 to April 2021.

Study design

A cross-sectional descriptive study.

Research subjects

Inclusion criteria: Patients diagnosed with COPD were prescribed breathing exercises by their doctors, had not participated in any breathing training program before and agreed to participate in the study.

Exclusion criteria: Patients with thoracic trauma, or recent thoracic surgery. Patients are unable to cooperate: psychosis, cognitive delay, dementia. healthy

Sample size: Apply the formula to calculate the estimated sample size according to the ratio:

$$n = \frac{z^2_{1-\alpha/2} - Xp(1-p)}{d^2}$$

Including

Type 1 error, alpha(α)=0.05

$Z_{1-\alpha/2} = Z_{0.975} = 1.96$ (Z: value from the normal distribution)

Because no research documents have been found on the rate of adherence with breathing exercises in patients with chronic obstructive pulmonary disease both at home and abroad $p = 0.5$

Allowed error $d = 0.1$

$n = 100$

To select a feasible sample size for collection, we choose a sample size $n = 100$

The method of data collection

Step 1: Review and approve the research ethics file by the ethics committee of the University of Medicine and Pharmacy in Ho Chi Minh City and the place where the samples were taken.

Step 2: Make a list of patients, patients who are in inpatient treatment at the internal departments of the two hospitals where the samples are taken have been diagnosed with COPD and assigned to practice breathing. Then through the head nurse of the hospital, make a list of patients by day.

Step 3: Approach each patient and choose a convenient time during the day to ensure the patient has time to rest to explain the purpose of the study. When the subject consents, have the patients participating in the study sign a written consent to participate in the study.

Step 4: Direct interview with the patient and answer questions if any.

Step 5: Train 42 nurses on breathing exercises (puffy-lip breathing and diaphragmatic breathing) so that caregivers can better understand the steps in breathing exercises according to checklists and assessment methods after 5 days of patients breathing exercises. Previously, the nurse knew breathing exercises and instructed the patient to practice breathing as prescribed by the doctor.

Step 6: The nurse guides the patient to practice breathing

according to the checklist in the guidelines for diagnosis and treatment of chronic obstructive pulmonary disease of the Ministry of Health in 2018 (Decision No. 2866/QD-BYT). Patients will be trained for 5 days in the hospital.

Step 7: The nurse will evaluate the adherence with breathing exercises after 5 days with the checklist of breathing exercises (Decision No. 2866/QD-BYT) and practice for 5 days. Use the CAT scale to assess the patient's quality of life. The researcher collects the checklist, checks the raw data fully supplemented, sends greetings, thanks.

Step 8: Input data into data management and analysis software. From there, the results are presented and discussed.

Data collection tool

-Adherence: measured by 2 values including the checklist of breathing exercises and the number of days of practice.

+Adherence: when the patient has fully and correctly performed the steps in the checklist of 2 exercises of pursed-lip breathing and diaphragmatic breathing (Decision No. 2866/QD-BYT) and practised breathing for 5 days at the same time.

+Non- Adherence: wrong practice ≥ 1 step or not enough steps or not enough time 5 days to practice.

-CAT quality of life scale: the CAT scale includes 8 questions with problems of cough, sputum production, shortness of breath, chest heaviness, activity, social communication, sleep and health. Each question will have a scale from 0 (no influence) to 5 (severe influence). The overall average score is calculated by adding together the scores of 8 questions. The total score ranges from 0 to 40. The lower the total score, the better the quality of life.

Data analysis and processing

After data collection, data will be entered and analyzed using SPSS 20.0 software. Descriptive statistics calculate the frequency and proportions of variables. Use Fisher's exact test, T-test to determine the relationship between adherence and quality of life.

Medical ethics

Review and approval of the research ethics file by the ethics committee of the University of Medicine and Pharmacy in Ho Chi Minh City and where to get research data.

This study was approved by the Ethics Committee in Biomedical Research, University of Medicine and Pharmacy, Ho Chi Minh City. HCM No. 822/HDDD, November 2, 2020

Informed consent was obtained from study participants.

Results

The study was conducted on 100 patients, the results showed that: The percentage of age group ≥ 60 accounted for the majority (76%) and up to 74% of patients were male. However, the Body Mass Index (BMI) thin and thin accounted for a high proportion (44%). Education level in primary and lower secondary schools accounts for a high proportion of 54.0% and 30.0%, respectively. Farmer occupation accounts for the highest proportion (53%). Officials accounted for the proportion (12%) and pensioners accounted for (12%). Besides, people with a family account for the percentage (72%). Disease duration from 1-5 years accounts for (54%). Disease duration >10 years accounted for the lowest rate (5%). The study also found that 84% of the study subjects had comorbidities.

The adherence rate with pursed-lip breathing exercises in COPD was 79.0%. The rate of adherence with diaphragmatic breathing exercises in COPD was 23.0% and patients practice enough times as indicated with the rate of 51.0%. The rate of adherence with breathing exercises of patients with COPD was low at 16%, non-adherence with breathing exercises accounts for a high rate of 84%.

COPD affects the quality of life from moderate to very severe. Moderate influence (10-20 points) accounts for 22%; severely affected (21-30 points) accounted for 44%; very severely affected (31-40 points), accounting for 32%.

The percentage of patients who adhered to moderate-influenced breathing exercises was the highest (9/16 (56.2%). Instead, the percentage of patients who did not comply with breathing exercises with severe and very severe effects was high (39/84 (46.4%) and (32/84 (38.1%).) the life of the adherence group was lower than that of the non-adherent group (18.50 < 27.77) The relationship between adherence with breathing exercises and quality of life in patients with the chronic obstructive pulmonary disease was statistically significant with $p<0.05$.

Discussion

Research object characteristics

Research results show that the majority of patients with COPD is 74% higher than female patients, accounting for 26%. Most patients in the age group of 60 years and older account for 76%. This result is consistent with the study of Luong Manh Truong, which concluded that men have higher rates of COPD than women [4] and the research results of Pham Thi Bich Ngoc in 2019 and the study of Liliane PS Mendes in 2018 showed that men accounted for 88% and the average age of COPD was 65 ± 7 [5,6].

