LUNG CENTER OF THE PHILIPPINES

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WHAT'S INSIDE

https://lcp.gov.ph

CLINICAL RESEARCH DEPARTMENT

The Clinical Research Department (CRD) oversees all research projects at the Lung Center of the Philippines (LCP). It receives, evaluates and coordinates all research activities. It establishes policies and guidelines for the development, writing, presentation and approval of research proposals. Thru its Technical Review Board (TRB), it provides guidance and technical expertise on protocol development, including sample size calculation and statistical analysis plan. It spearheads institutional researches and coordinates with other national and international agencies for clinical trials, student undergraduate and graduate research, and collaborative research. It runs the TB Research Team at the LCP's National Center for Pulmonary Research (NCPR) as well as spearheads the Lung Cancer Registry to gather and collate the comprehensive local data on pulmonary tuberculosis and lung cancer, respectively. It maintains the Clinical Research Facility (CRF), an establishment that provides room, space and storage facilities for clinical trials and research.

The CRD publishes the Scientific Proceedings, the official journal of the LCP, to share local relevant educational material in the field of pulmonary medicine. The Scientific Proceedings Journal publishes original clinical investigations, epidemiological studies, case reports, review articles, evaluation of diagnostic and surgical techniques, and latest updates on management guidelines.

In 2019, the CRD started to align with the vision and strategic direction of the LCP on research. The current challenges involve providing resources to support priority programs and projects with other departments to undertake institutional research on advanced procedures to support new clinical pathways, programs and policies and contribute to impact healthy lungs and healthy environment.

The department likewise is aligned with the National Unified Health Research Agenda 2021–2025 on [1] responsive health system [2] research to enhance and extend healthy lives [3] holistic approaches to health and wellness [4] health resiliency [5] global competitiveness and innovation in health and [6] research in equity and health.

In order to achieve these proposed strategic directions, the CRD reviews its accomplishment using the perspectives of the Balanced Scorecard in [1] learning and growth [2] internal business processes [3] customer satisfaction and [4] financial perspective. From these perspectives, the CRD hopes to monitor the outcomes of all action plans and to evaluate the implementation of such plans.

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Registration of researches to be conducted at the LCP : processes all applications for Institutional Research, Clinical Trials, Student Undergraduate Research, Graduate Research and Collaborative Research.

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The **Scientific Proceedings**, the official journal of the Lung Center of the Philippines, is an open-access, English language, medical science journal, published biannually by the Lung Center of the Philippines. The journal intends toshare local relevant scientific findings in the field of respiratory medicine through publication of high quality original clinical investigations, epidemiological studies, case reports, review articles, evaluations of diagnostic and surgical techniques, and the latest updates on management guidelines. The journal's target audience are clinicians, surgeons, specialists, laboratorians, scientists, and researchers working on pulmonary medicine. The Scientific Proceedings does not charge any subscription, review, or manuscript processing fees.

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Scientific Proceedings

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THE PEER REVIEW PROCESS

The Good, the Bad, and the Ugly

Jubert P. Benedicto, MD, FPCCP
Editor-in-Chief

I cannot believe it. We are well past the maiden issue of the *Scientific Proceedings* and we were able to sustain this initiative during this post-pandemic period. What an accomplishment! I could feel that slowly (but surely) we are creating some traction.... our community is becoming more aware that this journal is a viable venue for publications. I have received very encouraging feedback from stakeholders including the alumni for the "professional and very scientific look" of our publication. Kudos not only to the staff for making this possible, but also to the administration for its unwavering support.

Now, as we push further and establish *Scientific Proceedings* as THE local journal for researches performed at the Lung Center of the Philippines, we must grapple with the most important issue that makes a journal an acknowledged medium for publication – the **Peer Review process**.

As it bestows integrity and credibility to the scientific publication, Peer Review is certainly difficult for all of those involved, from the authors, to the editors, and the reviewers themselves. This becomes more gut-wrenching and even uncomfortable, when the authors receive the comments and recommendations from the reviewers.

As a researcher, scientific writer, and peer reviewer myself, and now as a journal editor, I always attempt to possibly highlight and focus on the positive aspects of this process so that it can be appreciated more by all of those who are involved including myself. Unfortunately, this does not seem to be the case most of the time. And the way I see (and experience) it, we must take the peer review process in its entirety-both the so-called "good" and "bad" aspects. And probably, just like any change, there may be painful steps before we can see a beautiful product.

In general, the Peer Review is designed to assess the validity, quality and often the originality of articles for publication. Its ultimate purpose is to maintain the integrity of Science by filtering out invalid or poor-quality articles (https://authorservices.wiley.com/Reviewers/journal-reviewers/what-is-peer-review). Because of this inherent purpose, Peer Review confers truthfulness into scientific publications. Trust becomes an essential component for the whole process to run smoothly.

We have taken great efforts to implement and integrate Peer Review into our existing systems for publication. We identified a pool of peer reviewers and provided them with a virtual training. The whole process – with its significance and step-by-step implementation – was extensively laid out. This was complemented by a follow-up workshop and strategically placed open forum. The workshop was specifically designed for the Lung Center of the Philippines so that all concerns, peculiarities, even fears, from the participants were addressed head on. In the end, we all realized that Peer Review is vital and should be regularly and consistently executed. We also anticipated the amount of work that this would entail. Not easy but cumbersome. Not straightforward but will involve a lot of critical communication. Not a simple task but necessary.

Although the entire process is methodologically sound, there may still be steps that may be entry points for "concerns". What if the reviewer is "so strict"? *Malas ko naman*. What if the reviewer is just in a bad mood or just in a hurry? What if *di lang kami nagkaintindihan*? We certainly hope that reviewers will fend off any tendency to be "non-constructive", to simply just be critical, and to communicate better. At the end of the day, we always go back to the primordial intention and altruistic aim of Peer Review as mentioned above.

To the authors: be open to criticisms and take these as opportunities to further grow and improve your manuscripts. The scientific cycle really involves failed attempts but please do not stop trying. Do not be discouraged. Communicate well in writing. Answer reviewer and editor queries completely and in a timely manner. It might also help to answer items one-by-one and maybe not all immediately. I always feel that some space may be needed for one not to be overwhelmed, as this may reflect in your responses. Be intentional with your responses.

This issue is the first product of this process. I encourage the authors and reviewers to possibly scrutinize the end-product and marvel at their work. I was amazed at the transformation of the main output- a truly awe-inspiring evolution from the first manuscript that was initially submitted. The end-products were more professionally written, imbued with more clarity, and scientifically more appealing to the target audience.

I know a lot of challenges still lie ahead. Consistency is the key. I am just inspired to be assured that the whole LCP community is behind us as we embark on bringing back the prestige in our publication. *Kakayanin. Unti-unti lang*. Let us all focus on the final product. I can assure everyone; you will be proud of the Scientific Proceedings. ***Aba, tatak-LCP yan*** !!!!

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ABOUT THE JOURNAL

The **Scientific Proceedings**, the official journal of the Lung Center of the Philippines, is an open-access, English language, medical science journal, published by the Lung Center of the Philippines. Its policies are guided by the latest version of the International Committee of Medical Journal Editors (ICMJE) **"Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals."**

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The **Scientific Proceedings** intends to share local relevant scientific findings in the field of respiratory medicine through publication of high quality original clinical investigations, epidemiological studies, case reports, review articles, evaluations of diagnostic and surgical techniques, and the latest updates on management guidelines. The journal's target audience are clinicians, surgeons, specialists, respiratory therapists, laboratorians, scientists, researchers working on pulmonary medicine, and policy makers.

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ORIGINAL ARTICLE

CLINICAL OUTCOMES OF PATIENTS WITH POST COVID–19 CONDITION WHO UNDERWENT PULMONARY TELEREHABILITATION AT THE LUNG CENTER OF THE PHILIPPINES

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ABSTRACT

Introduction. Pulmonary telerehabilitation is an indispensable technology for enhancing the clinical outcomes of patients with post COVID–19 conditions. In this age of physical distance, we must acclimate to the new standard.

Objective. This study aimed to describe the clinical outcomes (exercise capacity, functional performance, perceived breathlessness, health–related quality of life, and maximal inspiratory volume) of patients with Post COVID–19 condition who underwent pulmonary telerehabilitation at the Lung Center of the Philippines (LCP).

Methodology. This study is a retrospective cohort chart review of post COVID–19 patients who enrolled in the Pulmonary Telerehabilitation program from June 2021 to June 2022. Inclusion of charts were done via total enumeration sampling. Mean, standard deviation, and t–test were used for statistical analysis.

Results. Only 59 of the 77 charts evaluated met the inclusion criteria. Most participants were women (54.24%) aged 53–67 (40.68%). The 6–minute walk test (6–MWT) revealed a substantial increase in step count from 402.05 (SD= +206.39) to 678.66 (SD= +194.22) (p=<0.0001) and 6–minute walk distance (6–MWD) from 305.86m (SD= +157.37) to 516.73m (SD= +147.90) (p=<0.0001). The Pulmonary Telerehabilitation program increased functional status based on the modified Medical Research Council (mMRC) Dyspnea Scale Score from 2.27 (SD= +0.91) to 1.32 (SD= +0.68). Telerehabilitation reduced perceived breathlessness in the Filipino–modified Borg Scale (MBS) from 2.24 (SD= ±1.00) to 1.08 (SD= ±0.70). Telerehabilitation improved health–related quality of life from 2.42 (SD= +1.28) to 1.08 (SD= +1.10) on the Post COVID–19 Functional Scale (PCFS). Maximal inspiratory volume increased from 847.41ml (SD=+525.69) to 1455.17ml (SD=+525.96).

Conclusion. The 4–week Pulmonary Telerehabilitation Program improved exercise capacity, functional performance, perceived breathlessness, health–related quality of life, and maximal inspiratory volume of patients with post COVID–19 conditions.

Keywords. *Clinical outcomes, pulmonary telerehabilitation, post COVID–19 condition*

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INTRODUCTION

SARS-CoV-2 is the causative agent of coronavirus disease 2019 (COVID-19) which emerged in the province of Wuhan, China.[1] The disease has resulted in around 73 million cases and more than 1 million cases of death across the world. This pandemic has caused a devastating impact on the community, economy, and health sectors.[2] Most people who recovered from COVID-19 are left with symptoms such as dyspnea, muscle pain, persistent cough, fatigue, poor endurance, headache as well as insomnia. Collectively, it has been called Post COVID-19 Condition. The World Health Organization has developed a working clinical case definition of post COVID-19 condition: "Post COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, and cognitive dysfunction but also others that generally have an impact on everyday functioning. Symptoms may be new onset, following initial recovery from an acute COVID-19 episode, or persist from the initial illness. Symptoms may also fluctuate or relapse over time".[3] The need to maintain physical distancing has dramatically reduced the number of face-to-face healthcare appointments and other health procedures and one of the challenges is the access to pulmonary rehabilitation. Due to challenges with distance and travel for both parties as well as worries about the therapist's safety in addition to the safety of the patients, this may be a limiting factor. Through the introduction of telehealth and telerehabilitation, it has been urged to employ technologies like online video and phone communication in place of face-to-face interaction to promote and enable healthcare follow-ups and consultations.[4] In seven primary care facilities in Chile, Dalbosco-Salas et al. conducted an observational, prospective study. The study involved adult patients (>18 years) who had previously contracted the SARS-CoV-2. The study's 24 sessions of supervised home exercise training delivered via a telerehabilitation program significantly improved fatigue and dyspnea. Although limited by the absence of a control group, this report showed that a telerehabilitation program applied in primary health care is feasible and was effective in improving exercise capacity, quality of life, and symptoms in adult survivors of COVID-19.[5]

Considering how little is known about pulmonary telerehabilitation for patients with post COVID-19 conditions, this is the study's greatest strength. This study is important because it offers a different way to deliver pulmonary rehabilitation programs that can lessen symptoms, enhance health status, and limit the risk of viral transmission, which can help solve the care gap for patients with post COVID-19 conditions.

The aim of the study was to describe the clinical outcomes in terms of exercise capacity, functional performance, perceived breathlessness, health-related quality of life, and maximal inspiratory volume of patients with post COVID-19 condition after 4 weeks of pulmonary telerehabilitation.

METHODOLOGY

This study is a retrospective chart review of patients with post COVID-19 conditions who enrolled in pulmonary telerehabilitation.

Total enumeration sampling was used. Participants' charts are gathered from the Pulmonary Rehabilitation section in the LCP from June 2021 to June 2022 were reviewed. Only 59 of the 77 charts that were included for review met all the following criteria: 1) age >19 years old; 2) completion of the 4-week telerehabilitation program; 3) performance of the 6-MWT; 4) completion of the PCFS questionnaire; and 5) measurement of the maximal inspiratory volume. Ten charts had no information on maximum inspiratory volume, and eight participants failed to finish the 4-week pulmonary telerehabilitation program; thus, those charts were excluded.

The 6-MWT was used to assess exercise capacity in both pre- and post-telerehabilitation. The mMRC scale, which goes from 0 to 4, with 0 representing no dyspnea and 4 representing maximal dyspnea, was used to evaluate functional performance.[6] Filipino translation of the Modified Borg Scale (MBS) was used to check participants' breathlessness.[7] It is a numerical rating system with a scale that goes from 0, which indicates that breathing is not difficult, to level 10, which indicates that breathing is most difficult. It is typically administered during the 6-MWT to quantify the amount of dyspnea that participants report experiencing while exercising.[8]

A scale known as the Post COVID-19 Functional Status (PCFS) scale was created to rate the functional progress of COVID-19 patients. The PCFS categorizes post-COVID-19 functional impairments into five levels (D = death; 0 = no limitation; 1 = no significant functional limitation; 2 = mild functional limitation; 3 = moderate functional limitation; 4 = severe functional limitation).[9] Incentive spirometry was used to determine the maximum inspiratory volume.

Through the Zoom platform, pulmonary telerehabilitation was carried out, where patients were observed and given instructions to complete a 6-MWT, respond to questions from the PCFS Scale, and do incentive spirometry. The physical therapist, during telerehabilitation, inquired about the MBS and mMRC scale scores in Filipino. Patients who underwent pulmonary telerehabilitation had their post-telerehabilitation outcomes compared to their pre-telerehabilitation status.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences Version 2.0 software. Descriptive statistics were used to describe the frequency, mean, and standard deviation. Comparatively, inferential statistics such as the t-test were used to determine if there is a statistically significant difference in the clinical outcomes of pre- and post-pulmonary telerehabilitation programs.

Ethical Considerations

The study was conducted with the Lung Center of the Philippines Institutional Ethics Research Board's (LCP-IERB) approval (LCP-PF-009-2022) and in accordance with the Data Privacy Act of 2012. Waiver of the Informed Consent process was sought from LCP-IERB.

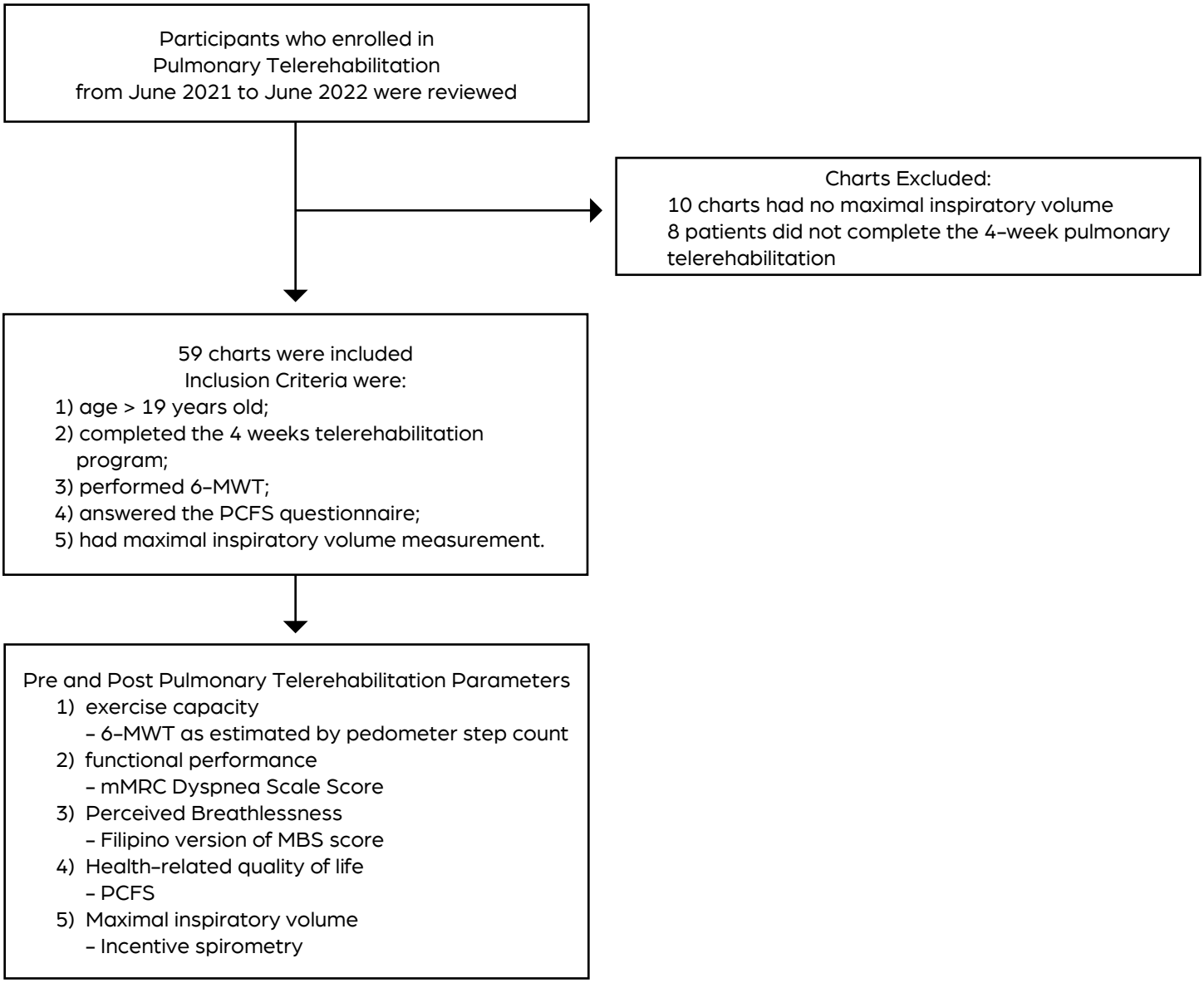

Figure 1. *Process flowchart of the Study*

RESULTS

The population was composed mostly of females (54.24%). Most of the participants were aged 53–67 years (40.68%), followed by patients aged 38–52 years (37.29%). A large percentage of the group were non-smokers (84.75%). In relation to co-morbidities, most of the patients had hypertension (35.59%) and post-TB bronchiectasis (20.34%) (Table 1).