Breathing exercise adherence rate

The adherence rate with pursed-lip breathing exercises was lower than that of diaphragmatic breathing exercises. The adherence rate to practice diaphragmatic breathing in COPD is 23.0% and the adherence rate to practice pursed-lip breathing in COPD is 79.0%. Pursed-lip breathing exercises are simpler than diaphragmatic breathing exercises. For the pursed-lip breathing exercise, there are 3 steps, while the diaphragmatic breathing exercise consists of 4 more complicated steps. The mean respiratory rates were 15.0 and 4.32 breaths/min in diaphragmatic breathing, and 12.8 and 3.53 breaths/min is pursed-lip breathing. Oxygen consumption for diaphragmatic breathing is 165.8 ± 22.3 mL O^2/min, 164.8 ± 20.9 mL O^2/min for pursed-lip breathing [7].

The rate of adherence to breathing exercises is very low, accounting for 16%. The results of this study are consistent with the results of Ly Cam Hon in 2016 showing that only 11.5% of patients adhered to physical therapy - rehabilitation and 88.5% did not comply [6]. And the 2020 Ierodiakonou study on inhaler adherence and comorbidities in COPD patients showed that 74.1% of COPD patients had poor adherence to treatment, while the majority of them were characterized by intentional non-adherence (69.5%) [8]. Or the study of author Ngo Quy Chau in 2019 on 70 patients with COPD. The rates of non-adherence were: "ignorant" (77.1%), "incoherent" (58.6%) and "intentionally" (55.7%) [9]. But this result is lower than the research result of Nguyen Dinh Phuong. The adherence rate with inhalers is nearly 59%, and the best practice is 48% [10]. The residents of the study sample are in 2 large hospitals in Ho Chi Minh City, with high education levels, stable occupation, so the adherence rate is high. From the results of the study as well as other studies, it can be seen that the adherence rate in patients with COPD is relatively low. It may be due to the severity of the disease, the symptoms occurring or the age, place of residence

Quality of life of patients with COPD

The proportion of patients who did not adhere to breathing exercises that affected their quality of life was very high (46.4%) and (38.1%), respectively. The relationship between adherence to breathing exercises and quality of life in patients with COPD was statistically significant with $p<0.05$. The average quality of life of the compliant group was lower than that of the non-adherent group (18.50<27.77). The results of the study are similar to the results of the author Nguyen Huong Lan as well as the results of the author Ierodiakonou: In the multivariate analysis, the results of COPD had a significant relationship with poor adherence [8,10]. Research results show that treatment adherence has a significant effect on the quality of life. When the patient adheres to treatment, not only improves the health status here, but also improves the patient's lung function, but also improves mobility, spirit, personal care, and quality of life. Thereby reducing the economic burden, treatment costs, dependence on treatment drugs, hospital stay, complications and family support.

Conclusion

The percentage of patients who adhered to breathing exercises was determined to be very low, 16%. The relationship between

adherence to breathing exercises and quality of life was statistically significant (P=0.000). The average quality of life of the group that adhered to breathing exercises was lower than that of the group that did not adhere to breathing exercises (18.50<27.77).

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Commentary

Time to Test More Anti-Cancer Treatment Strategies in the Elderly

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Abstract

Cancer is linked to ageing, which is a well-known risk factor. Because of the growing senior population, the number of new cancer diagnoses has increased globally. Many theories have been proposed over the years to explain this increased risk, including higher genetic and epigenetic alterations, as well as the idea of immunosenescence. The best therapeutic options for this cancer-stricken population are unknown. Older cancer patients have historically been underrepresented in clinical trials designed to establish best practises, resulting in undertreatment or higher toxicity. With this in mind, it's critical to look into new anti-cancer agents, such as immune-checkpoint inhibitors, that have recently been discovered, in order to manage these daily clinical issues and eventually combine them with alternative antiblastic drug administration strategies, such as metronomic chemotherapy.

Keywords: Older Patients • Cancer • Immunosenesce • Metronomic Chemotherapy • Immunotherapy

Introduction

Although older cancer patients make up the majority of clinical oncology practise, there are fewer data on the risks and benefits of cancer treatment in this group, owing to their under-representation in most clinical trials that establish international standards of care [1,2,3]. This problem is exacerbated in the elderly population (over 80 years old) and, in general, leads to undertreatment of this group due to a lack of understanding of anti-cancer drug tolerability and efficacy [4].

As a result, further research into this subject is required to gain a better understanding of the potential treatment plans for older cancer patients, including engaging them in clinical trials aimed at determining their optimal standard of care and alternative treatment techniques. We looked at the most common cancer therapy options for older cancer patients, with a particular focus on a potential novel therapeutic technique for this group of individuals.

Epidemiologic and Mechanistic Data

Patients over the age of 65 account for approximately 50% of new cancer diagnoses and 70% of cancer-related death in the United States [5]. A similar trend may be seen in Europe, where more than half of newly diagnosed cancers are in those over the age of 65 [6]. Aging is a well-known risk factor for cancer development due to numerous causes [7,8]. The most researched variables include genetic and epigenetic alterations, mitochondrial malfunction, endocrine and cytokine-mediated mechanisms, mutations in aged stem cells, and telomere shortening [9,10]. Immunosenescence is another mechanism underlying the link between ageing and cancer growth. This is marked by a decrease in the number of naive CD8 T+ and CD4 T+ cells in the peripheral blood, which is caused by the involution of immune system components. The ability of T-cells to be activated and fulfil their activities is reduced as a result of these elements, even in tumour growth control, boosting immune escape, which is one of the key hallmarks of cancer cell proliferation.

3. Chemotherapy Maximum Tolerated Dose

The maximum tolerated dose (MTD) idea underpins traditional chemotherapy, which is infusing a chemotherapeutic medication at the highest dose that causes manageable side effects. This approach has been used to treat haematological malignancies since the 1960s, demonstrating for the first time an effective treatment strategy for these disorders. However, due to the loss of a significant fraction of highly reproducing normal cells, such as those lining the gastrointestinal system and bone marrow cells, MTD chemotherapy is associated with a not insignificant set of adverse effects.

In general, in the younger population, the cost-effectiveness of toxicity is well balanced, especially with the development of supportive medications such as antinausea or granulocyte-stimulating factors (G-CSF), which reduce the most prevalent side effects associated with chemotherapy regimens.

For a variety of reasons, the same outcomes are not accessible for older cancer patients. The loss in function of end organs is linked to ageing. Slower drug metabolism, for example, may affect liver function, which is linked to greater chemotherapy dose exposure for longer periods if hepatically cleared. The similar thing happens with renally cleared drugs as glomerular filtration decreases over time. The reserve in the bone marrow declines with age, causing patients to have extended cytopenias. Myelosuppression is a "qualitative" issue that ought to be explored, not only a quantitative one of MTD treatment. High-dose chemotherapy, in particular, impairs immunological tolerance by causing natural killer (NK) and γδT cell malfunction. Furthermore, high-dose chemotherapy can harm dendritic cells (DCs), diminishing their antigen-presenting function, decreasing their motility, and suppressing the expression of cell surface markers. Other considerations include the fact that elderly cancer patients are typically fragile, have a variety of comorbidities at the time of diagnosis that may limit chemotherapy tolerability, and use a large number of medicines that may interact with anti-cancer treatment. Finally, in recent decades, more and more data on chemotherapy-induced cognitive deficits has been documented.

All these aspects limit clinicians in treatment decision making, leading to recommendations of best supportive care rather than chemotherapy given the potential risks. Several prediction tools have been developed specifically on this topic, such as: Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score, able to stratify the patients in four risk categories of severe toxicity; chemotherapy toxicity calculator from the Cancer and Aging Research Group (CARG score), a predictive model for chemotherapy toxicity in patients ≥65 years old; and Geriatric 8 score (G8), a screening tool to determine which older cancer patients should undergo full geriatric evaluation prior to commencing chemotherapy.

4. Metronomic Chemotherapy

Low-dose metronomic chemotherapy (MC), an alternate method, has been studied in recent years to reduce the drawbacks of MTD chemotherapy and to try to overcome resistance mechanisms. Its purpose is to deliver low-dose chemotherapy without interruption, and it has been evaluated in a number of studies including a variety of histologies.

Through a variety of ways, this new scenario offers numerous options for combating cancer cell proliferation and acquired tumour resistance. The effect of MC on tumour cell development pathways and its impact on the tumour microenvironment are its most intriguing features. Tumor cells, in particular, require the formation of new blood vessels in order to meet their high energy demands as a result of their fast growth, a process known as angiogenesis. Blood vessel genesis is aided by vascular endothelial growth factor (VEGF), fibroblast growth factors (FGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF), and thrombospondin-1 (TSP-1). Tumor cells produce a large percentage of them. In this context, MC has been demonstrated to cause apoptosis and endothelial migration in

activated endothelial cells, as well as inhibit the function of key angiogenesis factors.

The immune system has another effect on the tumour cell microenvironment. Immune escape is one of the most essential and well-studied characteristics of cancer cell proliferation, as previously stated. It entails the creation and stimulation of immunosuppressive molecules in order to suppress both the innate and adaptive immune responses and prevent tumour invasion and elimination.

Treg cells, which suppress tumor-specific effectors (CD8+ T lymphocytes, CD4+ T helper cells, and NK cells), and myeloid-derived suppressors (MDSCs), which suppress T and NK cells through distinct pathways, are both implicated in this challenge. MC has been shown to augment host immunity through a variety of immunomodulatory mechanisms in recent years. Continuous exposure to a low dose of cyclophosphamide, for example, stimulated the release of pro-inflammatory factors (IL-6 and IL-12) through macrophages, downregulated anti-inflammatory cytokines (TGF-) and IL-10, and reduced Treg numbers in vitro. Methotrexate, paclitaxel, vincristine, and vinblastine at low concentrations increase DC maturation and antigen-presenting function.

The benefits of MC are not only biological, but they are also important in clinical settings. MC, in particular, has a strong anti-cancer activity and survival benefit in the most important oncologic outcomes, such as overall survival and progression-free survival, in a variety of histologies, as well as a favourable safety profile, particularly in older cancer patients. Capecitabine and vinorelbine are the two most investigated drugs in this situation. Even when these medications were given in combination at a metronomic dosage, the advantages were maintained in older cancer patients. Indeed, doctors are increasingly using this method to treat frail older patients who are unable to undergo a regular chemotherapy regimen.

5. Immunotherapy

The immune system's antitumoral role has been known since William Coley observed that injecting inactivated bacteria into sarcoma sites could cause tumour shrinking.

In recent years, several types of immunotherapies have been studied. Immune checkpoints, specifically cytotoxic T-lymphocyte antigen 4 (CTLA-4) and programmed cell death 1 (PD-1), also known as immune checkpoint inhibitors (ICIs), have been of special interest in this respect.

CTLA-4 is expressed on the cell surface of CD4+ and CD8+ T lymphocytes, while PD-1 is found on the surface of T cells, B cells, and NK cells in the immune system. All of these can activate inhibitor pathways in these cells, resulting in a shift in the immunosuppressive landscape, such as in Treg cells. Blocking these inhibitory cell surface proteins has shown to be effective in a variety of cancers, including renal cell carcinoma, melanoma, non-small cell lung cancer, and breast cancer, among others.

These findings were also validated in the senior group, indicating that this therapy technique is effective even in the elderly. The benefit of ICIs in terms of survival is consistent across a 65-year-old age cut-off. However, more information is needed to fully comprehend these findings in people beyond the age of 75. Given that these medications have a diverse side effect profile but are typically well tolerated even in individuals with reduced performance status, this method offers a frequently bearable choice.

6. Metronomic Chemotherapy and Immunotherapy: A New Horizon?

In older individuals requiring combination chemo-immunotherapy, a new model of anti-neoplastic treatment could be combination of low-dose metronomic chemotherapy and immunotherapy. There are data suggesting that certain cytotoxic agents could enhance the efficacy of immunotherapy and further data outlining the immunostimulatory potential of metronomic therapy. Several recent preclinical studies have explored this field outlining promising results .

In one trial, 28 metastatic melanoma patients with progressive disease were treated with a metronomic dose of cyclophosphamide (50 mg twice a day for 1 week altering with off treatment) and celecoxib (200 mg daily throughout the study) followed by vaccination with DCs, showing improved survival compared to retrospective data of treatment without chemotherapy and celecoxib . Encouraging results were found even with the new class of ICI drugs. Karachi et al. demonstrated a relationship between peripheral and tumor immune microenvironment transformation and dose modulation of temozolomide in murine models. Moreover, some data show that the anti-PD1 activity dampens glycolysis, providing cytotoxic lymphocytes with an additional competitive advantage.

Conclusion

In conclusion, both MC and immunotherapy appear to boost immune cell activation, with the former increasing tumor-specific activation and the latter maintaining it. MC has the ability to influence the tumour microenvironment, facilitating tumour invasion and cytotoxicity.

The synergistic effect of low-dose metronomic chemotherapy and immunotherapy provides an encouraging possibility, allowing efficacious treatment while minimising quality of life in frailer patients and opening up a prospective option for those who may have only received supportive care.