Table 1. *Baseline Characteristics of post COVID-19 patients*

Variable	Frequency (n = 59)	Relative Frequency (%)
Age (years)		
23 – 37	7	11.86
38 – 52	22	37.29
53 – 67	24	40.68
68 – 81	6	10.17
Gender		
Male	27	45.76
Female	32	54.24
Smoking History		
Smoker	9	15.25
Non-smoker	50	84.75
Co-morbities		
COPD	6	10.17
DMT2	6	10.17
Post TB Bronchiectasis	12	20.34
Hypertension	21	35.59
Coronary Artery Disease	1	1.69

Table 2 displays the exercise capacity of post-COVID-19 patients before and after telerehabilitation, as measured by the number of steps taken and the distance traveled during the 6-MWT. The results indicated an increase in steps, with a mean average value of 402.05 (SD= ±206.39) before telerehabilitation and 678.66 (SD= ±194.22) after telerehabilitation (p= <0.0001). The 6-MWT mean average value increased from 305.86 (SD= ±157.37) to 516.73 (SD= ±147.90) due to the increase in distance traveled (p= <0.0001). Table 2 demonstrates that following pulmonary telerehabilitation, patients' exercise capacity improved significantly.

Table 2. *Pedometer step count and distance in 6-MWT*

Variable Capacity Parameters	Pre Telerehab Average ±SD	Post Telerehab Average ±SD	p=value
Pedometer step count	402.05 ±206.39	678.66 ±194.22	<0.0001
Distance, m	305.86 ± 157.37	516.73 ± 147.90	<0.0001

Table 3 shows a 210.86m (SD= ±130.02) average difference between the 6-MWD in pre- and post-pulmonary telerehabilitation, which means that there is a significant difference between the mean distance and the improved standard of 54m (p= <0.0001). The significant difference in the result of this study may be attributed to the heterogeneity of the sample population. Most of the subjects who participated in the study were age between 38–67 years old.

Table 3. *Evaluation of the 6-minute walk distance (6-MWD) difference between the pre- and post-telerehabilitation and the improvement standard*

	Average ± SD	p-value
6MWD difference, m	210.86 ± 130.02	<0.0001

*Test value/improvement standard: 54 m[10]

Table 4 shows that there is a significant change in the 6-MWD between the younger age group and the older age group, with a difference of 327.78%.

Table 4: *Percentage change on 6-MWD based on age group between pre and post telerehabilitation*

Age	% Change
23 – 37	327.78
38 – 52	211.31
53 – 67	206.89
68 – 81	166.14

Table 5 displays the secondary outcomes for pre- and post-pulmonary telerehabilitation. Using the mMRC scale, functional performance was evaluated, yielding results of 2.27 (SD= ±0.91) pre-telerehabilitation versus 1.32 (SD= ±0.68) post-telerehabilitation, with a statistically significant p-value of <0.0001. The perceived dyspnea score on the Filipino version of the MBS decreased from 2.24 (SD= ±1.00) prior to telerehabilitation to 1.08 (SD= ±0.70) after telerehabilitation, with a statistically significant p<0.0001 (p 0.0001). In terms of health-related quality of life, the pre-telerehabilitation mean average was 2.42 (SD= ±1.28) and the post-telerehabilitation mean average was

1.08 (SD= ±1.10), with a statistically significant p-value of <0.0001. Maximal inspiratory volume as determined by incentive spirometry was 847.41ml (SD=525.69) before telerehabilitation and 1455.17ml (SD= 525.96) after telerehabilitation, with a statistically significant difference (p= <0.0001) between the two groups

Table 5: *Secondary Outcome measures in the pre and post Pulmonary Telerehabilitation*

Study Outcomes	Pre-Telerehab Average ± SD	Post-Telerehab Average ± SD	p-value
Functional Performance mMRC Dyspnea Scale Score	2.27 ± 0.91	1.32 ± 0.68	<0.0001
Perceived Breathlessness Filipino version of MBS Score	2.24 ± 1.00	1.08 ± 0.70	<0.0001
Health-related Quality of Life PCFS Scale Score	2.42 ± 1.28	1.08 ± 1.10	<0.0001
Maximal Inspiratory Volume Incentive spirometry (ml)	847.41 ± 525.69	1455.17 ± 525.96	<0.0001

mMRC: modified Medical Research Council, MBS: modified Borg Scale, PCFS: Post COVID Functional Status

DISCUSSION

The benefits of telerehabilitation are comparable to those of face-to-face supervised rehabilitation, decreasing the obstacles of distance, time, expenses, and hazards. Telerehabilitation employs telecommunication resources to provide rehabilitation remotely, whether in real-time or not.[11] A previous study by Cabrera-Martimbianco et al. linked advanced age and female gender to post-COVID-19 syndrome and found that post-COVID conditions are most common in patients with comorbidities like diabetes and hypertension.[12] The majority of patients with post-COVID syndrome in this study were aged 53 to 67 and predominantly women. A new meta-analysis by Ceban (2022) showed that a third of patients with post-COVID had persistent symptoms for twelve or more weeks after infection.[13] Dyspnea and fatigue are most prevalent for post-COVID-19 syndrome and among the proposed treatments are respiratory physiotherapy, which plays a key role in increasing endurance, decreasing dyspnea and fatigue, as well as improving functionality and quality of life. Numerous studies opt for respiratory physiotherapy protocols to be conducted remotely.[14] A wide range of virtual reality applications motivates patients to exercise, improving therapy adherence and self-efficacy, adherence to the telerehabilitation is satisfactory and no serious adverse events occur. Telerehabilitation with an integrative and person-centered approach is reported to be feasible and well accepted by patients in comparison with standard rehabilitation, although sometimes technology is perceived as difficult to use or patients are simply not familiar with smartphone technology.

Exercise Capacity

The average 6-MWD recorded by Enright et al. among healthy individuals ranges from 400 to 700 meters[15], and this range matches results from Britto et al. in other populations.[16] The results of this study showed a significant improvement in the 6-MWT after four weeks of pulmonary telerehabilitation with a mean average distance of 516m which is in congruence with a multicenter, parallel-group randomized controlled trial by Jian'an Li et al. in which the primary outcome was 6-MWD in meters. In the study, the mean 6-MWD in the control group increased by 17.1m from baseline post-telerehabilitation assessment, whereas 6-MWD in the study group improved by 80.2m and the adjusted between-group difference in change in 6-MWD from baseline was 65.45.[17] Another study by Ines et al. compared a telerehabilitation program that patients hospitalized for severe or critical COVID-19 underwent to a control group of patients who declined the program. In the study, after the telerehabilitation program, the improvement was clinically and statistically greater.[18] After five weeks of aerobic training and breathing exercises, Ahmed et al. prospective interventional experiment with 20 volunteers discovered that performance at the 6-MWT of 635m improved statistically significantly from a baseline of 560 m.[19]

Physical activity can also be measured by daily step count or pedometer which is a readily accessible tool.[20] It was discovered that pedometers were a cheap and convenient alternative to monitoring physical activity in a study investigating the validity of pedometer step counts

in measuring physical activity among patients with chronic respiratory disease.[21] Smartwatches were used in a one-year multicenter observational research by Hunter et al. to track changes in activity throughout critical illness recovery after COVID-19 critical care admission. It was found that smartwatches can be used to observe an increase in activity among patients following hospital admission with COVID-19.[22]

Functional Performance

This study showed that most of the subjects started with a baseline score of 2, with a description of "I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking at my own pace on the level". After 4 weeks of pulmonary telerehabilitation, the mMRC score was reduced to 1.32, describing "I get short breath when hurrying on the level or walking up a slight hill". Some studies have shown the effectiveness of telerehabilitation exercise programs for COVID-19 subjects post discharged. It was noted that there was significant improvement at the end of the program in the telerehabilitation group regarding mMRC.[23] In one case series by Wootton et al., wherein each subject received a telerehabilitation program, patients showed improvement in their mMRC score at the end of the six-week rehabilitation period.[24] Bickton et al. case report showed improvement on the mMRC scale when doing an improvised pulmonary telerehabilitation program for post-acute COVID-19 patients. According to their study, telerehabilitation programs for COVID-19 patients may be practical and well-tolerated in settings with limited resources.[25]

Perceived Breathlessness

Based on the MBS score, this study demonstrated an improvement in the patient's perceived breathlessness. The average MBS score for patients is 2.24, which is approximately halfway between a slight and a moderate perception of breathlessness. The participant's breathlessness decreased to 1.08 after 4-weeks of telerehabilitation, with a description of very slight breathlessness. The result was a remarkable indication that telerehabilitation was able to improve the breathing of post COVID-19 patients. Out of 704 publications, six studies were included in a systematic review and meta-analysis by Alessandro de Sire et al. to assess the effectiveness of rehabilitation treatment on fatigue in post COVID-19 patients. The telerehabilitation program was successfully used during the pandemic in two of these studies. Nearly all the study's participants had COVID-19-related fatigue, and only 17% of participants stated that their symptoms persisted after receiving rehabilitative therapy. The overall impact size showed a 1.40 reduction in the Borg Category Ratio of 10, highlighting the importance of rehabilitation in reducing fatigue in post-COVID-19 syndrome patients.[26] It is possible that physiological adaptation to exercise training is the cause of the decrease in dyspnea perception during exercise training.[27] This decrease in dyspnea enables patients to go about their regular lives without feeling out of breath, which may enhance their quality of life.

Health-Related Quality of Life

This study demonstrated an improvement in the quality of life connected to one's health, which was supported by the PCFS scale used before and after telerehabilitation. Most of the respondents in this study showed mild functional restrictions on routine tasks or activities at home or at work. The majority of patients saw an improvement in health-related quality of life after the 4-week pulmonary telerehabilitation, with a mean average PFCS score of 1.08 post-rehabilitation, which was deemed to have minimal functional limits. Our findings were consistent with the Nopp et al. study, which involved the outpatient rehabilitation of COVID-19 survivors and showed that the PCFS score improved after six weeks of rehabilitation.[28] The functional status was assessed using PCFS in a different study by Luana et al., a clinical trial of post-COVID-19 patients who followed a pulmonary and functional rehabilitation program. Their PCFS score improved from 2.1 to 1 in this study.[29]

Maximal Inspiratory Volume

The study's findings revealed a striking improvement in the maximal inspiratory volume during telerehabilitation, going from a mean average of 847 ml prior to rehabilitation to 1455 ml following rehabilitation. Incentive spirometry is a lung expansion technique used to promote sustained maximal inspiration which reflects diaphragm strength and ventilation ability. It encourages deep inspiratory and expiratory breathing by having the patient take long, deep breaths with subsequent pauses. This maneuver emphasizes lung inflation, increasing tidal volume, and maintaining patency of the smaller airway. Numerous studies have shown that simple instruction of performing ten deep inspirations while awake every hour can significantly enhance lung function and reduce pulmonary consequences, including pneumonia and atelectasis. It is proposed to help patients by improving ventilation/perfusion mismatch and alveolar-PaO2 gradient. These effects reduce intrapulmonary shunting and the risk of atelectasis.[30] Recent research on subjects who used incentive spirometry for eight weeks revealed a significant improvement in pulmonary function parameters such as forced vital capacity, forced expiratory volume in one second, and peak expiratory flow rate. The immediate visual feedback from the incentive spirometer is thought to have an impact on the improvement of pulmonary function. It might motivate the participants to induce a prolonged maximal inspiration that improves lung volume and makes the best use of the respiratory muscles.[31]

LIMITATIONS OF THE STUDY

The study was limited by the small sample size and absence of a control group, although it confirms the feasibility and safety of a telerehabilitation program for patients with post COVID-19 conditions. As with chronic cardiopulmonary diseases, telerehabilitation may help to avoid a gap in service delivery following the hospital discharge of COVID-19 patients and should be integrated into their follow-up. Technical problems such as internet availability and operation of mobile phones especially in the elderly were also limited in the study.

CONCLUSION

This study showed that the 4-week Pulmonary Telerehabilitation program of the LCP improved the exercise capacity, functional performance, perceived breathlessness, health-related quality of life, and maximal inspiratory volume of COVID-19 survivors. The findings suggested that telerehabilitation might play a key role in patients with post COVID-19 conditions especially its impact on quality of life. An early rehabilitation program should be incorporated to improve the quality of life in post COVID-19 patients. This research study will provide an important assessment regarding the clinical outcomes of patients with post COVID-19 conditions who underwent the pulmonary telerehabilitation program of the LCP. The data that was obtained from this research paper could be used as a basis for the further improvement of the telerehabilitation system of the institution. Through this, patients need not personally visit the hospital thus preventing further exposure not only to COVID-19 but also to other infectious diseases. This investigation will serve as a springboard for medical studies focusing on this particular topic.

Future studies should include the type of exercise training to determine the appropriate intensity of exercise in COVID-19 survivors. Given the limited studies on the use of incentive spirometry for post COVID-19, we recommend a correlation of incentive spirometry to quality of life, perceive breathlessness, and functional status to determine the effectiveness of such a simple procedure.

FUNDING

None.

CONFLICT OF INTEREST

None declared.

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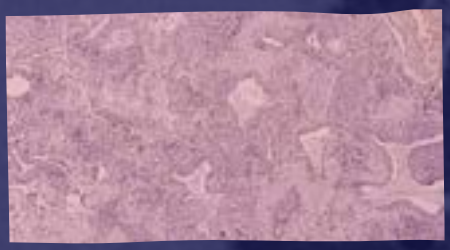

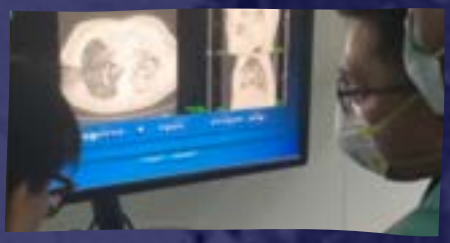

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ORIGINAL ARTICLE

TUBERCULOSIS TREATMENT OUTCOMES AMONG COVID-19 PATIENTS ADMITTED AT THE LUNG CENTER OF THE PHILIPPINES

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ABSTRACT

Background. With the previous COVID-19 pandemic and the ongoing threat of tuberculosis (TB) in the country, there is difficulty in implementing proper healthcare services to patients with TB. In addition, limited literature exists pertaining to the mechanism, sequelae, and prognosis of COVID-19 and TB co-infection. This retrospective study aims to investigate the clinical characteristics and treatment outcomes of COVID-19 patients with Tuberculosis.

Objectives. The study aimed to determine the TB treatment outcomes among COVID-19 patients with tuberculosis admitted at a Lung Center of the Philippines (LCP) from March 2020 to March 2021.

Methods. This is a one-year retrospective single center study. Clinical characteristics, imaging, and treatment outcomes of 49 patients were collected via chart review of admitted patients from March 2020 to March 2021.

Results. The overall TB treatment outcomes of COVID-19 with TB were: 47% success rate (majority belongs to severe and critical COVID-19) and 22% died. 80% of COVID-19 with TB patients were classified under moderate and critical COVID, 16% as severe and 2% as mild COVID. 63% were male and belonged to the age range 35-49 (35%). Most common comorbidities were: diabetes (31%) and hypertension (31%). Cough (94%) and dyspnea (80%) were the prominent manifestations. 88% presented with bilateral opacities on chest imaging. In addition, the National TB Figures showed treatment-success rate of 90% and 61% for 2020 and 2021, respectively.

Conclusions. TB and COVID-19 remains to be prevalent and may co-exist. In this single-center study, COVID-19 with TB patients were classified as moderate and critical COVID and had high TB treatment success rates. In line with this, emphasis on early detection of TB (bi-directional screening) in COVID-19 patients should be done to improve TB treatment outcomes

Keywords. *Tuberculosis, COVID-19, treatment outcomes, clinical profile*

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INTRODUCTION

We have lived through a global pandemic which has claimed millions of lives worldwide. The substantial impact of the coronavirus disease 2019 (COVID-19) on a multitude of diseases and the repercussions of the countrywide lockdowns to contain the virus are slowly unveiling. The deleterious effects on health care services and even the economy are still being felt up to this moment.

In spite of the COVID-19 pandemic, tuberculosis (TB) still remained a threat especially in Asia. In the World Health Organization (WHO) report last 2019, the Philippines had the highest TB incidence in Asia with 554 cases per 100,0000 people. TB is still one of the top 10 causes of death in which roughly 74 Filipinos die every day due to tuberculosis.[1] Due to the series of public health restrictions that were made to control the spread of COVID-19 worldwide, WHO reported an increase in TB deaths last 2020 for the first time in over a decade. They have estimated that there would be a further rise in global TB mortality of about 13%.[2,3] In addition, the Department of Health (DOH) in the Philippines also noted a steep decline in the number of TB cases that were reported last 2020. This staggering aftermath was mainly attributable to the disruption of TB health services secondary to the multiple lockdowns, quarantine, and lack of manpower due to healthcare workers getting infected with COVID-19.[4] In addition, the development of poor health seeking behavior due to the lockdowns itself and the fear of acquiring COVID may have also contributed to this dilemma.