Result

Because this cohort is under-represented in clinical trials, anti-neoplastic treatment in older patients remains a challenge. The scientific community should emphasise the need of performing clinical trials in geriatric populations to examine therapy efficacy and safety. The care of these individuals should be interdisciplinary; involving disease specialists and geriatricians, in order to properly evaluate them using proven techniques that can better anticipate how well they will tolerate medicines and how effective they will be. Data from the elderly population has demonstrated that toxicity often prevents older patients from receiving the same dose intensity as younger patients, and the vast majority of geriatric patients will receive less effective and occasionally harmful therapies.

As a result, traditional chemotherapy regimens, including monotherapy and combination regimens, are adjusted in terms of their schedules and dose intensities, lowering efficacy.

To address this problem, current research has shown that combining "new" and "old" medicines, such as immunotherapy with ICIs and MC, may be a viable strategy for preventing cancer progression and resistance. Emerging data has been promising, but it is also premature because it is based on limited clinical experience or in vitro models. Such approaches must be verified in larger, placebo-controlled, randomised studies involving the elderly population, as well as proper clinical evaluation using recognised geriatric instruments. The solid preclinical rationale and favourable toxicity profile of this anti-cancer therapeutic combination appear to be the winning step. It's critical to continue researching these approaches in clinical settings.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Editorial

It's past time to figure out how comorbidities contribute to the severity of COVID-19.

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Introduction

The introduction of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from China has put human lives in jeopardy. Asymptomatic, mild, or severe pneumonia-like symptoms characterise Coronavirus Disease 2019 (COVID-19). COVID-19 people with diabetes, COPD, CVD, hypertension, cancer, HIV, and other comorbidities may face a life-threatening scenario. To enter the cell, SARS-CoV-2 uses ACE-2 receptors present on the surface of the host cell. Certain comorbidities are linked to increased ACE-2 receptor expression and proprotein convertase release, which aids viral entrance into host cells. The COVID-19 patient enters a vicious infectious loop of life as a result of the comorbidities, which are strongly linked to severe morbidity and mortality. Individuals with comorbid conditions must take extra precautions and be managed carefully. In this study, we concentrated on the impact of common morbidities in COVID-19 patients and reviewed therapy methods in light of recent developments. We discovered few materials describing the relationship between COVID-19 and comorbidities; nonetheless, this review defines the broader spectrum of comorbidities that COVID-19 patients face.

At the end of December 2019, the Chinese city of Wuhan reported pneumonia cases of unclear origin. The causal agent was discovered as a novel coronavirus (2019-nCoV), now known as SARS-CoV-2, and coronavirus illness as COVID-19 on January 7, 2020 [1]. The disease quickly spread across China and crossed international borders, resulting in approximately 7 million confirmed cases and >0.4 million deaths worldwide [2]. The four genera of Coronaviruses (CoVs) are αCoV, βCoV, γCoV, and δCoV. Only αCoV and βCoV are known to cause illness in mammals among these taxa. Severe acute respiratory syndrome (SARS) in 2003 and Middle East respiratory syndrome (MERS) in 2012 were recognised to be caused by βCoVs, which were known to induce serious life-threatening respiratory illnesses. SARS-CoV-2 is also a member of the βCoV family, which is an enveloped virus with a positive sense-RNA genome that is responsible for COVID-19 [3]. SARS-genome CoV-2's has 96 percent resemblance to bat CoV RaTG13, according to genomic study. SARS-CoV shares evolutionary similarities with Rhinolophus affinis, Bat-SL-CoVZC21, and then Bat-SL-CoVZC45, indicating that it originated in the Chinese chrysanthemum bat. The genomic sequencing and evolutionary investigation of SARS-CoV-2 revealed that 79.5 percent of the genome matched that of SARS-CoV, and bats have been suggested as probable reservoirs for the virus that transmitted it to humans via an unnamed intermediary host. Pangolin has recently been discovered to have 99 percent genomic similarity with SARS-CoV-2, implying that it plays an important role in viral transmission and infection [4]. SARS-CoV-2 is spread via zoonotic animals or human-to-human contact via respiratory droplets.

For the past two years, a novel coronavirus known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been responsible for a global pandemic, with nearly 280 million infections and 5.4 million fatalities by the end of 2021. Bedside observations indicated individuals at higher risk of severe coronavirus disease-2019 (COVID-19)-related pneumonia and death as soon as the pandemic broke out. The most significant factor related with death was age. Diabetes, obesity, previous hypertension, cancer, and chronic renal, cardiovascular, and respiratory disorders were all linked to a higher risk of severe respiratory symptoms, which could lead to hospitalisation or possibly ICU admission. The most severe individuals died from refractory acute respiratory injury despite the use of high-flux oxygen, mechanical ventilation, and even extracorporeal membrane oxygenation, as well as bacterial and mycological super infections, thromboembolic sequelae, and multi organ failure. Anti-COVID-19 treatments such as repurposed antiviral, immunomodulatory, and anticoagulant medicines were widely employed in addition to supportive care, however they were ineffective [5].

The question of how comorbidities may add to the severity of COVID-19 remains unsolved. It's worth looking into whether underlying comorbidities increase the risk of contamination by facilitating SARS-CoV-2 entry or replication in the targeted cells, thereby increasing the viral load; whether they alter the host's immune response to the viral infection by precipitating the cytokine storm; or whether they simply increase the disease burden in frailer patients. Understanding the molecular pathways that may be involved can aid in the development of extremely effective targeted anti-COVID-19 treatments in the future. A propensity to severe COVID-19 manifestations was first suggested to be due to a gene polymorphism. The discovery of heightened vulnerability in specific patient subgroups prompted a search for gene signals engaged in important host antiviral defence mechanisms and/or mediators of inflammatory organ damage using genome-wide association (GWAS) [6]. In four critically ill SARS-CoV-2 infected young males, putative loss-of-function variants of X-chromosomal Toll-like receptor (TLR)7 associated with impaired type-I and II interferon responses were identified, providing insight into COVID-19 pathogenesis and underlying the essential protective role of type-I interferon immunity against SARS-CoV-2 [7]. Later, it was discovered that X-linked recessive TLR7 deficiency is a highly penetrant genetic aetiology of serious COVID-19 pneumonia, with a prevalence of 1.8 percent in male patients under 60 years old. Other gene possibilities were explored for their potential to aid viral replication, change the immune response, and/or explain interindividual variability in innate and adaptive immune responses. COVID-19 pneumonia is caused by inborn defects of type-I interferon immunity that are dependent on TLR3 and IRF7. B cell autoimmune phenocopy of inborn defects of type-I interferon immunity was found to be responsible for life-threatening COVID-19 pneumonia in at least 2.6 percent of women and 12.5 percent of men in international cohorts. Type-I autoantibodies neutralise it. 2 of 4 interferons were shown to account for 20% of severely ill COVID-19 patients over 80 and overall mortality, predating SARS-CoV-2 infection and significantly rising in prevalence after the age of 70 years. A global network of researchers also established a mechanism for discovering, recruiting, and genetically profiling individuals who are naturally resistant to SARS-CoV-2 infection. The protective effect of the O allele among the ABO blood classes, which may function as co-receptors for SARS-CoV-2, was validated in a meta-analysis involving 50,000 patients from 46 studies. GWAS has discovered a variation near the angiotensin-converting enzyme-2 (ACE2), the major cell receptor of SARS-CoV2, as able to give protection, potentially through lowering ACE2 expression on SARS-CoV-2-targeted cells. An endoplasmic reticulum transmembrane protein called Transmembrane Protein 41B (TMEM41B) was identified as essential for permissive infection using a genome-wide CRISPR knockout screen for SARS-CoV-2 infection, with a potential relationship between its level of expression and COVID-19 severity. Gene polymorphism, on the other hand, could not account for all individual vulnerabilities. Changes in the expression of genes involved in type-I interferon signalling and viral replication pathways have been linked to comorbiditiesHeparan sulphate proteoglycans, in addition to ACE2, have been discovered to interact with the viral spike protein, explaining why changes in their expression could lead to higher sensitivity to COVID-19 . Because SARS-CoV-2 entry necessitates sequential cleavage of the spike protein, which is synthesised as an inactive precursor, at the S1/S2 and S20 cleavage sites to mediate membrane fusion, proteases involved in these processes may influence individual susceptibility to COVID-19 if their baseline activity varies according to comorbidities. During attachment to the cell surface, cell surface proteolytic enzymes such as the transmembrane serine protease isoform 2 (TMPRSS2) and the human airway trypsin-like protease (HAT or TMPRSS11D) break the SARS-CoV-2 spike protein. Other endolysosomal transmembrane serine proteases (TTSPs) and cathepsins (mainly cathepsin L) help prime the spike protein and degrade the extracellular matrix, allowing SARS-CoV-2 to infect the host cells. Furthermore, the discovery of a four-amino-acid insertion (PRRA) at the S1/S2 boundary in the SARS-CoV-2 spike protein sequence suggested that furin or furin-like proteases may be involved in the production of virions in host cells, influencing the level of viral replication and thus the severity of the disease. The renin-angiotensin-aldosterone and kinin–kallikrein systems have both been linked to the cytokine storm seen in COVID-19 patients. Because ACE2 inactivates des-Arg9-bradykinin, SARS-CoV-2-induced

ACE2 inhibition enhances bradykinin 1-receptor effects. a metabolite of bradykinin SARS-CoV-2 reduces the effects of the bradykinin 2-receptor by blocking cathepsin L, which is present at the infection site and implicated in bradykinin production. Vasoconstriction and promotion of pro-fibrotic, apoptotic, and inflammatory signalling in SARS-CoV-2-targeted tissues could be caused by dysregulation of the renin-angiotensin-aldosterone balance and overactivation of the angiotensin II type-I receptor axis. Breidenbach and colleagues investigated the expression of various genes that might facilitate SARS-CoV-2 entry using various SARS-CoV-2-targeted organ tissues obtained from 1968 patients with common comorbidities known to increase the risk of COVID-19 severity in a study published in the journal. Gene expression in whole-tissue homogenate was mapped using single-cell RNA sequencing and compared to international databases. Surprisingly, the tissue region with the highest gene expression differed depending on the comorbidity, implying complicated and non-uniform underlying mechanisms that support patient susceptibility. Accordingly, the highest levels of ACE2 expression were found in cancer patients' pulmonary tissues, obese patients' renal tissues, diabetic heart failure patients' cardiac tissues, and coronary disease patients' peripheral blood mononuclear cells. In patients with hypertension, cancer, and a history of smoking, there was a significant increase in the expression of TTSPs, including TMPRSS2 and HAT, across the SARS-CoV-2-targeted organ systems as compared to healthy persons. Breidenbach's findings, when combined with molecular biology research looking at gene activation, inhibition, or deletion, corroborated the role of SARS-CoV-2 entry-related gene expression patterns in the outcome of COVID-19 patients. However, since SARS-CoV-2-mediated endothelial alterations are a well-established non-organ-specific injury related at least in part to modifications in bradykinin receptor expression and activity, these researchers' findings were limited by their whole-tissue-homogenate-based approach, which included the vascular component of each tissue type, their findings were limited by their whole-tissue-homogenate-based approach, which included the vascular component of each tissue type. As a result, before linking the identified tissue-specific gene expression patterns with the relevant comorbidities, these preliminary data must be evaluated with caution. To summarise, we still have a long way to go in terms of better understanding the sensitivity of patients with comorbidities to severe COVID-19 patterns. All of the work done so far will be extremely important in understanding the pathophysiology of SARS-CoV-2 infection and developing particular curative and preventive medicines in the coming years to protect at-risk groups and reduce morbidity and mortality.

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Myopericarditis and COVID-19: a systematic review of cases

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Discussion

We recently published a systematic review on the electrocardiographic (ECG) findings in patients with coronavirus disease-19 (COVID-19) [1]. In the abovementioned study, we observed myopericarditis as one of the possible patterns of cardiac involvement in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Earlier studies show that myopericarditis was most frequently linked to post-viral inflammations with different viruses, and SARS-CoV-2 might be another virus causing this condition [2]. Therefore, we aimed to closely inspect the published studies (mostly case reports) regarding this pattern.

We systematically searched PubMed (29 results), Embase (26 results), Scopus (25 results), and Cochrane (no results) databases for the following key-terms: "Myopericarditis" and "COVID-19", "SARS-CoV-2", "SARS-CoV2", "2019-nCoV" or "Novel coronavirus." We included the original studies investigating myopericarditis in patients with COVID-19. Articles without a retrievable full-text were excluded, including abstracts and conference abstracts.