In a prospective multi-country European study by Migliori et al, they concluded that high mortality was observed in patients with COVID-19 and TB, hence, TB should be considered as a risk factor for severe COVID and should also be prioritized.[5] A study by Visca et al, noted that both COVID-19 and tuberculosis impair the body's immune response but there is still insufficient data for the synergistic effect between the two infections.[6] The available evidence on clinical aspects suggests that COVID-19 happens regardless of TB occurrence (either before, during or after an active TB diagnosis) and that TB infection might possibly have a role in the development and severity of COVID-19 infection based on a systematic evaluation of transcriptomic disease risk and diagnostic markers.[7] On the other hand, recent evidence suggests that the suppression of the cell-mediated immunity caused by COVID-19 induces the activation of latent TB, imposing a severe impediment to eradicating TB by 2035.[8] A meta-analysis done by Song et al in China last 2021 investigated the outcomes of COVID-TB cases and the subsequent effect of TB co-infection on the prognosis of COVID-19 patients. Their results revealed that patients with COVID-TB coinfection are 2.21 times more likely to die and 2.27 times more likely to develop severe disease than COVID-19 patients alone. Hence, they recommended routine TB screening among suspected or confirmed cases of COVID-19 especially in countries with high TB burden. [9]

In contrast, the predicament of whether COVID-19 may reactivate or worsen active TB disease still remains unanswered. Experience and studies pertaining to the mechanism, sequelae and prognosis of COVID-19 and TB co-infection are extremely limited locally and even internationally hence, Tadolini et al suggested further analyses of interactions and determinants of outcomes in patients with both diseases.[10] Despite the multitude of scientific research on COVID-19, there remains little evidence to quantify the impact of COVID-19 on the outcomes of TB infection.[11] Since TB continues to be a global burden despite the ongoing COVID-19 pandemic, patients with active TB may need special attention and be given appropriate interventions. A data-driven understanding of the impact of COVID-19 to TB outcomes is necessary to support the efforts to mitigate it and to revise the implementation of TB services that would lead to optimistic outcomes.[10] To date, there is still insufficient local data regarding impact of COVID-19 to TB treatment outcomes.

This study then aims to determine the TB treatment outcomes, clinical profile, and radiological presentation of TB patients who were co-infected with COVID-19. Specifically, we aim to determine the proportion of COVID-19 with TB co-infection among the specific classifications of COVID-19 severity as well as the proportion of treatment outcomes of COVID-19 with TB admitted at LCP compared to the national TB figures of the Philippines.

METHODOLOGY

Study Design, Setting, Sample size and Population

This descriptive, retrospective, single-center study was done at the Lung Center of the Philippines in Quezon City, Philippines. It is a specialized government-owned hospital for chest diseases with a 179 bed capacity. It was one of the COVID-19 designated hospitals in the National Capital Region which catered to a variety of COVID-19 patients. For data collection, purposive sampling was used, which included all inpatients aged >18 years old with an admitting diagnosis of "COVID-19" and "tuberculosis". We excluded patients who were not treated as an active tuberculosis infection, those with negative SARS-CoV-2 RT-PCR results, and those with incomplete data. We obtained the demographic information, clinical history and imaging from each patient's chart record and were organized using a standardized electronic data collection form. Treatment outcomes of tuberculosis were followed up via the hospital's own Public Health Domiciliary Department (PHDD) and the Integrated Tuberculosis Information System (ITIS).

The manuscript followed the STrengthening the Reporting of Observational studies in Epidemiology (STROBE) reporting standards.

Study Procedure

A total of 61 patients admitted last March 2020 to March 2021 at the Lung Center of the Philippines with an admitting diagnosis of "COVID-19" and "Tuberculosis" in the medical records database were included (Figure 1). These data were cross-referenced with the data from the pulmonary fellows' patient census. 12 patient charts were excluded: 1 patient chart turned out to be negative in SARS-CoV 2 RT-PCR, 8 were managed as TB bronchiectasis and not as active infection, 3 were initially categorized as Presumptive PTB but turned out negative for TB Gene Xpert, thus, not managed as active TB infection. The included 49 patients were cross-referenced with the hospital's PHDD in which 23 patients were referred and being managed by PHDD. The remaining 26 patients were not referred to PHDD and were either managed by their own private physician or referred to their own barangay's health center.

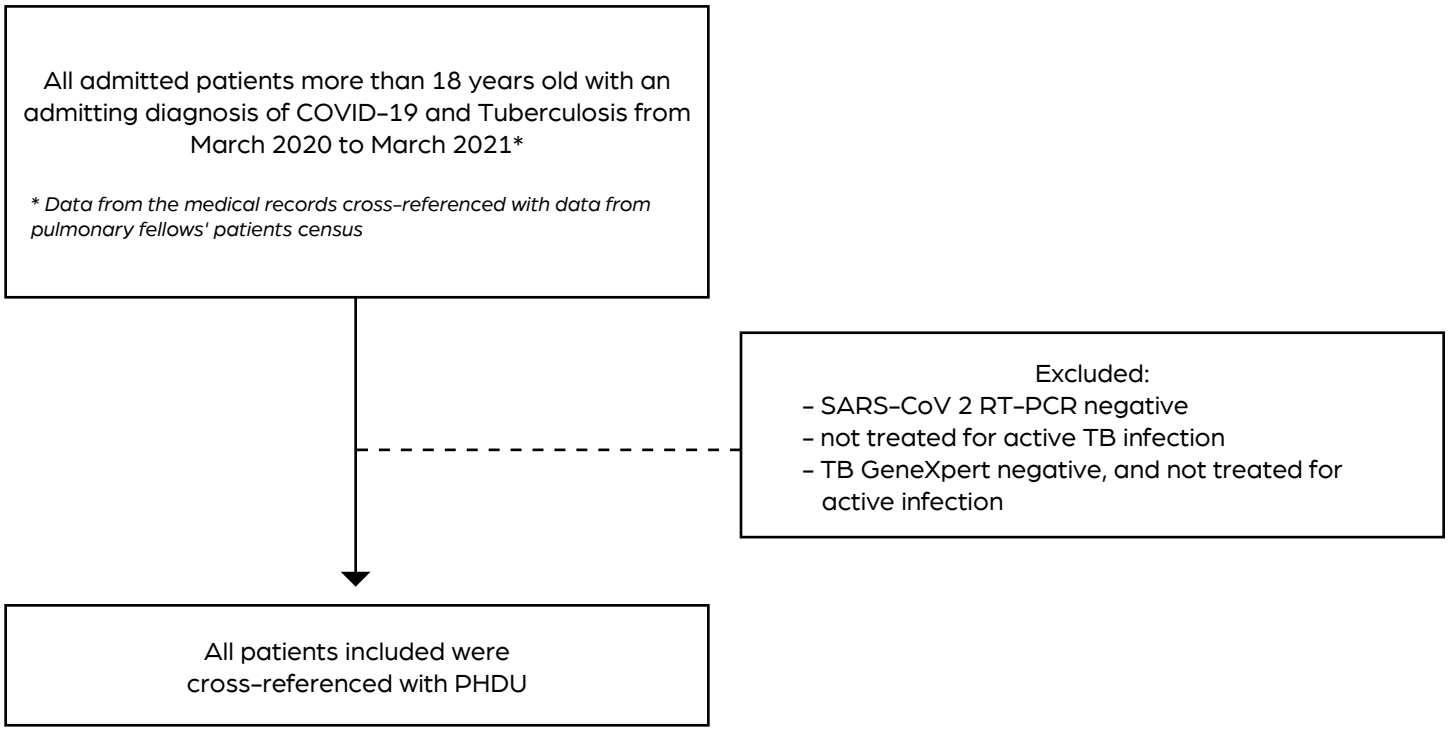

Figure 1. *Flowchart of data collection*

Outcome Measures

This study aimed to determine the tuberculosis treatment outcomes based on the NTP Manual of Procedures (MOP) 6th edition (Appendix A) among COVID-19 patients with Tuberculosis admitted at LCP from March 2020 to March 2021.

Statistical Analysis

Descriptive statistics was used to summarize the treatment outcomes, demographic profile, and clinical characteristics of the patients. Quantitative variables were expressed as frequency and percentage statistics, allowing for a clear understanding of the distribution and representation of data.

Ethical Considerations

This study was conducted in accordance with the amended Declaration of Helsinki 2013, the National Ethical Guidelines for Health and Health Related Research 2021, and the Data Privacy Act of 2012. The study protocol was approved by the Institutional Ethics Review Board (IERB) prior to implementation. Consent was waived by the IERB.

RESULTS

A total of 49 patients categorized under the COVID-19 with TB co-infection cohort were included in the study. (Figure 2).

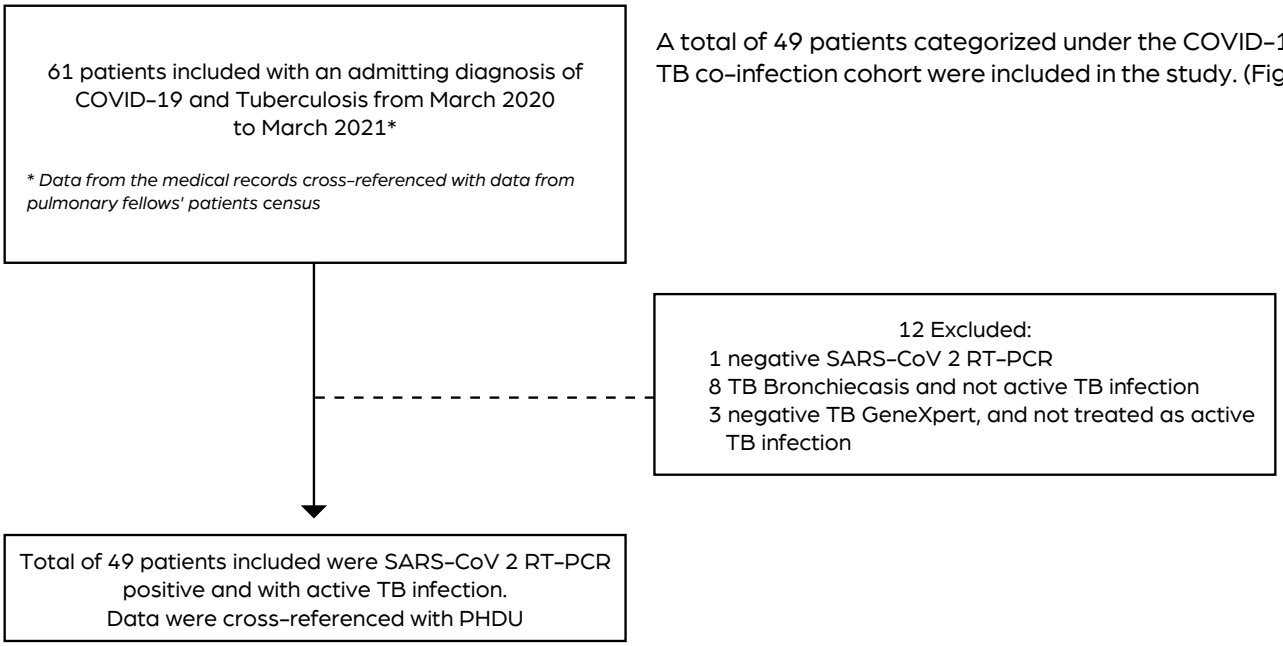

Figure 2. *Study Population*

Table 1. *Demographic and clinical characteristics of COVID-19 with TB*

	Total Cases of COVID-19 with TB (n = 49)	Mild (n = 1)	Moderate (n = 20)	Severe (n = 8)	Critical (n = 20)
AGE					
18–34	9 (18.4%)	0 (0%)	3 (15%)	3 (37.5%)	3 (14.3%)
35–49	17 (34.7%)	0 (0%)	7 (35%)	1 (12.5%)	9 (42.9%)
50–64	6 (12.2%)	0 (0%)	9 (45%)	3 (37.5%)	5 (23.8%)
>65	6 (12.2%)	1 (100%)	1 (5%)	1 (12.5%)	3 (14.3%)
SEX					
Male	31 (63.3%)	0 (0%)	14 (70%)	4 (50%)	13 (65%)
Female	18 (36.7%)	1 (100%)	6 (30%)	4 (50%)	7 (35%)
COMORBIDITIES					
COPD	3 (6.1%)	0 (0%)	1 (5%)	0 (0%)	2 (10%)
Asthma	1 (2%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)
DM	15 (30.6%)	0 (0%)	7 (35%)	4 (50%)	4 (20%)
Hypertension	15 (30.6%)	0 (0%)	9 (45%)	1 (12.5%)	5 (25%)
Heart disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Liver disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
CKD	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Malignancy	1 (2%)	0 (0%)	0 (0%)	1 (12.5%)	0 (0%)
Auto-immune disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
HIV/AIDS	2 (4.1%)	0 (0%)	1 (5%)	1 (12.5%)	0 (0%)

**TB tuberculosis; CD clinically diagnosed; BC bacteriologically confirmed*
***COPD chronic obstructive pulmonary disease; DM diabetes mellitus; CKD chronic kidney disease; HIV/AIDS human immunodeficiency virus/acquired immunodeficiency syndrome*

More than half of the total cases of COVID–19 with TB cohort were male (63%). Among the critical COVID–19 with TB, the majority are again male comprising 65% (13 out of 20) while the remaining 35% are female (7 out of 20). Among the mild COVID–19 with TB, only one female was reported in the study (Table 1). Most of the total cases of COVID–19 with TB cohort belong to ages 35–49 (35%, 17 out of 49) which also comprise the almost half of the critical COVID–19 with TB cases (43%, 9 out of 20). COVID–19 with TB cohort cases of ages 18–34 were evenly distributed among the moderate, severe and critical COVID–19 with three cases each respectively. In contrast, half of the elderly population ages >65 was categorized under the critical COVID–19 with TB cohort (Table 1).

Twenty (41%) out of the 49 cases of COVID–19 with TB cohort have no comorbidities. Whereas for the top comorbidities, most of the population had diabetes mellitus (DM) and hypertension comprising 31% each of the population (Table 1). Interestingly, only three (6%) out of 49 total cases of COVID–19 with TB cohort have chronic obstructive pulmonary disease (COPD) and only one (2%) have bronchial asthma. There were also two cases (4%) of HIV/AIDS and also one (2%) case of malignancy (i.e. lung malignancy). Of note, there were no reported cases of heart disease, liver disease, chronic kidney disease and auto–immune diseases.

Table 2. *Proportion of COVID–19 with TB co–infection based on the Severity Classification of COVID–19*

	Mild COVID	Moderate COVID	Severe COVID	Critical COVID
Total Cases of COVID–19 with TB (n = 49)	1 (2.04%)	20 (40.8%)	8 (16.3%)	20 (40.8%)

The severity classification of COVID–19 infection that was used is based on DOH's Interim Guidelines and was adapted from WHO (Appendix B).[12] Majority are classified as moderate and critical COVID comprising 40% each of the population. Eight patients (16%) had severe COVID while only one out of the 49 (2%) patients had mild COVID (Table 2). In particular, a total of 18 (36%) COVID–19 with TB patients were classified as clinically diagnosed (CD) while 31 (63.3%) were bacteriologically confirmed (BC). Almost half of those who were classified as BC TB had critical COVID–19 co–infection. On the other hand, 44% of those who were classified as CD TB had moderate COVID–19 co–infection (Appendix C).

Table 3. *Proportion of TB treatment outcomes in COVID–19 with TB co–infection*

	Treatment completed*	Cured**	Died†	Not evaluated††
Total Cases of COVID–19 with TB (n = 49)	15 (30.6%)	8 (16.3%)	11 (22.4%)	15 (30.6%)
COVID–19 Severity Classification§				
Mild (n = 1)	0 (0%)	0 (0%)	0 (0%)	1 (100%)
Moderate (n = 20)	9 (45%)	2 (10%)	0 (0%)	9 (45%)
Severe (n = 8)	4 (50%)	2 (25%)	0 (0%)	2 (25%)
Critical (n = 20)	2 (10%)	4 (20%)	11 (55%)	3 (15%)

§COVID–19 with TB patient cohort based on COVID severity
**patient who completes treatment without evidence of failure but with no sputum smear negative results in the last month of treatment and on at least one previous occasion, either because tests were not done or results are unavailable*
***patient with bacteriologically confirmed TB at the beginning of treatment and who was smear– or culture–negative in the last month of treatment (6th month) and on at least one previous occasion in the continuation phase*
†patient who dies for any reason during the course of treatment
††patient whom no treatment outcome was assigned (includes transfer to another facility for treatment continuation but final outcome was not determined

The TB treatment outcomes that were used are based on the National TB Control Program, Manual of Procedures 6th Edition (Appendix A).[13] The overall TB treatment outcomes of COVID–19 with TB cohort were as follows: 31% in both treatment–completed and not–evaluated, 22% were classified as died and 16% as cured (Table 3).

In particular, for the CD TB sub–cohort (Appendix D), 50% of those who had moderate COVID–19 with CD TB were classified under treatment–completed while the remaining half were not evaluated. Among patients with severe COVID–19 infection with CD TB, more than half (67%) were also categorized as treatment–completed while the remaining (33%) had not been evaluated. Among patients who had critical COVID–19 with CD TB, majority (71%) of them died while only 14% were classified as treatment–completed. On the other hand, for the BC TB subcohort (Table 5), 41% of those who had moderate COVID–19 with

BC TB completed treatment, 16% were categorized as cured and the remaining 41% were not evaluated. For severe COVID-19 with BC TB, half were categorized as cured and the other half were under treatment-completed. For critical COVID-19 with BC TB, majority of them (43%) died and only 7% were categorized as treatment-completed.

Only one patient was diagnosed with mild COVID-19 with BC TB and was categorized as not evaluated.