We found a total of 24 cases in 20 studies (19 case reports and a case series). Among the 19 patients with available age, gender, and comorbidity data, 10 (52.6%) were female. The mean age was 50.6 ± 8.9, with one of the cases being a pediatric patient [3]. Seven (36.8%) had no known previous comorbidities. Two patients had a history of previous myopericarditis [4,5]. Of these 19 patients, eight (42.1%) and 10 (52.6%) presented with chest pain and dyspnea respectively.

Ten of 21 patients (47.6%) with ECG data had typical or mostly-typical findings of pericarditis: diffuse ST elevations with PR depressions in non-aVR leads and reverse changes in the aVR. In 14 cases with reports of left ventricular (LV) function on echocardiography, a decreased LV ejection fraction (LVEF) (LVEF <50% (6, 7)) was observed in 7/14 (50%). Five of 24 (20.8%) patients developed cardiac tamponade, and 4/24 (16.7%) died. Table 1 presents patient characteristics, symptoms, physical examinations,

Table 1: Summary of the findings in the included studies

Study (Ref)	Patient characteristics and comorbidities	Symptoms on admission	Physical examination	1) ECG* and 2) cardiac biomarkers at presentation	Echocardiographic findings	Complication	Management
3	1-year-10-month-old girl with no previous cardiovascular history	Persistent fever,	1) Vital signs: HR: 120 bpm, RR: 26, SpO_2: 92%, T: 38.6 °C	1) N/A	Normal cardiac chambers size,	Pericardial thickening, minor effusion without signs of tamponade; survived	Antibiotics (azithromycin, ampicillin/sulbactam), paracetamol, and intravenous hydration
		conjunctivitis, generalized rash, edema in eyelids, hands, and feet, general discomfort, occasional cough, and light arthralgia.	2) Heart: normal sounds and rhythm, no murmurs.	2) Troponin T: 29.1 pg/ml	normal diameter of coronary arteries, and		
			3) Lungs: preserved vesicular murmur.	CK-MB; 18.1 ng/ml	light pericardial effusion more evident in right chambers, without signs of cardiac tamponade		
4	47-year-old woman with previous myopericarditis	Chest pain, breathlessness, dry cough, and subjective fevers	1) Vital signs:	1) Sinus tachycardia and concave infero-lateral ST elevation	Initial echocardiogram: normal LV function and a global pericardial effusion with a	Cardiac tamponade; survived	Pericardiocentesis, IV fluid resuscitation, transferred to the ITU for vasopressor support.
			BP: 80/50, HR: 110, T: 36.9 °C	2) Troponin T levels were 225 and 253 ng/L.	maximum depth of 1.1 cm and no tamponade, Repeat		
					echocardiogram: further accumulation of		
					pericardial effusion to a maximal depth of 2 cm, with evidence of cardiac tamponade		

5	50-year-old woman with a history of hypertension, reactive arthritis, and previous myeopericarditis in 2012	Central chest pain (worse on lying flat and deep inspiration), without dyspnea and cough	1) Vital signs: BP:116/74 mmHg, HR: 85 bpm, SatO2: 97%, afebrile	1) Poor R-wave progression and small QRS complexes	Trivial anterior pericardial effusion with good biventricular function	Myopericarditis, myositis; survived	Colchicine, ibuprofen, and prednisolone
			2) Heart: normal	2) Troponin T: 77 ng/L			
			3) Lungs: normal				
			Examination findings were normal				
9	60-year-old man with no comorbities	Severe ongoing asthenia for a week, and acute anosmia	1) Stable hemodynamic parameters, T= 39°C, no need for oxygen therapy.	1) Normal sinus rhythm and flattened T waves in lateral leads	N/A	COVID-19 myopericarditis, AF; survived	Colchicine,
			2) The physical examination was normal	2) High-sensitivity cardiac troponin I peak: 639 ng/L			Flecainide.
							Discharged with maintenance dose of colchicine
12	38-year-old woman with no comorbidities	Palpitations and general malaise without dyspnea, chest pain, or respiratory symptoms	1) Vital signs: HR: 137 bpm, BP: 98/54, SpO2: 95%, T: 36.5 °C	1) Diffuse concave ST elevation,	Global LV hypokinesia, severely reduce LV systolic function (LVEF <30%), mild pericardial effusion (2 mm), no valvular disease	Fulminant myocarditis with stage B cardiogenic shock, COVID-19 pneumonia; survived	ICU admission, O_2 supplementaion, methylprednisolone, IVIg, HCQ, azithromycin, lopinavir/ritonavir, norepinephrine, dobutamine, and levosimendan; Furosmide
			2) Heart: Tachycardia without elevated JVP or heart murmurs	PR segment depression, Spodick's sign			
			3) Lungs: Bibasal soft inspiratory crackles	2) Troponin I: 1,190 ng/L, BNP: 13,000 pg/ml			
13	25-year-old man with no comorbidities	Acute-onset chest pain, dyspnea, fatigue and fever	1) Vital signs	1) Sinus tachycardia with ST segment elevation and PR depression in leads I, aVL, and V5-V6, and	Diffuse LV hypokinesia with EF= 35%, and PAP= 30 mmHg	Myopericarditis; survived	Ampicillin-sulbactam, clarithromycin, oseltamivir, acetylsalicylic acid, metoprolol
			BP: 130/80, HR: 140 bpm, SpO2: 98%, T: 37.1 °C	ST depression and PR elevation in aVR			
			2) Lungs: coarse crackles in the both lower lungs	2) Troponin: 21.471 ng/m, CK-MB: 37.1 ng/mL, troponin I: 6.499 ng/mL			