Table 4. *Presenting Signs and Symptoms of COVID-19 with TB*

Signs and Symptoms	Total Cases of COVID-19 with TB (n = 49)	Mild (n = 1)	Moderate (n = 20)	Severe (n = 8)	Critical (n = 20)
Fever	19 (38.8%)	1 (100%)	8 (40%)	2 (25%)	8 (40%)
Cough	46 (93.9%)	0 (0%)	18 (90%)	8 (100%)	20 (100%)
Dyspnea	39 (79.6%)	1 (100%)	14 (70%)	8 (100%)	16 (80%)
Hemoptysis	2 (4.1%)	0 (0%)	1 (5%)	0 (0%)	1 (5%)
Anosmia	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1 (5%)
Ageusia	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1 (5%)
Sore throat	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Diarrhea	3 (6.1%)	0 (0%)	1 (5%)	1 (12.5%)	1 (5%)
Weight loss	5 (10.2%)	0 (0%)	1 (5%)	2 (25%)	2 (10%)

Cough and dyspnea were the prominent presenting symptoms with 94% and 80% of cases respectively in the COVID-19 with TB cohort. For the mild COVID-19 with TB, only fever and dyspnea were reported. For the moderate and severe COVID-19 with TB cohort, fever, dyspnea, cough, and diarrhea were the common complaints with cough and dyspnea (70-100%) being the most predominant. For the critical COVID-19 with TB, besides the fever, dyspnea, cough, and diarrhea, patients also presented with hemoptysis, anosmia and ageusia (Table 4).

Table 5. *Chest CT scan of admitted patients with COVID-19 with TB co-infection*

	n=49
Consolidation	29 (59%)
Nodules	26 (53%)
Ground-glass opacity	25 (51%)
Bronchiectasis	24 (49%)
Cavities	19 (39%)
Reticules	18 (37%)
Fibrosis	16 (33%)
Atelectasis	10 (20%)
Pleural Effusion	10 (20%)
Tree-in-bud	9 (18%)
Pleural thickening	5 (10%)
Infiltrates	2 (4%)
Air bronchogram	1 (2%)
Calcification	1 (2%)
Laterality of Presentation	
Unilateral	6 (12%)
Bilateral	43 (88%)

The 10 most common lung imaging features (Table 5) of patients admitted for COVID-19 with TB coinfection include: consolidation (59%), nodules (53%), ground-glass opacity (51%), bronchiectasis (49%), cavitary lesions (39%), reticules (37%), fibrosis (33%), atelectasis (20%), pleural effusion (20%), and tree-in-bud (18%). Majority of imaging features present bilaterally (88%), and only 12% present as unilateral lesions.

Table 6. *Proportion of TB Treatment Outcomes of COVID-19 with Tuberculosis* Co-infection admitted at the Hospital vs the National TB figure*

	COVID-19 with Tuberculosis*	National TB Figure Year for 2020	National TB Figure Year for 2021
Treatment Success†	47%	90%	61%
Not Evaluated††	30%	55%	85%
Death	11%	1%	1%
Failed	0%	1%	1%
Lost to follow-up	0%	23%	20%

**Admitted COVID-19 with TB co-infection last March 2020 to March 2021*
†The sum of cured and treatment completed
††No treatment outcome was assigned (includes transfer to another facility for treatment continuation but final outcome was not determined

For the year 2020 to 2021, 47% of admitted patients were classified as treatment success (Table 6). In contrast to the National TB Figures,[14] 90% and 61%, were classified as treatment success for the year 2020 and 2021 respectively. Of note, there is an apparent decrease in trend of the treatment success rate between year 2020 and 2021 of the national TB figures. For the treatment not evaluated, there is an increasing trend from year 2020 (55%) to year 2021 (85%) nationwide based on the National TB Figure.

DISCUSSION

This is the first data from the Philippines that reports on the potential indirect impact of COVID-19 pandemic on the tuberculosis treatment outcomes. This is a retrospective cohort study which provides a summary of the clinical profile, demographics, and TB treatment outcomes of the 49 COVID-19 with TB patients.

The Philippines is the fourth largest contributor to the number of tuberculosis cases worldwide with 500 people affected per 100,000 and was among the countries that contributed to global reduction in TB notification from the year 2019 to 2020.[15] Due to the current shift of priority towards COVID-19 in the past 2 years, management of tuberculosis was highly affected. It was anticipated that there would be difficulty in delivering appropriate services to TB patients such as: active case findings, timely diagnosis, regular follow-up, and distribution of medications.[4] The DOH has noted from March 2020 that there was a disruption in regular TB services from consultation, testing, to treatment due to limited mobility and resulted in a drastic drop in the number of TB cases notified in the country. By the end of 2020, approximately 268,816 new and relapse TB cases were notified to DOH, a 35% decrease from the 2019 data.[6] To date, there are no other studies that have included and compared the specific TB treatment outcomes of COVID-19 with TB patients. Furthermore, we have not found any studies that compared treatment outcomes and clinical profile for bacteriologically confirmed versus clinically diagnosed tuberculosis who had COVID-19 coinfection.

Proportion of TB Treatment Outcomes in Admitted COVID-19 with TB Patients in Comparison to National TB Figures

In the study, most of the population are classified as "moderate COVID-19 with TB" and "critical COVID-19 with TB" comprising 40% (20 out of 49) each of the population (Table 2). In addition, a total of 18 (36%) COVID-19 with TB patients were classified as clinically diagnosed (CD) while 31 (63.3%) were bacteriologically confirmed (BC). Almost half of those who were classified as BC TB had critical COVID-19 coinfection. On the other hand, 44% of those who were classified as CD TB had moderate COVID-19 co-infection (Appendix C). Most of the "COVID-19 with CD TB" sub-cohort

(Appendix D) were classified as treatment-completed (39%, 7 out of 18) whereas majority of the "COVID-19 with BC TB" sub-cohort were classified as treatment-completed (26%, 8 out of 31) and not-evaluated (32%, 10 out of 31).

The overall TB treatment outcomes of COVID-19 with TB in the study were as follows: 47% treatmentsuccess rate (31% as treatment-completed and 16% as cured), 31% (15 out of 49) as not-evaluated, and 22% (11 out of 49) died. The "critical COVID-19 with TB" cohort comprises all the treatment-outcome categorized as died (55%) whereas the "moderate COVID-19 with TB cohort" mostly comprises both the treatment outcomes categorized as treatment-completed (45%) and not-evaluated (45%) (Table 3). The WHO's "End TB Strategy" program recommended a target level of >/90% in TB treatment coverage and TB treatment success rate which applies to all countries.[21] The Philippines' treatment-success was always on target during the years 2017 to 2018, achieving 90-91%.[13] However, as seen on the study, 47% treatment-success rate was noted which pales in comparison with the TB targets and the NTP's national figures. Moreover, an evident decrease also in the treatment-success and a rise in the not-evaluated outcomes were noted during 2020 to 2021 nationwide based on the NTP figures. This outcome is probably due to the impaired health-seeking behavior, public health restrictions and the logistics of each health care facility that prioritized COVID-19 over TB in the past 2 years. In a similar study done by Liu et al, it revealed substantial reductions (>50%) in TB notifications in 2020 compared to 2015-2019 in Jiangsu province of China which suggests lower TB case detection in the province. Moreover, they've noted a decrease in patient treatment success and screening for MDR among the new and high-risk tuberculosis patients.[16]

Mortality rates for TB infection was continuously on the rise for the past 2 years wherein majority was diagnosed with concomitant COVID-19 infection. Multiple case-control studies corroborated findings that showed an altered disease pathology in COVID-19/TB co-infection which leads to two-fold increase in the mortality of coinfected patients.[22] A similar unpublished study on the profile and outcomes of COVID-19/TB done by a tertiary hospital in Cebu, Philippines included 35 patients with a mortality rate of 43%. They concluded that having a positive sputum AFB smear is associated with higher mortality in COVID-19 patients co-infected with TB.[23] Internationally, COVID-19 with TB patients were also discussed in the studies done by Tadolini (12.3%), Motta (11.6%) and the TB/COVID19 Global Study Group (11.08%) with the latter study showing that the presence of TB in COVID-19 was higher among the patients who died than in those who survived but the difference was not statistically significant (p .069). In addition, those with active TB were noted to have a higher probability of death (OR 1.5) compared to those with previous TB.[9,17,5] In contrast, the TB treatment-outcome of death in this study was at 22%. The higher value may probably be due to the small sample size of the study and mostly due to the geographic area, since Asia is the top contributor of TB cases worldwide whereas the previous studies were mostly done in Europe. Nonetheless, identifying the exact cause of death (whether due to COVID-19 itself or the co-infection) is not within the scope of the study. The concomitant COVID-19 and TB infection adds to the complexity of management of each of these respiratory diseases. The impact of COVID-19 on the chronic pulmonary sequelae of TB is yet to be determined.

Clinical Characteristics of COVID-19 with TB co-infection

The clinical characteristics of the COVID-19 with TB cohort were mostly male (63%) and belonged to ages 35-49 (35%, 17 out of 49) and 50-64 (35%, 17 out of 49). These were comparable to a study done by the TB/COVID-19 Global Study Group[5] in which most of their patients were also male (70%) and had a mean age of 44 (31-58 y.o) with the male gender noted as an independent contributor to mortality.[8] This may possibly be related to a report that suggests men are less likely to seek medical care and participate in self-report screening of signs and symptoms for early detection of TB as noted in the meta-analysis done by Horton et al. According to Horton, men were influenced by stigma, financial difficulties, and feelings of inadequacy hence are less likely to seek consultation.[18] In a study done by Bwire, it showed that females are less likely to acquire COVID-19 infection compared to men due to sex hormone differences in immunologic response. It was revealed that blocking estrogen receptors in mice increases mortality for COVID-19 infection. Men also produce high expression of coronavirus receptors (Angiotensinconverting enzyme-2) which facilitates route for pathogenesis of COVID-19 infection.[19] For the elderly population ages >65, half of them were categorized under the critical COVID-19 with TB cohort (Table 1). This was comparable to a study done by Song et al[8] in which it was concluded that older age (>65 y/o) may be a risk factor for death from COVID-TB. Hence, the elderly population with COVID-19 may benefit from early TB screening.

Among the clinical manifestations of COVID-19 with TB cohort, fever (39%), cough (94%) and dyspnea (80%) are the most common symptoms which coincides with the existing studies (Table 4). While both COVID-19 and TB

present with respiratory symptoms as mentioned above, COVID-19 usually occurs in a rapid onset with an incubation period of one to two weeks in contrast to TB which typically develops gradually over a period of time. For uncomplicated COVID-19 infection, the cough is usually dry compared to the productive coughing with expectoration of sputum or blood in patients with TB. In this study, majority of features of the lung imaging among patients with COVID-19 with TB include bilateral distribution of consolidation, ground-glass opacity, nodules, bronchiectasis, cavitary lesions, reticules, fibrosis, atelectasis, pleural effusions, and tree-in bud (Table 5) which are similar to the studies done by TB/COVID19 Global study and Song et al.[5,8] Majority of evidence in the previous years described lung imaging in COVID-19 as having bilateral involvement, peripheral distribution, mixed ground-glass opacity and consolidation[20] whereas the most common radiological findings of COVID-TB also include bilateral lesions and ground-glass opacities with specific findings of cavities, nodules, pleural effusion, and fibrosis. Fever, cough, and dyspnea were the most common encountered presenting symptoms for COVID-19 with TB. Since both diseases present with respiratory symptoms, correlation with imaging studies could be of benefit in finding clues as to whether the patient has COVID alone or with TB co-infection. Therefore, clinicians should be vigilant and consider a possible COVID-19 with TB coinfection upon encountering the above radiological imaging and clinical manifestations instead of just focusing on COVID-19 alone.

Twenty (41%) out of the 49 cases of COVID-19 with TB cohort in this study have no comorbidities. Whereas, the majority of those who have comorbidities (59%) were noted to have DM and hypertension comprising 31% each respectively (Table 1). This may probably be due to the evidence that people with DM are at greater risk of presenting with different types of infections, specifically lower respiratory tract infections [21]; hence, may increase the predisposition of patients to COVID-19 and TB. Surprisingly, only 6% (3 out of 49) have chronic obstructive pulmonary disease (COPD) and 2% (1 out of 49) have bronchial asthma. There were two cases (4%) of HIV/AIDS and also one (2%) case of malignancy (i.e. lung malignancy). These results were comparable with Song et al[8] in which a total of 56% of their COVID-TB population also had comorbidities. DM and hypertension were also the most common followed by HIV infection, hepatitis, chronic kidney disease, and cerebrovascular disease. Only 2% each of their population also had COPD and asthma. Of note in this study, there were no reported cases of heart disease, liver disease, chronic kidney disease and auto-immune diseases. In the TB/COVID Global Study Group,[5] they noted that patients with more than one comorbidity were more frequently observed among those who died (86%).

The COVID-19 pandemic did pose a major public health problem in most countries, especially in the implementation of public health services for TB patients in the Philippines. An inquiry on the TB outcomes before and after the pandemic would contribute to the knowledge gap of the impact of COVID-19 pandemic on TB patients in the Philippines. While the study is not specifically designed to answer this inquiry, we have found that there's still a higher treatment success of COVID-19 with TB outcomes in LCP despite the pandemic. There was a relatively little difference in the treatment outcomes of TB patients in general before and after the pandemic. The outcome rates for the treatment-success vs not-evaluated were as follows: 93% vs 2% before pandemic and 89% vs 2% after pandemic respectively. Despite the COVID-19 pandemic, the hospital's PHDD treatment-success rates seems to be still acceptable as compared to TB targets. The PHDD's accomplishment in following the recommendations of the DOH guidelines in early detection and screening of TB patients were made possible by the center's effort through: open service despite the pandemic restrictions, engaging patient virtually for proper information dissemination, and lastly active barangay visits within the area for case finding and patient follow-up. Nonetheless, the previous data is only reflective of a single-center in Metro Manila and not generalizable to the whole country.

LIMITATIONS OF THE STUDY

This study was limited to a single center only and involved a small sample size. In addition, no comparisons were made between TB treatment outcomes observed in this study with other institutions. The duration of the study was done in a one-year period hence, the scope was limited only to the first COVID-19 pandemic year. All of the subjects that were included were drug-sensitive TB cases upon review of the data from the PHDD, so the results of the TB outcome were limited only to this subset of patients. Since this study solely focused on the TB outcomes of patients who were admitted for COVID-19 with TB co-infection, the exact cause of mortality was not included and specified.

CONCLUSION

TB and COVID-19 remain to be prevalent and may co-exist. In this single-center study, COVID-19 with TB patients were classified as moderate and critical COVID and had high TB treatment success rates. TB and COVID-19 are prevalent diseases worldwide and its coexistence may lead to worse TB outcomes. This study demonstrated that TB in COVID-19 patients may be associated with higher TB treatment-

success rates. In line with this, emphasis on early detection of TB (bi-directional screening) in COVID-19 patients should be done to improve TB treatment outcomes.

To further investigate the TB treatment outcomes of patients diagnosed as COVID-19 with TB co-infection, we recommend extending the duration of the study to more than a year and to possibly include drug-resistant TB patients. A comparative study between those who had TB alone vs COVID-19 with TB may be done to determine the impact of COVID-19 on mortality rates of TB. Since this study focuses solely on the TB outcomes, a follow-up study can also be made for these patients who have COVID-19 with TB co-infection to check for post-COVID-19 and Post-TB lung disease sequelae. An investigation may also be done to compare the TB treatment outcomes between pandemic vs pre-pandemic years to associate impact of COVID-19 in the management of TB in the country. In addition, a post-pandemic investigation on COVID-19 and TB co-infection rates and outcomes may also be done with particular focus on the impact of high COVID-19 vaccination rates and leniency of COVID-19 restrictions such as implementation of mask-down policies nationwide.

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CONFLICT OF INTEREST

None declared.

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APPENDIX A

Treatment Outcome based on NTP Manual of Procedures 6th edition

1. Cured – a patient with bacteriologically confirmed TB at the beginning of treatment and who was smear- or culture-negative in the last month of treatment (6th month) and on at least one previous occasion in the continuation phase
2. Treatment completed – a patient who completes treatment without evidence of failure but with no sputum smear negative results in the last month of treatment and on at least one previous occasion, either because tests were not done or results are unavailable
3. Treatment failed – a patient whose sputum smear or culture is positive at five months or later during treatment, treatment terminated because of evidence of acquired resistance to drugs used, a patient whom follow-up sputum examination was not done and does not show clinical improvement anytime during treatment, and severe uncontrolled adverse drug reaction
4. Died – a patient who dies for any reason during the course of treatment
5. Lost to follow up (LTFU) – a patient whose treatment was interrupted for at least two consecutive months, and a patient diagnosed with active TB but was not started on treatment
6. Not Evaluated – a patient whom no treatment outcome was assigned (includes transfer to another facility for treatment continuation but final outcome was not determined

APPENDIX B

DOH COVID-19 severity classification:

1. Asymptomatic – a patient who test positive for COVID-19 using virologic test (NAAT) or an antigen test but without signs and symptoms that are consistent with COVID-19
2. Mild illness – a patient with signs and symptoms of COVID-19 (fever, cough, sore throat, malaise, headache, nausea, vomiting, diarrhea, loss of taste and smell) but without pneumonia or hypoxia
3. Moderate illness – a patient with clinical signs of non-severe pneumonia (e.g. fever, cough, dyspnea, respiratory rate (RR) = 21-30 breaths/minute, peripheral capillary oxygen saturation (SpO2) >92% on room air)
4. Severe illness – a patient with clinical signs of severe pneumonia or severe acute respiratory infection as follows: fever, cough, dyspnea, RR>30 breaths/minute, severe respiratory distress or SpO2 < 92% on room air
5. Critical illness – patients manifesting with acute respiratory distress syndrome, sepsis and/or septic shock
    a. Acute Respiratory Distress Syndrome (ARDS) – patients with onset within 1 week of known clinical insult (pneumonia) or new or worsening respiratory symptoms, progressing infiltrates on chest Xray or chest CT scan, with respiratory failure not fully explained by cardiac failure or fluid overload
    b. Sepsis – adults with life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection. Signs of organ dysfunction include altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of II. coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinemia
    c. Septic Shock – adults with persistent hypotension despite volume resuscitation, requiring vasopressors to maintain MAP > 65 mmHg and serum lactate level >2 mmol/L

APPENDIX C

Proportion of COVID–19 with TB (Clinically Diagnosed TB vs Bacteriologically Confirmed TB) Among the COVID–19 Severity Classification

	Mild COVID	Moderate COVID	Severe COVID	Critical COVID
Clinically Diagnosed TB† (n=18)	0 (0%)	8 (44.4%)	3 (16.7%)	7 (38.9%)
Bacteriologically Confirmed TB†† (n=31)	1 (3.2%)	12 (38.7%)	5 (16.1%)	13 (49.9%)

**TB tuberculosis*
†refers to patients with no biological specimen confirmation but diagnosis is made by the physician on the basis of physical exam, history, and imaging abnormalities
††refers to patients with either sputum or non-sputum sample (CSF, tissue, blood, urine, stool, gastric aspirate) which is positive for TB by smear microscopy, culture, or rapid diagnostic tests (Xpert MTB/RIF, line probe assay, TB LAMP)

APPENDIX D

TB Treatment Outcomes in COVID–19 with TB (CD vs BC)

	CD TB co–infection with COVID (n=18)				BC TB co–infection with COVID (n=31)			
	Mild (n=0)	Moderate (n=8)	Severe (n=3)	Critical (n=7)	Mild (n=1)	Moderate (n=12)	Severe (n=5)	Critical (n=13)
Cured	0 (0%)	0 (0%)	0 (0%)	1 (14.3%)	0 (0%)	2 (16.7%)	2 (40%)	3 (23.1%)
Treatment Completed	0 (0%)	4 (50%)	2 (66.7%)	1 (14.3%)	0 (0%)	5 (41.7%)	2 (40%)	1 (7.7%)
Treatment failed	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Died	0 (0%)	0 (0%)	0 (0%)	5 (71.4%)	0 (0%)	0 (0%)	0 (0%)	6 (46.2%)
Lost to follow–up	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not evaluated	0 (0%)	4 (50%)	1 (33.3%)	0 (0%)	1 (100%)	5 (41.7%)	1 (20%)	3 (23.1%)
Total	0 (0%)	8 (44.4%)	3 (16.7%)	7 (38.9%)	1 (3.2%)	12 (38.7%)	5 (16.1%)	13 (41.9%)

**TB tuberculosis; CD clinically diagnosed; BC bacteriologically confirmed*

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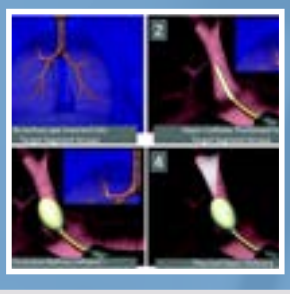

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ORIGINAL ARTICLE

CLINICAL PROFILE AND OUTCOMES OF PATIENTS WITH PRIMARY INTRATHORACIC CANCER ADMITTED DUE TO COVID–19 AT THE LUNG CENTER OF THE PHILIPPINES

Ivarrene E. Cahinde, MD, John Carlo C. Custodio, MD, Guia Elena Imelda R. Ladrera, MD, FPCP, FPCCP
Lung Center of the Philippines

ABSTRACT

Background. Before the end of 2019, an outbreak of COVID- 19 (SARS COV-2), a new respiratory disease was growing in Wuhan, China. There are much published literature and reports describing the clinical characteristics and outcomes of COVID-19 in non-cancer patients but less was published about patients with primary intrathoracic cancer.

Objectives. This study aimed to escribe the clinical profile and outcomes of patients with primary intrathoracic cancer with COVID-19.

Methodology. We report a single-center retrospective medical record review of the clinical profile and outcomes of intrathoracic cancer patients with COVID-19. We analyzed 22 patients admitted in a tertiary hospital who were SARS COV-2 real-time polymerase chain reaction-positive. A descriptive statistic was used and quantitative results were analyzed using frequency distributions or median whenever appropriate.

Results. A total of 22 subjects were identified. Majority were male (77%), the median age was 52 years old, and 42% had hypertension. The most common symptoms were cough and dyspnea. Majority of the patients who died were age 41-60 years old (75%), male (53%), non-smoker (63%), and with ECOG III (36%). Of the entire cohort, 73% had non-small cell carcinoma (NSCCA), 63% were COVID-19-critical and 63% had acute respiratory failure (ARF), 11 patients were discharged and 11 died.

Conclusions. Our data highlighted that patients with increasing age, male, hypertensive, COVID-19-critical, with ARF, with NSCCA, and poor ECOG performance status are more likely to die from COVID-19 infection. Patients with intrathoracic cancer are one of the vulnerable groups and should receive optimum delivery of care at the onset.

Keywords. *Intrathoracic cancer, cancer, COVID-19, SARS-CoV 2, clinical profile, outcomes.*

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INTRODUCTION

Patients with cancer have been one of the most affected groups during this pandemic. This is caused by a new strain of coronavirus, and the disease was officially named by World Health Organization (WHO) on February 11, 2020 as Coronavirus Disease 2019 COVID-19.[1] Tremendously affected are the vulnerable groups, which include patients with intrathoracic cancers. Individuals with cancer are more susceptible to infections due to coexisting chronic diseases and co-morbidities. The overall poor health status and systemic immunosuppressive states caused by both anticancer treatments and cancer itself make them vulnerable to various diseases,[2] including COVID-19. Patients with cancer infected by COVID should be given special consideration because they are at greater risk of progressing to serious COVID-19. The consequences of COVID-19 infection could have a wide range of effects in terms of increased morbidity and mortality. Available data confirm that cancer patients are more likely to be infected with COVID-19 and high risk of developing major complications.[3-7]

Questions posed are the demographic profile of these patients, how chronic diseases or co-morbidities, increasing age and could cancer treatment itself be observed to affect outcomes in this population group. There are many published literature and reports describing the clinical characteristics and outcomes of COVID-19 in non-cancer patients but fewer have been published about the cancer patient group, specifically among those having primary intrathoracic cancer.

During the pre-pandemic era, the Lung Center of the Philippines (LCP), a tertiary hospital, served as a cancer referral center with primary intrathoracic cancer catering mostly to indigent patients from all over the Philippines. This study was proposed because to date no local study has documented the clinical profile, treatment course, and outcomes of patients with intrathoracic cancer and Covid-19 infection. The Lung Center of the Philippines was one of the hard-hit institutions during this COVID-19 pandemic. Here, we studied the clinical profile and analyzed the data from the medical records.

METHODOLOGY

Study Design

The study is a descriptive retrospective study design.

Study Setting

The study site is the Lung Center of the Philippines located at Quezon Avenue, Quezon City, National Capital Region. It is a government tertiary specialty hospital for lung diseases and was designated as a COVID-19 referral center by the DOH during the pandemic. The covered period of the study is from April 1, 2020 to March 31, 2022.

Study Population

The study included patients > 18 years old with COVID-19 infection (by realtime PCR or SARS-CoV 2 GeneXpert Xpress) and primary intrathoracic cancer who were admitted at LCP from April 1, 2020 to March 31, 2022. All patients > 18 years old who were admitted due to COVID-19 symptoms but later noted to have primary intrathoracic cancer, and patients who came in for chemotherapy and other cancer-related management and procedure but turned out to have a positive result on the routine swab for COVID-19 were included. Pathologically confirmed primary intrathoracic cancer during or prior to admission included, but were not limited non-small cancer, small cell cancer, pleural mesothelioma, thymoma, mediastinal tumor such as Hodgkin and non-Hodgkin lymphoma, germ cell tumor, and thymic cancer.

We excluded intrathoracic cancer patients who were managed in other hospitals for more than 48 hours and transferred to our institution, primary intrathoracic cancer patients with COVID-19 but during the course of admission at LCP were discharged against medical advice, patients with malignancy that are metastatic to the thorax, and those whose medical records had incomplete data.

Study Procedure

A masterlist from the medical records of all COVID-19 patients admitted from April 1, 2020 to March 31, 2022 were asked from the medical records section. Charts of all patients with a diagnosis of primary intrathoracic cancer and COVID-19 were retrieved and reviewed. Other information and or laboratory results, and histopathologic diagnosis needed were reviewed and extracted from the existing LCP database (Bizbox, WebLis system, and Voyager). Demographic and clinical profiles were collected from the eligible patient's chart and recorded in the data collection form that was coded. Data variables were encoded and transformed into frequencies for tabulations and counting.

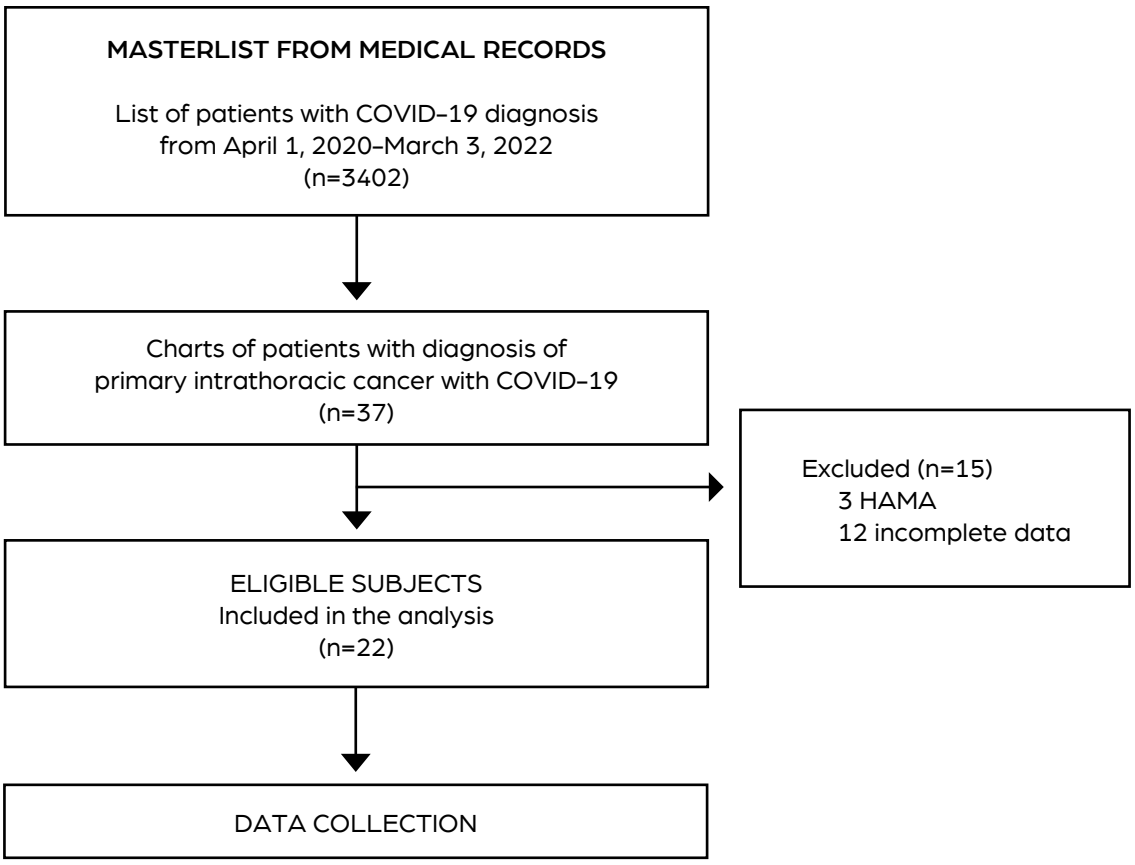


Figure 1. *Flowchart of patient included in the study*

Statistical Analysis

Quantitative results obtained were analyzed using frequency distributions or median whenever appropriate. Microsoft Excel was employed in the computation.

Ethical Considerations

The study was conducted after approval was sought and granted (LCP-PF-019-2022) by the LCP Institutional Ethics Review Board (LCP IERB). This research study followed the National Ethical Guidelines for Health and Health Related Research and abided by the principles of the Data Privacy Act of 2012. A waiver of informed consent was requested through the IERB for this retrospective cohort study. The anonymity and confidentially of the eligible patients were preserved by not revealing their identity in the data collection form, statistical analysis, and reporting of the study findings, alpha numeric codes were used instead. Data collection and analysis were simultaneously conducted and shared with the statistician only with the alphanumeric codes of the patients. The final results of the analysis were encoded and stored in an encrypted device shared only by the three investigators. Both written and electronic data will have proper disposal after 1 year. Written data were kept only by the investigators and were secured in a locker in the office of Adult Pulmonary Medicine at the Lung Center of the Philippines. Only the three investigators can gain access to all data. The research involved no more than minimal risk to the participants.

RESULTS

Study Participants

Of the 37 charts reviewed, 22 patients with intrathoracic cancer with COVID-19 infections were included: all patients were diagnosed with SARS COV-2 RT-PCR. Eligible patients were admitted between April 1, 2020 to March 31, 2022.

Baseline Characteristics

Table 1 summarizes demographic characteristics categorized by whether patients are discharged (alive) or dead, in terms of both age and sex. After exclusion criteria, ultimately, 22 patients (77% male) were analyzed. The median age is 52 years old, which is also the median age for discharged and expired patients. From the eight patients in the age range 41-60 years old, six died, while from the eight patients whose age is more than 60-year-old, two died.

On the profile of sex in the entire cohort, 77% are males, of whom 53% (nine out of 17) died.

Table 1. *Demographic Profile*

Profile	Entire Cohort (n=22)	Discharged (n=11)	Died (n=11)
Age, (n [%])	Median = 52 y.o.	Median = 52 y.o.	Median = 52 y.o.
19–40 y.o.	6 (27)	3 (27)	3 (27.3) 27
41–60 y.o.	8 (36)	2 (18)	6 (54.6) 55
>60 y.o.	8 (36)	6 (55)	2 (18.2) 18
Sex, (n [%])			
Male	17 (77)	8 (73)	9 (82)
Female	5 (24)	3 (27)	2 (18)

Baseline clinical profile

Figure 2 shows the baseline clinical profile of the 22 patients. Nine (81%) of those who died experienced dyspnea, while two (18%) had cough.

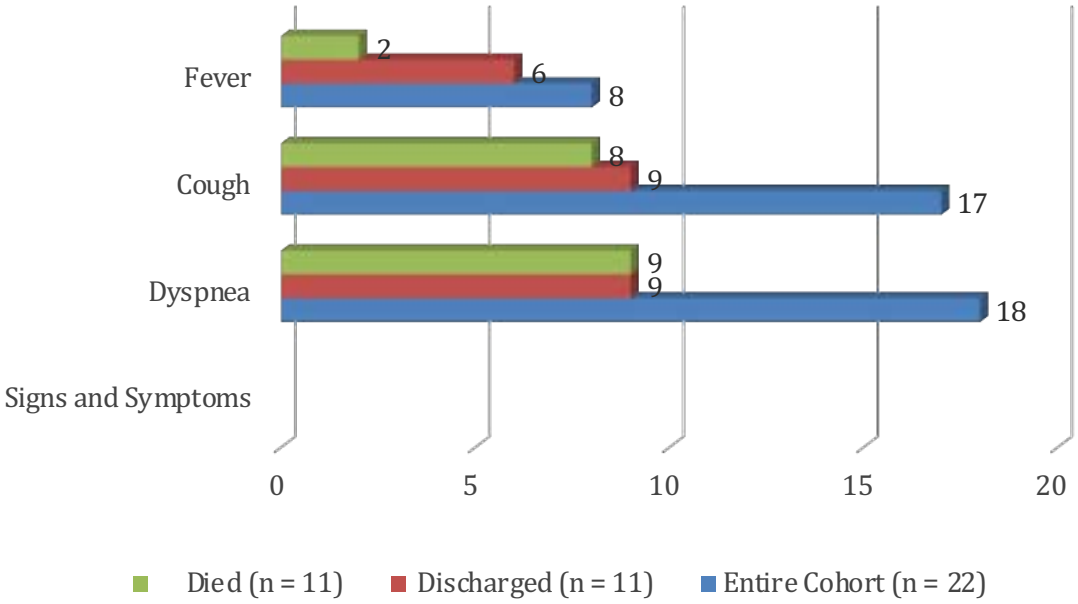
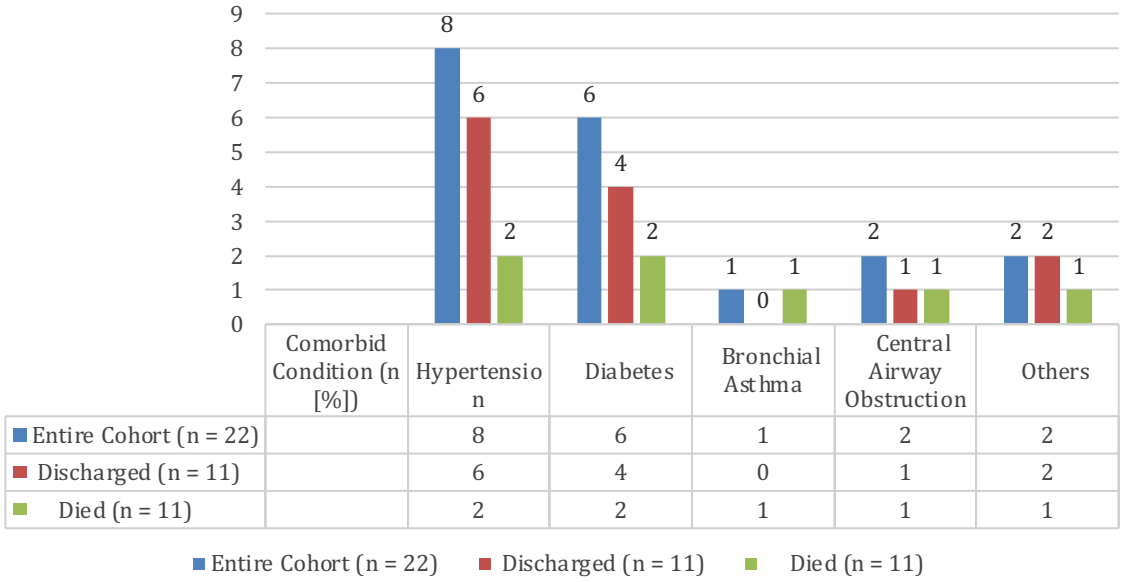


Figure 2. *Signs and symptoms (n=22)*

Figure 3 shows the comorbid conditions acquired before contracting COVID-19, eight (42%) patients had hypertension, 6 (32%) had diabetes, while the rest had bronchial asthma (5%), central airway obstruction (11%), and other co-morbid conditions (11%). While each of the hypertensive and diabetic patients, two (27%) died.