14	60-year-old male with hypertension	fevers, cough, and worsening dyspnea, with	1)Vital signs:	1) Diffuse ST elevation, with QTc interval= 437 ms	Severe segmental LV systolic dysfunction (EF= 15–20%) with hypokinesis of the apex, distal anterior septum, anterior and lateral walls, with a small pericardial effusion. Normal RV size and function.	Myopericarditis, acute	IVIg, methylprednisolone, intubation, HCQ, epinephrine
	and hyperlipidemia	mild abdominal pain and diarrhea, without chest pain, nausea, or vomiting	T: 37.4, HR: 96 bpm, SpO2: 87%,	2) LDH: 588 U/L, High-sensitivity troponin: 582 ng/L, CK-MB: 28.2 ng/mL, pro-BNP: 15642 pg/mL		hypoxemic respiratory failure; survived	
			2) Lungs: clear lungs and tachypnoea				
15	39-year-old man with no comorbidities	Chest pain, dyspnea, without fever or cough	N/A	1) Diffuse ST elevation and PQ depression	Moderate circumferential pericardial effusion, without any sign of tamponade	Myopericarditis, rhabdomyolysis, acute liver injury, pleural effusion (exudative), an episode of paroxysmal AF, mild acute	Colchicine, low doses of diuretics, insulin, fluid restricted diet, amiodarone
				2) Troponin: 15.4 µg/L, NT-pro-BNP: 4473 pg/mL		renal failure; survived	
16	71-year-old woman with a history of breast cancer	Flu-like symptoms, mild fever (38 °C), chest pain,	1) Vital signs:	1) Diffuse inverted T waves and elongated	Infero-septal and infero-apical LV wall hypokinesia, LVEF= 56%, and a	Acute myopericarditis (moderate pericardial effusion); survived	N/A
	treated with surgery, chemotherapy, radiotherapy, and hormonotherapy		SpO2: 91%, T: 38 °C	QT up to 700 ms	moderate pericardial effusion		
				2) High-sensitivity troponin T: 60 ng/L, BNP: 474 ng/L			
17	78-year-old man with hypertension	chest pain and dyspnea	N/A	1) AF with 150 beat/min and concave ST elevation except for aVR lead	N/A	Acute respiratory distress, mild pericardial effusion; survived	Intubation, Furosemide, beta-blocker, ACE inhibitor,
				2)Troponin T: 998.1 ng/L			COVID-19 specific therapy

18	50-year-old man with hypertension and past history of ischemic stroke	fevers, chills, generalized malaise, non-productive cough, dyspnea for 3-4 days and an episode of near-syncope	N/A	1) Sinus tachycardia, ST elevation in II, III, and	Severe global LV systolic dysfunction,	ACS, purulent fulminant myopericarditis, cardiac tamponade, circulatory shock, acute hypoxemic	Intubation, Mechanical ventilator, Pericardiocenentesis, vasopressin, norepinephrine, dobutamine, HCQ, azithromyci, Vancomycin, Cefepime, IVIg, methylprednisolone, Methylene blue, Remdesivir
				aVF and ST-depression in I and aVL	RV enlargement and systolic dysfunction, Moderate-to-large pericardial effusion anterior to the RV with	respiratory failure, AKI, gastro-intestinal bleeding, multi-organ failure; Expired	
				2) LDH: 3332 U/L, high	organizing material (suggesting an inflammatory process),		
				sensitivity troponin: 544 ng/L, creatine kinase: 2135 U/L, CK-MB: 54.3 ng/mL	intermittent RV impaired filling and collapse suggestive of tamponade physiology		
19	53-year-old woman with no comorbidities	Fever, dry cough, severe fatigue, without chest pain, dyspnea, and further symptoms. The patient did not show any respiratory involvement during the clinical course.	1) Vital signs:	1) Low voltage in the limb leads, minimal diffuse ST-segment elevation (more prominent in the inferior and lateral leads), and	Regional wall motion abnormalities, normal LV dimensions with increased wall thickness	Acute myopericarditis (pericardial effusion) with systolic dysfunction; survived	Dobutamine, antiviral drugs (lopinavir/ ritonavir),
			BP: 90/50, HR: 100 bpm, SpO2: 98%, T:36.6 °C	ST-segment depression with T-wave inversion in V1 and	(interventricular septum: 14 mm, posterior wall: 14 mm),		steroids, chloroquine, kanrenone, furosemide, bisoprolol, kayexalate, glucose and insulin solution, sodium bicarbonate, aspirin
				aVR	diffuse echo-bright appearance of the myocardium, diffuse hypokinesis, estimated LVEF= 40%., no evidence of heart valve disease,		
				2) Troponin T: 0.24	midly impaired LV diastolic function with		
				ng/mL, CK-MB: 20.3 ng/mL, NT-pro-BNP: 5647 pg/mL	mitral inflow patterns, an E/A ratio of 0.7 and an average		
					E/e' ratio of 12, circumferential pericardial effusion most notable around the right cardiac chambers (maximum, 11 mm), without signs of tamponade.		

20	51-year-old man with a history of hypertension.	Dry cough, fatigue,	1) Vital signs:	1) Diffuse ST elevation	Enlarged heart with a marked decrease in ventricular	Fulminant	HCQ,
		dyspnea, fever, multiple episodes of	T: 39.6 °C, RR: 26, BP: 141/89, HR: 97 bpm, SpO2: 91%	2) Troponin: 18 ng/mL, CK-MB: 14.7 ng/mL, BNP: 1,287 pg/mL	systolic function (EF= 20%)	myopericarditis, ARDS with bilateral pleural effusion; expired	azithromycin, dobutamine, remdesivir, ventilatory support,
		epigastric pain and nausea partially improved with omeprazole treatment two days prior to	2) Lungs: bilateral wheezing and rhonchi, agonal respiration, and a symmetrical decrease in chest				acetaminophen IV drip, ceftriaxone, vancomycin, remdesivir, dobutamine, indomethacin, Intravenous
		hospitalization. No chills,	expansion.				methylprednisolone, and colchicine
		diaphoresis, chest pain, or change in bowel or urinary habits.	3) Heart: pericardial friction rub (in day 7 of hospitalization)				
21	58-year-old woman on a background of	Fever, diarrhea and vomiting and poor oral intake	1) Vital signs:	1) N/A	1.5 cm pericardial effusion initially, over	Cardiogenic shock, and	Pericardial drain, vasopressor support in the ITU,
	type 2 Diabetes and Hypertension	with no respiratory symptoms	BP: 85/45, RR: 18, SpO2: 96%, HR: 91 bpm, T: 34.7 °C	2) Raised LDH, High sensitivity troponin: 388.8 ng/L,	7 hours the effusion progressed to 3–4 cm with evidence of cardiac tamponade	cardiac tamponade; survived	IV Amoxicillin and oral Doxycycline initially, then escalated to Piperacillin/ Tazobactam,
			2) Heart: raised JVP and pulsus paradoxus				furosemide
			3) Abdomen: generalized				
			abdominal tenderness				
22	61-year-old man with obesity	5 days of progressive dyspnea leading to respiratory failure and severe hypoxemia	Hemodynamic and pulmonary instability	1) Diffuse concave elevation of the ST segment	Day 1: Severe RV dysfunction with paradoxical movement of the septum due to overload of the right chambers,	Acute myopericarditis, severe COVID-19 pneumonia, massive pulmonary thromboembolism of both main pulmonary arteries; survived	ICU admission, O_2 supplementation
				2) N/A	in addition to severe TR suggesting pulmonary embolism		
					Day 7: Normal LVEF with		
					Mild to moderate pericardial effusion		