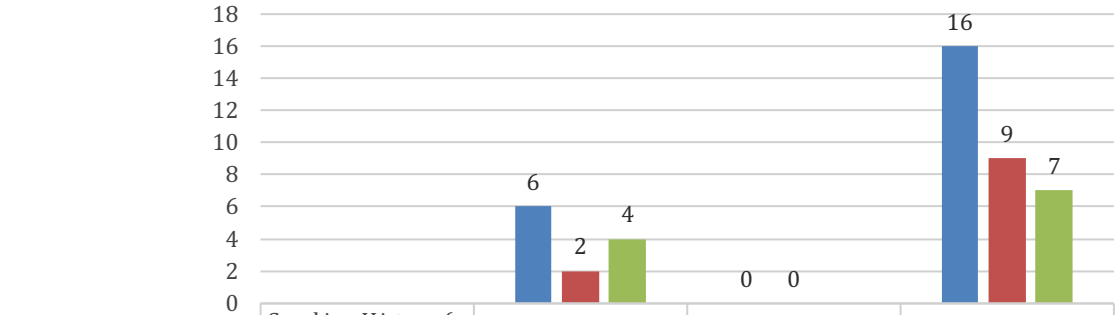


Comorbid Condition (n [%])	Hypertension	Diabetes	Bronchial Asthma	Central Airway Obstruction	Others
Entire Cohort (n = 22)	8	6	1	2	2
Discharged (n = 11)	6	4	0	1	2
Died (n = 11)	2	2	1	1	1

Entire Cohort (n = 22) Discharged (n = 11) Died (n = 11)

Figure 3. *Comorbidities (n=22)*

Figure 4 shows the profile of smoking history, 16 (73%) never smoked, while the remaining six (27%) were previous smokers. Of the six patients who previously smoked, four (67%) died; and from the 16 who never experienced smoking, seven (44%) died.



Smoking History (n [%])	Previous Smoker	Current Smoker	Never Smoker
Entire Cohort (n = 22)	6	0	16
Discharged (n = 11)	2	0	9
Died (n = 11)	4		7

Entire Cohort (n = 22) Discharged (n = 11) Died (n = 11)

Figure 4. *Smoking History (n=22)*

Figure 5 shows COVID-19 disease severity, of three (14%) and five (23%) of the entire cohort were moderate and severe, respectively. All of these eight patients were discharged. Fourteen (63%) of all patients had critical COVID-19 severity, of which 11 (79%) died.

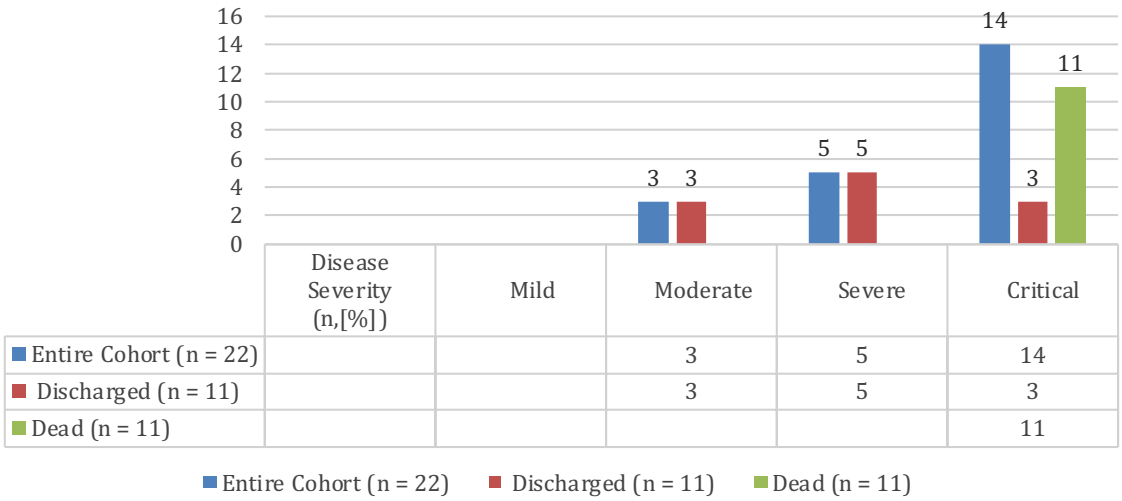


Figure 5. *COVID-19 Disease Severity (n=22)*

Table 2 summarizes cancer diagnosis and staging, a total of 16 patients had non-small cancer adenocarcinoma, with seven patients under stage IVA and eight with stage IVB. From the eight patients with stage IVB lung adenocarcinoma patients, 4 died. Two patients had stage IVB small cell cancer and were discharged. Only one patient was diagnosed with stage IV Non-Hodgkin's Lymphoma, and another single patient had a stage IIIA Yolk Sac tumor. All of these patients expired while contracting COVID-19.

Interestingly, seven patients (32%) were under ECOG Status I and one died. Another seven patients (32%) were under ECOG Status II of which two expired, while all eight (36%) patients in the cohort under ECOG status III died. A total of eleven (50%) of the patients received no treatment (palliative care), of whom five (46%) died. From the 10 (46%) of the cohort who underwent chemotherapy, five (50%) died. One (5%) patient received radiation therapy.

Table 2. *Cancer Diagnosis, Staging, ECOG Status and Treatment Received.*

Cancer Diagnosis and Staging			
	Entire Cohort (n= 22)	**Discharged (n= 11)**	**Died (n= 11)**
Non-Small Cell Cancer Adenocarcinoma	Stage IIIB, = 1 Stage IVA, = 7 Stage IVB, = 8	Stage IVA, = 4 Stage IVB, = 4	Stage IIIB, = 1 Stage IVA = 3 Stage IVB, = 4
Squamous Cell Carcinoma	Stage IVA, = 1	Stage IVA, = 1	-
Small Cell Cancer	Stage IVB, = 2	Stage IVB, = 2	-
Hodgkin's Lymphoma	Stage IV, = 1	-	Stage IV, = 1
Non-Hodgkin's Lymphoma	Stage IV, = 1	-	Stage IV, = 1
Yolk Sac Tumor	Stage IIIA, = 1	-	Stage IIIA, = 1
ECOG Status (n [%])			
I	32%	55%	9%
II	32%	45%	18%
III	36%	-	73%
Treatment Received, (n [%])			
Chemotherapy	46%	45%	45%
Radiation Therapy	5%	-	9%
(None) Palliative	50%	55%	45%

In-hospital complications data shows that among the 14 (64%) of those who had acute respiratory failure, 11 (77%) died. A total of six out of the eight (75%) patients who had ARDS also expired. There were three out of four (75%) of those who acquired acute kidney injury died.

We identified one patient each who acquired transaminitis, acute coronary syndrome, and septic shock, respectively, while two patients had hospital-acquired pneumonia. All five patients died. Finally, five (23%) of the entire cohort did not acquire any in-hospital complications and were eventually discharged.

Table 3. *COVID-19 Clinical Course – In Hospital Complications and Outcomes*

COVID-19 Clinical Course and Outcomes	Entire Cohort (n=22)	Discharged (n=11)	Dead (n=11)
In-hospital complications, (n, [%])			
Acute Respiratory Failure	14	3	11
ARDS	8	2	6
Acute Kidney Injury	4	1	3
Transaminitis	1	-	1
Acute Coronary Syndrome	1	-	1
Hospital Acquired Pneumonia	11	-	2
Septic Shock	1	-	1
None	5	5	

The median length of hospital stay for the entire cohort was eight days, with 16 median days among those discharged, and seven median days for those who died.

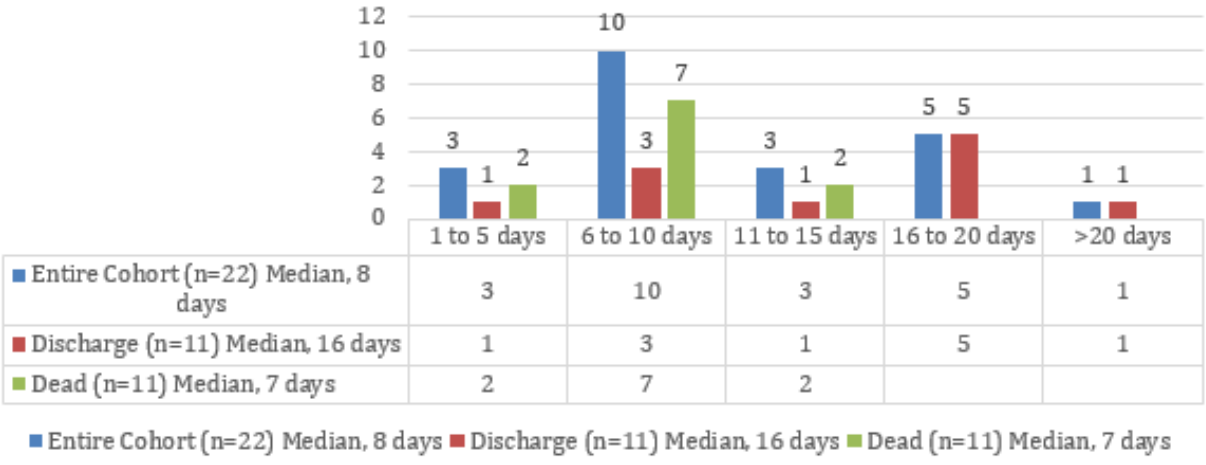


Figure 6. *Length of Hospital Stay (n=22)*

In terms of the status of discharge, figure 5 shows that 11 (50%) of the 22 patients expired, while four (18%) of those discharged were sent home, improved without the need for O_2 support, and severe (32%) were sent home, improved with the need of O_2 support.

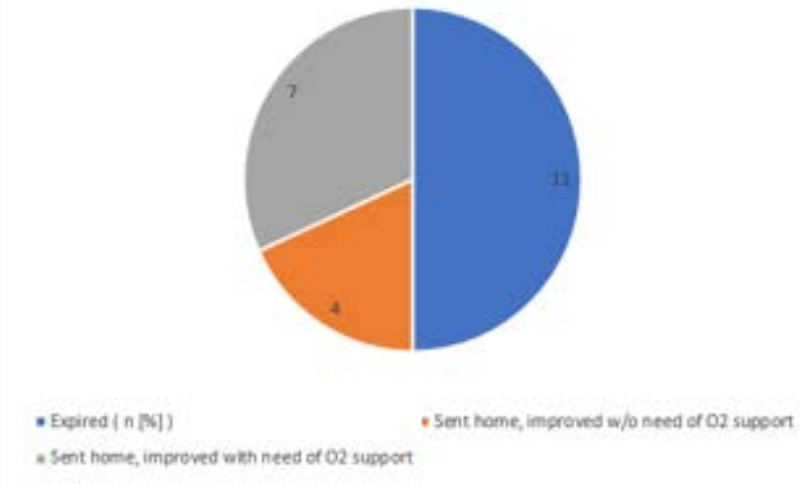


Figure 7. *Status Upon Discharge*

DISCUSSION

This study of 22 patients with intrathoracic cancer and COVID–19 infection at Lung Center of the Philippines confirms 100% mortality for COVID–19–critical patients. Our study projects a higher overall mortality rate (50%) compared with the global TERAVOLT study of thoracic cancer patients (25%) and the US study of lung cancer patients with COVID–19.[8,9] In a meta–analysis authored by Rolfo et al.[10] the published study resulted in a 32.4% COVID–19 mortality rate. This result strengthened the significance of the urgent focus on optimizing care in cancer patients with COVID–19.

Baseline Clinical Characteristics

The median age of patients is 52 years old which is also the median age both for patients who were discharged, and those who expired. Most of the patients who died were aged 41–60 (75%) and out of the 77% males from the entire cohort, 53% died. These findings were similar to the report of Fu et al.[11] wherein death occurred more frequently in males than in females (24% vs 19%),

Death occurred in patients with symptoms of cough and dyspnea, the latter (81%) being the most common presenting symptoms. Hypertension (42%) is the most common co–morbidity seen in this study, followed by Type 2 diabetes (32%), central airway obstruction (11%), and bronchial asthma (5%). In our study, out of the 11 patients who died, 18% had hypertension and 18% also had type 2 diabetes mellitus. Active cancer, increasing age, cardiovascular disease, and diabetes were associated with increased risk of mortality, were also reported by Fu et al.[11]

The majority of the patients were never smokers (73 %) and out of the entire cohort, most of those who died (64%) were non–smokers, a finding which is incongruent with Fu et al. wherein cumulative risk factors for COVID–19 complications and mortality were patients who had history of smoking.[11] Overall, 74% of patients have non–small small carcinoma–adenocarcinoma, 9% for small cell cancer and 4% for squamous cell carcinoma, similar to the study of Liang et al.[12]

With the 50% mortality rate, 63% of patients had stage 4 lung cancer and 18% had stage 3 lung cancer. Of the 68% of patients with adenocarcinoma, 45%, and 9%, died with stage IV and stage III Lung cancer, respectively. It has been observed that most of the patients with late–stage lung cancer expired. Several studies[7,13,14] reported that lung cancer patients suffer from an increased risk of mortality compared with other types of cancer but it was not mentioned what type of lung cancer had the highest mortality. In those studies, it was also highlighted that lung cancer patients have higher risks of pulmonary complications, severe lung injury, and higher risk of death because of the pathophysiological, clinical, and cancer–treatment–related risk factors resulting in immunosuppression. In each of the cases classified under Hodgkin and non–Hodgkin

lymphoma, non- seminomatous germ cell tumor (NSGCT) all of the patients under this type of malignancy expired. There are limited studies citing COVID-19 cases with these three types of intrathoracic malignancy. In an article by Kumar et al. NSGCT alone posted overall survival rate of 25%.[15] In a case report done by Li et al. a 26-year-old male with primary mediastinal large B-cell lymphoma with COVID-19 infection underwent chemotherapy and was subsequently discharged improved.[16]

In the study of Liang et al. the majority of the included patients had Eastern Cooperative Oncology performance status (ECOG) 0-1 in comparison with this study where 36% of patients from the entire cohort had ECOG status III of which all of them died.[12] It was noted that the mortality reported had ECOG status I. A total of 11 patients (50%) with ECOG I-II were discharged. Half of the total subjects in this study received no treatment and 46% died, of the patients who had chemotherapy 50% also died. In the original TERAVOLT analysis8 treatment with chemotherapy alone was associated with an increased risk of death compared with patients who had immunotherapy. In this study, there were no recorded patients who had immunotherapy, combined chemo-immunotherapy, or targeted therapy. We did not include the correlation between the delay of treatment and the outcome of these patients. In a retrospective study by Fujita et al.[6] cancer patients had a delay in their treatment during this pandemic. It was also pointed out in other studies that cancer patients may suffer worse respiratory outcomes when infected with COVID-19. [7,13] Coming to terms with the delay in cancer treatment will possibly add up to the overall poor prognosis of these patients.

In terms of disease severity, the majority of the patients were COVID-19-critical (64%) and out of this 64% of the entire study population, eleven COVID-19 critical patients died. The most common (63%) complication in this study was acute respiratory failure and the majority were not pulled out from this complication and eventually succumbed to death. Trend summarizes that once the patient had acute respiratory failure they would eventually die. We found out in this study that patients who died had shorter median hospital stay (7 days) until death occurred compared with those patients that had been discharged (16 days). A total of 50% of the total population in this study was discharged and 50% died.

LIMITATIONS OF THE STUDY

This study has some limitations. Because this is a retrospective study, we were not able to complete the needed data that would satisfy the inclusion criteria concerning our objectives, hence the large excluded population. Many patients also were discharged against medical advice contributing to the small sample size. Because this is also a single-center study, the sample size was small and will not represent generalizability to COVID-19 patients with intrathoracic cancer. Second, patients could have been admitted late in the disease of COVID-19 illness, therefore mortality was high in this retrospective study. Third, because we included only hospitalized patients the outcome of non-hospitalized patients will not be explored. Notwithstanding, our results seized that patient with intrathoracic cancer with COVID-19 infection has high mortality risk. A potential bias in this research is the unmeasured co-morbidity in this study that may influence the outcome. Treatment management depending on the severity of COVID-19 was also not included in this study, hence making it a potential bias also. Outcomes may also be influenced depending on the treatment recommendation received by the patient.

CONCLUSION

In summary, our data highlighted that the majority of the patients were male, the median age was 52 years old, most common symptoms were cough and dyspnea. Hypertension and type 2 diabetes mellitus were the most common co-morbidities. The majority of the patient who died belonged to the age group of 41-60 years old and were non-smokers. This finding suggests that smoking does not predict worse outcome. Patients with intrathoracic cancer with poor ECOG performance status were more likely to die during this pandemic. In this study, majority of the patients who expired had ECOG performance status III. Non-small cell carcinoma was the most common intrathoracic cancer and a majority have lung adenocarcinoma stage IV. We observed that all subjects with final diagnosis of COVID-19 critical expired. However, worse outcome was not compared in relation to treatment received based on initial presenting COVID-19 severity, hence a correlational study in the future is recommended. The most common complication was acute respiratory failure. The median hospital stay was 7 days for patients who died and 16 days for those who were discharged. Equal numbers of patients were discharged and expired. Majority of the patients who were discharged needed oxygen support. We conclude that patients with intrathoracic cancer are one of the vulnerable groups and may have high mortality risk during this pandemic and should receive optimum delivery of care at the onset. Our results can serve as baseline database for further studies in our institution targeting a bigger population and a multicenter investigation of patients with intrathoracic cancer and COVID-19 infection. A correlational or association study of COVID-19 vaccine in patient with intrathoracic cancer and its outcome is also recommended in future studies

FUNDING

None.

CONFLICT OF INTEREST

None declared.

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ORIGINAL ARTICLE

CLINICAL COURSE AND EXPOSURE CHARACTERISTICS OF BREAKTHROUGH COVID-19 INFECTION AMONG HEALTHCARE PERSONNEL OF THE LUNG CENTER OF THE PHILIPPINES

Maria Christina Angela L. Lukban, MD, Noel Raphael T. Villarete, MD,
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ABSTRACT

Background. COVID-19 infection has been a global pandemic resulting in biophysical, socio-economic, and psychological burden. Medical frontliners were the first to complete COVID-19 vaccination by early August 2021. However, despite this, breakthrough infections were still noted.

Objective. This study was conducted to determine the factors and exposure characteristics of fully vaccinated healthcare personnel in a tertiary institution who had breakthrough COVID-19 infection.

Methodology. This is a single center, one-year descriptive study of hospital-based healthcare workers with breakthrough infection.

Results. Majority of the 96 respondents were females (66%), nurses (49%), aged 31-40 (49%), with co-morbidities (65%). Work-related exposure for increased infections includes assignment in the COVID-19 wards, direct contact with confirmed patients (84%) and performance of aerosol generating procedures (93%). Identified exposure characteristic in the community setting was use of public transport (52.1%). Regardless of COVID-19 vaccine brand received, majority of infections documented were mild (93%). Only five were asymptomatic and there were only two documented cases, which presented with moderate and severe symptoms. Breakthrough infections began to increase six months after the initial primary series vaccination and nine months following the initial booster doses.

Conclusion. The severity of COVID-19 infection among healthcare workers is decreased with the use of any type of COVID-19 vaccine and its booster. Future studies are needed to investigate the increase of COVID-19 infection after 6th and 9th month from the last vaccination.

Keywords. *COVID-19, breakthrough infection, healthcare personnel, vaccination, exposure characteristics*

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INTRODUCTION

The COVID-19 virus, first noted in December 2019 and declared a global pandemic in March 2020, claimed millions of lives.[1] Through international efforts by January 2021, COVID-19 vaccines began to be mass produced and distributed.[2,3] However, despite the vaccination drive, many people still acquired COVID-19 infection. Defined as breakthrough infection as it was the acquisition of the same infection because of wanting protection from initial doses of a received vaccine.[4] Everyone, including medical frontliners, were not exempted from this breakthrough infection.[5,6] At the Lung Center of the Philippines, majority of the employees were fully vaccinated by August 2021, however some breakthrough infections began to be documented around the third quarter of the same year.

This study aims to investigate the work and community-related exposure characteristics which predisposed to breakthrough infections, and to classify the severity of breakthrough infection among fully vaccinated health personnel. Secondary objectives are to estimate vaccine effectiveness in preventing COVID-19 disease, and to establish demographic profile of populations predisposed to COVID-19 infection.

METHODOLOGY

Study Design

This study is a single center, one-year descriptive study of hospital-based healthcare workers with breakthrough infections in a tertiary government hospital. Data collection was conducted at the Lung Center of the Philippines (LCP), a designated COVID-19 referral center and a Level 3 institution with more than 500 vaccinated employees. Inclusion criterion included all LCP healthcare personnel who had breakthrough COVID-19 infections from May 1, 2021 to June 30, 2022. The researchers excluded those who have retired, resigned from service, and/or transferred to another institution within the study period.

Study Procedure

A master list of all fully vaccinated health care workers was obtained from the Employees' clinic database. The period of their breakthrough infection was noted. Their contact numbers and email addresses were taken from their Case Investigation Form (CIF) and from the hospital electronic laboratory. Some participants were approached individually and their responses collected through interview, others were contacted via call through their mobile or Viber numbers and a google form questionnaire was sent to their email addresses. This electronic questionnaire entitled: Exposure characteristics and clinical outcomes of fully vaccinated LCP employees was a modified questionnaire tailored from the World Health Organization Guidance document entitled: Cohort study to measure COVID-19 effectiveness among health workers in the WHO European Region. This contained a set of questions pertaining to the activities of health care personnel both inside the hospital and in the community setting which may predispose them to acquire breakthrough infection.[7]

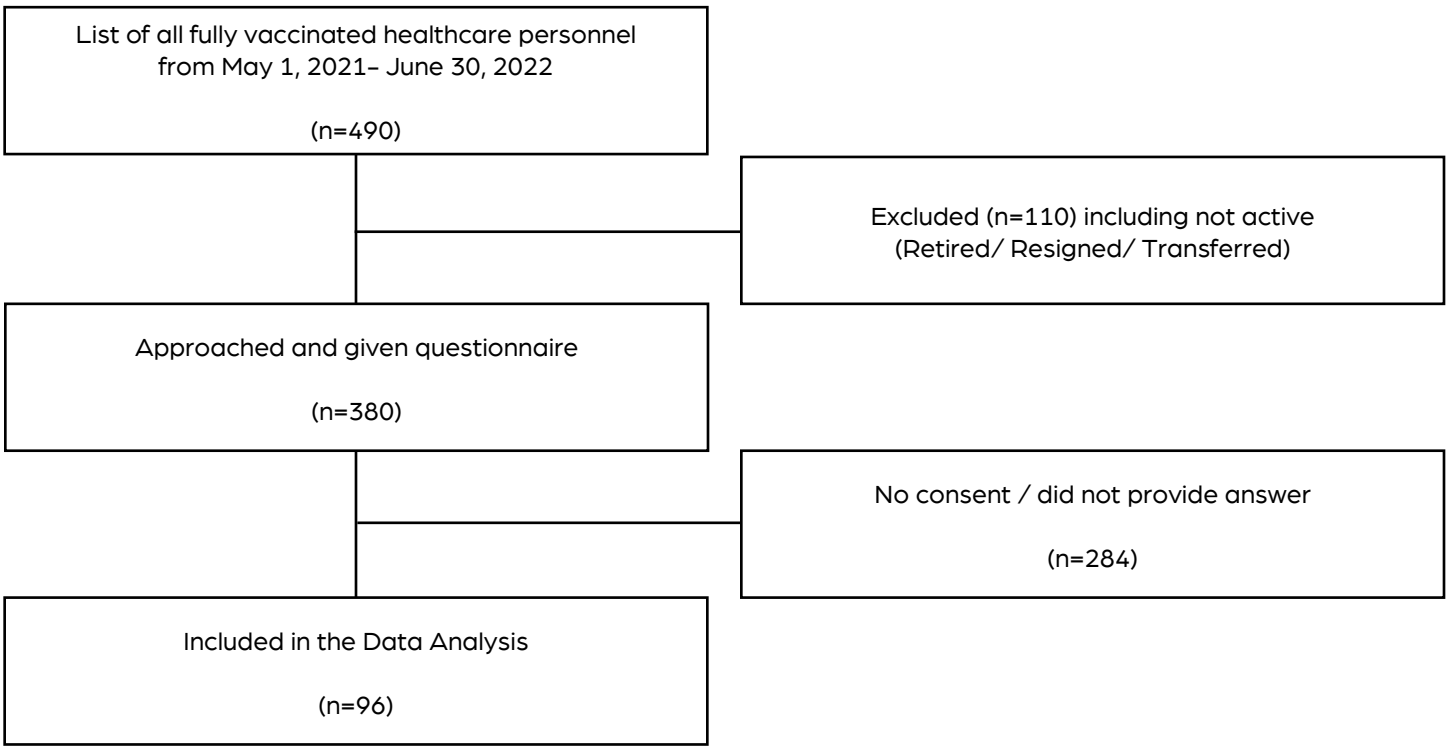

Figure 1. *Flowchart of patients included in the study.*

Statistical Analysis

Baseline socio-demographic characteristics of study participants were tabulated. All data were tallied and the percentage increase or decrease in frequency of COVID-19 breakthrough infection was reflected in terms of intrinsic and extrinsic work and community-related exposure characteristics.[7,8] The clinical course of infection was determined, in relation to the type of vaccine received and the presence or absence of booster dose. Lastly, the interval between the most recent dose of COVID-19 vaccine received and the occurrence of COVID-19 infection was also analyzed in terms of percentages.

Ethical Considerations

The study was conducted upon the approval of the LCP Institutional Ethics Review Board (LCP IERB) and was completed in accordance with the Data Privacy Act of 2012. Waiver of Informed Consent process was sought from LCP IERB. The participants' data: name and phone numbers, and other related information were treated with confidentiality. Participants' names were not used.

All documents, information and materials that were obtained during the conduct of this investigation were used for exclusive interpretation of results in accordance with the declared objectives of this research paper. Any form of raw data was deleted from the storage device of the proponent's computers, laptops, mobile phones and other electronic devices used in partial or in full for data safe keeping. In the drafting of the final research proposal, all data saved in these devices were deleted, put to an electronic trash bin, and erased completely from the devices' memories.

Table 1. Baseline socio-demographic and exposure characteristics of fully vaccinated healthcare personnel with breakthrough COVID-19 infection

	Parameter	Population (n)	Percentage (%)
Socio- Demographic	Age (years)		
	18-30	24	25%
	31-40	47	49%
	41-50	13	13.5%
	51-60	10	10.4%
	>60	2	2%
Sex	Male	33	34%
	Female	63	66%
Clinical	No Comorbidities	62	64.6%
	With Comorbidities	34	35.4%
	HTN	18	53%
	T2DM	7	21%
	Heart Disease	3	9%
	Lung Disease	9	26%
	Kidney Disease	2	6%
	Neurologic Disease	0	0%
Vaccine	Inactivated virus (Sinovac)	43	44.8%
	MRNA (Moderna)	5	5.2%
	Viral vector (AstraZeneca)	48	50%
Booster	Present	48	50%
	Absent	48	50%

The baseline socio-demographic and exposure characteristics of respondents were tallied as shown in Table 1. Majority of the respondents were females comprising 66% of the total participants. Most of the participants (49%) were aged 31-40 years, followed closely by participants from 18-30 years of age at 25%, and lastly, ages 41-50 years old at 13.5%. The least affected group were those from the 50-60 years age bracket and beyond. The comorbidities mostly identified were hypertension at 53%, lung disease and type 2 diabetes at 26% and 21% respectively. The COVID-19 vaccines mostly received were viral vector (AstraZeneca) 50%, inactivated virus (Sinovac) 44.8%, and mRNA (Moderna), 5.2%. There were equal number of participants with and without documented booster doses at the time of breakthrough infection.

Table 2a. *Frequency of COVID-19 infection among fully vaccinated healthcare personnel based on their work- related exposure characteristics*

Work- Related Exposure	Population (n)	Percentage (%)
Occupational Exposure		
Firstline		
Doctor	5	5.2%
Nurse	47	49%
Nursing Aide	17	17.7%
Med Tech (Specimen Collector)	8	8.3%
Respiratory	2	2.1%
Non-Firstline		
Radiology	2	2.1%
Nutritionist	0	0
Lab Personnel	0	0
Administrators	3	3%
Hospital Cleaner	1	1%
Access to COVID-19 Ward		
Yes	58	84.4%
No	38	15.6%
Contact to COVID-19 Confirmed Patients		
Yes	58	84.4%
No	38	15.6%
Use of Full PPE (Level IV/Standard) at all times while at the COVID-19 wards		
Yes	69	68.8%
No	25	31.2%
Involvement in Aerosol Generating Procedures		
Yes	89	92.7%
No	5	7.3%

Based on occupational exposure and line of work, most of the breakthrough infection occurred among the first line healthcare workers, namely: nursing service, 47 (49%) and nursing aides 17 (17.7%). This was followed by the medical technologists and medical doctors, having an incidence of eight (8.3%) and five (5.2%), respectively. In contrast, among the non-first line workers, the staff from administrative department, 3 (3%), followed by radiology technicians, 2 (2%), had the most infections. Most of those who contracted breakthrough infections had access to the COVID-19 wards and had direct contact with COVID-19 confirmed patients, 58 (84.4%). Majority were involved with aerosol-generating procedures, 89 (92.7%).

Table 2b. *Frequency of COVID-19 infection among fully vaccinated healthcare personnel based on their community-related exposure characteristics*

Community- Related Exposure	Population (n)	Percentage (%)
Contact with Confirmed COVID-19 case outside of the hospital		
Yes	15	15.6%
No	81	84.4%
Contact with a housemate/ household member with Confirmed COVID-19 case		
Yes	15	15.6%
No	81	84.4%
Participation in indoor gatherings		
Yes	37	38.5%
No	59	61.5%
Use of public transport		
Yes	50	52.1%
No	46	47.9%

Table 2b showed that among the 96 recorded responses, the majority 81 (84.4%) denied having been in contact with COVID-19 confirmed case outside of the hospital setting. Most of them refrained from participating in indoor gatherings 59 (61.5%). However, other identified risk factor for breakthrough infection was more in terms of using public vehicles (52.1%) other than those who do not as means of transportation.

Table 3. *Clinical Course of Breakthrough Infection*

		Population (n)	Percentage (%)
Clinical Course	Asymptomatic	5	5.21%
	Mild	89	92.71%
	Moderate	1	1.04%
	Severe	1	1.04%
	Critical	0	0%
Onset of Infection (from last dose of vaccine)	< 3 months	17	17.7%
	>3-<6 months	25	26%
	>6-<9 months	25	26%
	>9 months	29	30.2%
Booster	Present	48	50%
	Absent	48	50%

As shown in Table 3, most of the participants with breakthrough COVID-19 infection had mild symptoms (92.71%). Seven recorded responses were subdivided into five asymptomatic (5.21%), one with moderate (1.04%), and one with severe symptoms (1.04%). The onset of breakthrough infections recorded showed an increasing trend every quarter from the last dose of primary vaccination. It is shown as follows: 17.7% during the first quarter, during the 2nd and 3rd quarter, both are 26% and 30.2% during the last quarter.

Table 4a. *Severity of COVID-19 infection in relation to the type of Primary series Vaccine received*

	Inactivated Virus	mRNA		Viral Vector	
	Sinovac	Moderna	Pfizer BioNTech	AstraZeneca	Janssen
Total	43	5	0	48	0
Asymptomatic	0 (0%)	0 (0%)	0 (0%)	5 (10.4)	0 (0%)
Mild	41 (95.3%)	5 (100%)	0 (0%)	43 (89.6%)	0 (0%)
Moderate	1 (2.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	1 (2.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Critical	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

The severity of COVID-19 infection was almost identical regardless of the primary series of vaccines received. Majority of respondents recorded mild infection. [Inactivated virus - 41 (95.4%); mRNA - 5 (100%); Viral Vector -43 (89.6%)]. There were five asymptomatic respondents, all of whom received the viral vector vaccine. There were two respondents who both received the inactivated virus vaccine who presented with moderate and severe infections, both required hospitalizations.

Table 4b. *Severity of COVID-19 infection in relation to presence of booster dose*

	Presence of booster dose		Absence of booster dose	
	n	%	N	%
Total	48	50%	48	50%
Asymptomatic	3	6.2%	2	4.2%
Mild	45	93.8%	44	91.7%
Moderate	0	0%	1	2.1%
Severe	0	0%	1	2.1%
Critical	0	0%	0	0%

Regarding those with and without booster doses, the clinical severity of COVID-19 breakthrough infection was similar between the two groups. Among those with booster doses, most recorded infections had mild symptoms 45/96, (93.8%) compared with 44/96 (91.7%) among those without booster dose.

Table 5a. *Interval of COVID-19 infection after Primary COVID-19 Vaccine*

Type of Vaccine	<3 months	>3 months – <6 months	>6 months – <9 months	>9 months
Inactivated virus Sinovac	8 (18.6%)	10 (23.2%)	3 (6.9%)	22 (51%)
mRNA Moderna Pfizer	0 (0%) 0 (0%) 0 (0%)	5 (5.2%) 5 (5.2%) 0 (0%)	0 (0%) 0 (0%) 0 (0%)	0 (0%) 0 (0%) 0 (0%)
Viral vector Astra	9 (18.75%)	10 (20.8%)	22 (45.8%)	7 (14.5%)

Table 5a. This table shows that the incidence of breakthrough COVID-19 infection began to increase after the 3rd month of the primary series of inactivated vaccines. Further increases were noted after 9 months from the last dose of inactivated virus. As for the viral vector vaccine, the incidence of infection increases after 6 months from receiving the primary vaccine.

Table 5b. *Interval of COVID-19 infection after COVID-19 booster*

	<3 months	>3 months –	>6 months – <9 months	>9 months
Infection after Booster	1 (2.1%)	1 (2.1%)	19 (39.6%)	27 (56.3%)

Table 5b showed that the interval of infection began to increase 6 months from the last administration of the booster dose. One (2.1%) had breakthrough infection within the first quarter and another one (2.1%) had infection in the 2nd quarter. There was an increasing number of breakthrough infections after 6 months of booster dose, having 19 (39.6%) in the third quarter and 27 (56.3%) in the last quarter.

DISCUSSION

We have a total of 96 respondents composed mainly of females between the age range of 30-40 years 63 (66%), with a mean age of 34 years. Most respondents denied having comorbidities 62/96 (65%), only 34/96 (35%) have identified comorbid conditions, the most common of which were hypertension 18/34 (53%) and type 2 diabetes mellitus 7/34 (21%).[9,10] The findings were consistent with a study by Cortez, Bartolo, et al. which showed that majority subjects afflicted with COVID-19 are females with 1.8:1 ratio, and if with co-morbidities, the most identified as risk factors were hypertension and type 2 diabetes mellitus.[11] The most affected workforce belongs to the nursing service department, comprising nurses 47 (49%) and nursing aides 17 (17.7%), followed by medical technologists 8 (8.3%) and finally, medical doctors 5 (5.2%). The findings of this study were consistent with the study of Velasco et al. wherein among healthcare workers in the Philippines, the most infected with breakthrough infection were females in the 30-39 years age group.[12]

The exposure characteristics of the participants were divided into intrahospital and out of hospital exposure risks. Intrahospital exposure characteristics showed that most infections occurred among those who were assigned in the COVID-19 wards, as well as in direct contact with COVID-19 confirmed patients 58 (84.4%) and those performing aerosol generating procedures 89 (92.7%). Congruent with a study by Bautista et al. which showed that the incidence of infection increases with exposure to high-risk environments.8

With regards to community exposure characteristics, only 15 (15.6%) healthcare personnel had actual contact with known COVID-19 confirmed household contacts, other staff who contracted breakthrough infection used public utility vehicles (52.1%) more than the private vehicles as means of transportation. The findings of this study are consistent with Bandyopadhyay, where public transport was identified as playing a major role in disease transition of COVID-19.