23	82-year-old woman with hypertension, hyperlipidemia, iron-deficiency anemia, and paroxysmal AF, tachycardia -bradycardia syndrome	5 days of productive cough, fever with chills, intermittent diarrhea, without angina symptoms	1) Vital signs: afebrile, hemodynamically stable, and in no respiratory distress	1) Atrial paced rhythm with diffuse new, prominent T-wave inversions and a prolonged QT interval (>500 ms)	Day 1: LVEF= 55%, small circumferential pericardial effusion, and apical hypokinesis	COVID-19-induced inflammatory myopericarditis and pericardial effusion, cardiac tamponade; survived	No ICU admission or mechanical ventilation; physical isolation, antipyretics, hydration, and O_2 supplementation
				2) mildly elevated troponin I (peaked at 0.037 ng/ml)	Day 6: a moderately enlarging pericardial effusion with left pleural effusion		
					Day 8: circumferential pericardial effusion that had further enlarged since the previous study, a RV pacemaker wire 'piercing' the RV apex alongside early diastolic collapse of the right ventricle, suggesting echocardiographic tamponade		
24	5 patients	Respiratory failure requiring invasive ventilation	N/A	1) No significant characteristics of a myopericarditis	Pericardial effusion without signs of cardiac tamponade located predominantly around the right atrium and ventricle, presence of a quasi-floating fiber-like structure within the right-sided segment of the atrioventricular sulcus, and RV dilatation in 3/5 cases with PAP of 39, 35, 30 mmHg, respectively	COVID-19 associated myopericarditis, n=5;	ICU admission
	(Age, gender, comorbities: N/A)			2) Increased high-sensitivity troponin I: 5/5		Survived, n=3,	
						Expired, n=2	
25	19-year-old woman with no comorbidities	Fever, chest pain and cutaneous rash	1) Vital signs:	1) Sinus tachycardia and diffuse ST-segment elevation;	Normal ventricular function, with no signs of pericardial effusion	COVID-19 associated acute myopericarditis; survived	Ceftriaxone, LMWH, acetylsalicylic acid, pantoprazole, HCQ, lopinavir/ritonavir (antiviral and HCQ therapy was discontinued after 2 days because of nausea, diarrhea and anemia) Colchicine
			HR: 120 bpm,	2) Troponin T: 367 ng/L			
			T: 38.5 °C,				
			SpO_2: 97% in ambient air				
			2) Thorax and abdominal examination: normal.				
			3) Skin examination: showed a rash consisting in slightly erythematous confluent macules, involving the trunk and the limbs. On the palms and soles the macules merged into sharply edged areas of erythema with islands of spared skin				

26	73-year-old man with hypertension, dyslipidemia, type 2 diabetes mellitus, COVID-19 pneumonia and former nicotine dependence	Pressure-like, non-radiating and constant chest pain, 7 out of 10 in severity, started 3 hours prior arrival, worsened by deep breathing and movement, dyspnea on minimal exertion	1) Vital signs: within normal limits except for heart rate fluctuating between 100 to 110 bpm	1) Concave shaped ST elevations in leads I, II, aVF, V2-V6 of different magnitudes, with reciprocal ST depression seen in lead aVR, PR segment depression, Spodick's sign on V3 to V5	Small pericardial effusion,	COVID-19 associated acute myopericarditis (6-8 weeks after COVID-19 positive test); survived	N/A
				2) Elevated troponin I	grade I diastolic dysfunction, LVEF between 40-50%, increased wall thickness, and concentric hypertrophy		
27	45-year-old woman with no comorbidities	Progression of dyspnea, fever, myalgia and postural hypotension	Vital signs:	1) N/A	Normal biventricular function, with moderate pericardial effusion and diastolic restriction of the right ventricle	Fulminant COVID-19 associated myopericarditis, pleural effusion, cardiac tamponade and arrest; survived	Antibiotic therapy with azithromycin, piperacillin/ tazobactam and teicoplanin, ICU admission, unsuccessful pericardiocentesis followed by emergency thoracotomy, internal cardiac compression and pericardial drainage, noradrenaline, dobutamine, milrinone and vasopressin,
			HR: 125 bpm,	2) Initial troponin I: 867 pg/mL			venoarterial ECMO,
			BP: 105/72 mmHg, RR: 26 breaths/min and SpO_2:100% on room air	peak troponin levels reached 14,000 pg/ mL			tocilizumab,
				Initial BNP: 1840 pg/mL			immunoglobulin,
							convalescent plasma,
							methylprednisolone, UFH infusion

electrocardiographic and ECG findings, and subsequent complications and management.

Overall, myopericarditis seems to be a rare complication of COVID-19. Direct and indirect mechanisms can explain this pathology in the patients [8,9]. Viral entry through cardiac angiotensin-converting enzyme II (ACE-II) might directly cause myopericarditis [10]. Indirect injuries might result from the cytokine storm precipitated by the immune response to the virus and immune-cell recruitment [9,11]. This condition's incidence was not precisely studied, and future studies need to decipher the unknowns surrounding the subject.

Keywords: Anorectal disorders • Prevalence • Nepal

Abbrevations: ECG: Electrocardiography; HR: Heart rate; BPM: Beats per minute; BP: Blood pressure; SpO2: O2 saturation; T: Temperature; N/A: Not available; LV: Left ventricular; IV: Intravenous; AF: Atrial fibrillation; ITU: Intensive treatment unit; JVP: Jugular venous pressure; BNP: B-type natriuretic peptide; LVEF: Left ventricular ejection fraction; ICU: Intensive care unit; IVIg: Intravenous immunoglobulin; HCQ: Hydroxychloroquine; CK-MB: Creatinine kinase-MB; EF: Ejection fraction; PAP: Pulmonary artery pressure; RV: Right ventricle; ACE: Angiotensin-converting enzyme; ACS: Acute coronary syndrome; AKI: Acute Kidney injury; ARDS: Acute respiratory distress syndrome; ECMO: extracorporeal membrane oxygenation; LMWH: low-molecular weight heparin; RR: respiratory rate; TR: tricuspid regurgitation; UFH: unfractionated heparin.

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