The author identified factors such as longer waiting times resulting in non-compliance with recommended physical distance hence resulting in crowding in bus and jeepney stops as possible community exposure risks for spread of infection.[13]

Majority of the recorded breakthrough infections were mild, 89 (92.7%), only 5 (5.21%) respondents were asymptomatic, and only 1(1%) each presented with moderate and severe symptoms. The most common presenting symptoms were cough 71 (74%), sore throat 59 (61.5%), fever 49 (51%), and loss of taste and smell 22 (22.9%). The clinical course of the breakthrough infection belongs to the asymptomatic and mild group regardless of the primary vaccine received. Only one healthcare personnel respondent was noted to require oxygen supplementation. The findings of this study were consistent with Velasco et al., Bergwerk et al., wherein the clinical course of COVID-19 among healthcare workers who received complete primary series of vaccines with or without booster dose were mostly mild to asymptomatic, does not require hospitalization or use of supplemental oxygen.[5,12]

In relation to the types of COVID-19 vaccines received and the interval of breakthrough infection, a total of 43 (44.8%) respondents received inactivated virus vaccine (Sinovac), a total of 5 (5.2%) received mRNA (Moderna) and a total of 48 (50%) received viral vector vaccine (AstraZeneca). Regardless of the type of vaccine received, findings of this study showed that the incidence of breakthrough infections began to increase 6 months after the initial primary series vaccination.[14] Likewise, the incidence of breakthrough infection among those who received booster doses, began to increase after 9 months. There were only 48 (50%) respondents who received a booster during the time of their breakthrough infection; there was an increase in the number of infections six to nine months after initial administration of the booster dose.

Limitations of the Study

The study was conducted as a single-center one-year descriptive study of healthcare personnel of LCP with breakthrough COVID-19 infections. The study was patterned to the WHO prospective Cohort Study to measure COVID-19 Vaccine Effectiveness among Health workers in the WHO European Region, however, due to time constraint and the discontinuation of routine SARS-CoV-2 Reverse transcription polymerase chain reaction (RT PCR) testing at LCP among its employees, researchers decided to convert the study design into a descriptive study with prospective and retrospective data collection. If funding was available and time was not a problem, a prospective study would provide stronger data to support our hypothesis.

Another limitation of the study was the small sample size since most of the respondents did not consent or answer the questionnaire. Having data from all eligible subjects or at least a bigger sample size would provide more accurate and impactful data.

Other factors that might have affected the results of the study were recall and selection bias. In our study, the questionnaires were handed over to the participants after they had the breakthrough infection. The participants were asked to recall events that transpired weeks or months before the interview. Being in the medical field and frontlines, it was easier to follow up answered questionnaires in the same area.

The timing of the COVID-19 surge in the country and the different variants of SARS-CoV-2 virus can potentially skew the data. A SARS-CoV-2 variant testing aside from the routine swab could provide additional data to the kind of infection that a health worker could have acquired.

CONCLUSION AND RECOMMENDATIONS

This study provides evidence that modifiable and non-modifiable exposure characteristics contribute to acquisition of COVID-19 breakthrough infection. Intrahospital modifiable characteristics include length of exposure to, use of PPE and adherence to instituted infection protocols. Intrahospital non-modifiable factors include job description and involvement in life saving aerosol generating procedures. In the community setting, mostly modifiable exposure characteristics were identified such as participation in indoor gathering events, interaction with COVID-19-confirmed housemates, and use of public vehicles as means of transportation. In general, the severity of COVID-19 infection among healthcare workers is decreased with use of COVID-19 vaccines and its booster, ideally administered within the 6th month and 9th month from the last vaccination.

CONFLICT OF INTEREST

None declared.

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ORIGINAL ARTICLE

LUNG OPACITY SCORE OF COVID–19 PATIENTS AND ITS ASSOCIATION WITH CHEST CT SCAN FINDINGS AND FUNCTIONAL CAPACITY 9 TO 18 MONTHS AFTER DISCHARGE

Joseph Christopher C. Nash, MD, Steffi Joyce Marie C. Abrazaldo, MD, Eileen G. Aniceto, MD, FPCP, FPCCP, Lawrence O. Raymond MD, FPCP, FPCCP, Xanthe Marie G. Javier, MD, FPCR, Julius Zoilo Z. Oliveros, MD, FPCR
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Background. In the Philippines, the total COVID–19 cases have reached over 3.6 million. It has become apparent that not all COVID–19 patients have full symptom resolution, and some patients report the emergence of new symptoms over time.

Objectives. The study aimed to determine the association of Lung Opacity Score during admission with the chest CT scan findings and functional capacity at 9 to 18 months after discharge of COVID–19 patients.

Methodology. This is an ambispective cohort study. Subjects include those who were discharged from Lung Center of the Philippines from March 2021 to March 2022. Lung Opacity Score was determined using CT Pneumonia Analysis from the chest CT scan on admission. Participants were followed up at 9 to 18 months after discharge and underwent high–resolution chest CT scan and assessment of functional capacity.

Results. A total of 731 subjects were invited to participate in the study, and 31 agreed. Most of our patients were middle–aged, female, hypertensive and diabetic, with severe COVID–19 infection, and presenting commonly with symptoms of shortness of breath, cough, fatigue, fever, and myalgia. The majority were classified under Grade 2 (n=19, 61%), pertaining to a Lung Opacity Score of 6–15. More than 50% of the patients had the following CT abnormalities: nodule (90%), curvilinear lines (87%), ground–glass opacities (65%), and traction bronchiectasis (58%). Before admission due to COVID, 87% of patients rated their post–COVID–19 Functional Status (PCFS) as grade 0 (no functional limitation). After discharge, 35% of patients rated their functional capacity as having slight or moderate functional limitation. There were no noted significant association between Lung Opacity Score and chest CT scan findings (p–value > 0.05).

Conclusion. There were no significant association between Lung Opacity Score during admission with the chest CT scan findings and functional capacity 9 to 18 months after discharge of COVID–19 patients. Further studies with a larger sample size may be conducted to perform regression analysis to control for the effects of confounding variables.

Keywords. *COVID–19, lung opacity, computed tomography, chest CT scan, functional capacity*

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INTRODUCTION

In 2019, a novel coronavirus, designated as COVID-19 disease by the World Health Organization, was identified as the cause of pneumonia cases initially seen at Wuhan, China that rapidly spread with increasing number throughout the world.[1] As of May 27, 2022, cumulative COVID-19 cases globally have been 525,467,084 confirmed cases and deaths have reached 6,285,171.[2] In the Philippines alone, the total COVID-19 cases have reached over 3.6 million, and deaths have reached over 60,455 based on the DOH COVID-19 tracker data.[3] It has become apparent that not all patients experiencing COVID-19 have full symptom resolution, and some patients report the emergence of new symptoms over time. In the Patient-Led Research Collaborative, which was established in partnership with University College London, which included 3,762 respondents from 56 countries, 3,608 (96%) still have symptoms of more than 90 days.[4] In the prospective cohort study (Bergamo Project Italy), which is focused on follow up of high-risk COVID-19 patients, the following symptoms were commonly reported: dyspnea (509/1524, 33%), reduced diffusing capacity for carbon monoxide (DLCO) (346/1289, 28%) and post-traumatic stress disorder (PTSD) (477/1467, 32%).[5]

In the Lung Center of the Philippines (LCP), an average of 100-200 COVID-19 patients are admitted per month. In COVID-19 patients in whom imaging of the chest is indicated, chest radiography is initially requested. However, initial chest radiograph may be normal even in the setting of COVID-19 severe disease. In which case, chest CT scan is more effective in optimizing management and prognostication of COVID-19 patients. In a multicenter retrospective study done by Zhichao Feng, et al. lung severity scores on admission are independent risk factors for short-term progression during hospitalization. Currently there are limited studies available in the country determining its ability to predict clinical outcomes after discharge and predict development of post COVID-19 conditions.[6]

In this regard, we assessed the association of the lung opacity score with chest CT scan findings and functional capacity of COVID-19 patients, on admission and on follow-up at 9 to 18 months after discharge. Specifically, we aim to determine the baseline clinico-demographic profile of COVID-19 patients and the relationship of Lung Opacity Score on admission and the presence of the following chest CT scan findings at 9 to 18 months after discharge: architectural distortion, Bronchocele, consolidation, ground-glass opacities, honeycombing, mosaic attenuation pattern, nodule, perilobular consolidation, pneumatoceles, reticulations, curvilinear lines, pleural thickening or pleural effusion, mucus plugging and traction bronchiectasis or bronchiolectasis. We also aim to describe the functional capacity of patients based on the post-COVID-19 Functional Status Scale (PCFS) 1 month prior to admission and at 9 to 18 months after discharge.

METHODOLOGY

Study Design

This study used an ambispective study design.

Study Site

The study was conducted at the Lung Center of the Philippines (LCP), a government specialty hospital with a 210-hospital bed capacity. During the COVID-19 pandemic, LCP became one of the referral centers in Metro Manila for COVID-19 patients with moderate to critical condition. LCP allocated 160 beds dedicated for COVID-19 patients.

Study population

The participants of the study were patients 19 years old and above who were discharged from March 2021 to March 2022 with a final diagnosis of COVID-19 Moderate, Severe, or Critical, and with chest CT scan during admission performed in the institution. We excluded patients whose chest CT scan findings during admission were attributable to lung cancer and pleural effusion, those with COVID-19 infection who have died during their admission or after discharge, those who were currently pregnant at the time of recruitment, those who were non-ambulatory, homebound or residing outside of Metro Manila. We further excluded patients who refused to continue participation (repeat chest CT scan and post-COVID-19 Functional Status Scale questionnaire administration), and those whose chest CT scan findings were attributable to lung cancer and pleural effusion during follow-up.

Study Instrument/Intervention
Post-COVID-19 Functional Status Scale (PCFS)

Functional status was assessed according to the PCFS questionnaire, which consists of an ordinal scale (six grades) for assessment of patient-relevant functional limitations. **Grade 0** reflects the absence of any functional limitation; **Grade 1:** negligible limitations with persistent symptoms but this has no effect on everyday life; **Grade 2:** limitations in everyday life, occasionally needs to avoid or reduce usual activities; **Grade 3:** limitations in everyday life and the patient is not able to perform all usual activities; **Grade 4:** severe functional limitations requiring assistance with activities of daily living; and **Grade 5:** death. For this study, grade 5 was not included.

Additionally, patients were asked to retrospectively recount their functional status 1 month before COVID-19 infection using the PCFS scale as reference. The principal investigators (both licensed physicians and Pulmonary fellows-in-training) and research assistant conducted the interview to arrive at the patient's functional status scale. Assigning the appropriate PCFS scale grade was done using the patient questionnaire. The interviewers encouraged the participants to give a rating based on their ability to perform

the activity rather than whether they currently perform that activity. This prevented overestimation of the severity of the symptoms in patients who have chosen to abandon or who simply never performed certain activities during their COVID-19 diagnosis.

The PCFS scale by Klok, et al. is a European Respiratory Society (ERS) validated tool to identify people with persistent symptoms related to COVID-19 infection. The study, with acceptable validity according to the COSMIN (Consensus-based Standards for the selection of health Measurement Instruments) after comparing with other scales, showed that the PCFS scale is suitable in detecting functional limitations in relation to persistent symptoms.[7] PCFS is a validated tool in detecting functional status among post-COVID-19 patients but is not a validated tool to assess the patient's functional status prior to COVID-19 infection. The researchers obtained permission from the authors to use the English version of the PCFS scale.

Chest CT scan: Image Acquisition and Analysis

Patients underwent a high-resolution chest CT scan on the patient's follow-up within 9 to 18 months after discharge. All chest CT examinations were performed using one multidetector 16-slice CT scan (SOMATOM go.Now,® Siemens-Healthineers, Germany) with the following parameters: Tube voltage = 110 kvp, Tube current (quality reference mAs) = 71 mAs, Pitch = 1.5, Matrix = 512 x 512, Slice thickness = 1.5 mm and FOV= 300 mm. Patients were scanned in supine position during an inspiratory breath-hold, moving from the lung bases to the apex. Image reconstruction was done at a slice thickness of 1.5 mm. Multiplane reconstructions were performed in axial, coronal and sagittal planes as required. All images were reconstructed with lung and soft tissue kernels and stored in the local picture archiving and communication system (PACS).

Images done during admission and on follow-up were obtained for review. Two experienced radiologists (12 and 8 years of practice) independently reviewed the images. A final finding was reached via consensus when a discrepancy was found. The radiologists were blinded to the patients' clinical information or progress except for the knowledge that these images were obtained from patients with COVID-19.

Ancillary chest CT findings were defined in accordance with the Fleischner Society terminology.[8] The presence of the following chest CT patterns were visually assessed: consolidation, ground-glass opacities (focal, multifocal, diffuse), mosaic attenuation pattern (hypoattenuating areas, hyperattenuating areas), perilobular consolidation (organizing pneumonia-like pattern), reticulations, architectural distortion, honeycombing, traction bronchiectasis, pneumatoceles, curvilinear lines, nodules, pleural thickening or pleural effusion, mucus plugging, vascular abnormalities and additional findings were annotated separately. Additionally, pattern distribution was recorded (upper lobe, middle lobe/lingual, lower lobe). If no CT pattern could be clearly identified as predominant, the two most representative coexisting patterns were noted.

Quantitative Image Analysis

The CT Pneumonia Analysis system (Siemens Healthcare), an Artificial Intelligence algorithm, was used on each patient's CT scan during admission. The system was designed to automatically identify and quantify abnormal tomographic patterns in the lungs from chest CT for research purposes, particularly areas of increased opacities such as consolidations and ground glass opacities, which were common features of patients with COVID-19 pneumonia.[9] The system takes as input a non-contrast chest CT, identifies and 3D segments the lungs and lobes before segmenting the abnormalities.[9] It outputs two combined measures of the severity of lung/lobe involvement, quantifying both the extent of COVID-19 abnormalities and presence of high opacities.[9] High opacity abnormalities are shown to correlate with severe symptoms.[9]

Lung Opacity Score was calculated for each lobe by estimating the given region percent opacity as follows: score = 0, no involvement to a lobe (0%); score = 1, 1 to 25%; score = 2, 26 to 50%; score = 3, 51 to 75%; score = 4, 76 to 100%. The total score is the sum of these values.[10]

The scores for each of the five lobes were summed to calculate the result in a total score range from 0-20. A 0 score indicates that none of the lobes were involved and 20 indicates that all five lobes were severely affected. All these measurements were automatically obtained and computed by the AI system. To ensure the accuracy of the computations, the radiologists reviewed the images and ensured that the region of interests and abnormal tomographic patterns in the CT scans were properly identified by the AI system.[10]

Study Procedure

A master list was created from the monthly discharged database from March 2021 to March 2022 which included patient's initials, contact number, hospital number, date of discharge and discharge diagnosis (COVID-19 moderate, severe, or critical).

The primary investigators manually checked, using the patient's hospital number, the Radiology Information System whether a chest CT scan (non-contrast or contrast) was done during admission. Patients who do not have chest CT scans done during admission were excluded. Eligible participants were prospectively followed up at 9 to 18 months post-discharge.

Participants were contacted through phone calls for further screening and consent administration. The primary investigators explained the study objectives, procedure, risks, and benefits to the patient. To affirm voluntary participation, a copy of the informed consent was sent to them thru Viber, messenger, or email, depending on their preference. After they have signed the consent, it was sent back to the researchers. The investigators actively followed up the signed informed consent within 48 hours. Failure to secure the said consent within that time was considered as non-response. Once the consent form was signed, participants were scheduled for face-to-face interview and high-resolution chest CT scan.

Upon participation, the clinical-demographic information was obtained by chart review and recorded in a data collection form (Appendix A): age, sex, comorbidities, symptoms, date of discharge and disease severity. A structured face-to-face interview was conducted to administer the PCFS scale (Appendix B) for assessment of the functional capacity. Each patient was asked about their current functional capacity and their functional capacity 1 month prior to admission for COVID-19 infection.
The study obtained the Chest CT scan of patients by using CT Pneumonia Analysis algorithm where the lung opacity score and ancillary chest CT scan findings were obtained. The lung opacity score was obtained from the CT scan done during admission, whereas the ancillary chest CT scan findings were determined from the high-resolution chest CT scan that was done on follow up.

Sample Size and Sampling Design

The researchers utilized a purposive sampling technique to select study participants. A list of all patients discharged from LCP between March 2021 to March 2022 was retrieved from the COVID-19 census in the medical records.

However, due to the limited number of patients that were contacted for follow-up CT scan, the initial plan to include 100 patients in the study and to do stratified random sampling was no longer feasible. A total of 31 patients agreed to participate in the study.

Statistical Analysis

Data were encoded in Microsoft Excel by the researchers. Stata MP version 17 software was used for data processing and analysis. Continuous variables were presented as mean (standard deviation/SD) or median (interquartile range/IQR) depending on the data distribution. Categorical variables were expressed as frequencies and percentages. Fisher's exact test was performed to determine the association between Lung Opacity Score at baseline and the following outcomes: 1) ancillary chest CT findings, and 2) functional capacity 9-18 months after discharge (dichotomized to Grade 0 and Grade 1-4). P values ≤0.05 were considered statistically significant.

Ethical Considerations

This study was approved by the Lung Center of the Philippines Technical Review Board (TRB) and Institutional Ethics Review Board (IERB) prior to implementation and was conducted in compliance with publication standards and the National Ethical Guidelines for Health and Health-related Research. They were also informed of any amendments made to the protocol and sought their approval prior to proceeding with the study.

RESULTS

Patient Recruitment

Between March 2021-March 2022, there were 731 discharges at the Lung Center of the Philippines related to COVID-19 infection (Moderate, Severe, and Critical). A total of 700 patients were excluded from the study: 400 did not consent due to unavailability and 300 could not be contacted either due to wrong contact number information, cannot be reached, unattended, or no response. A total of 31 subjects were included in the data analysis of this study (Figure 1).

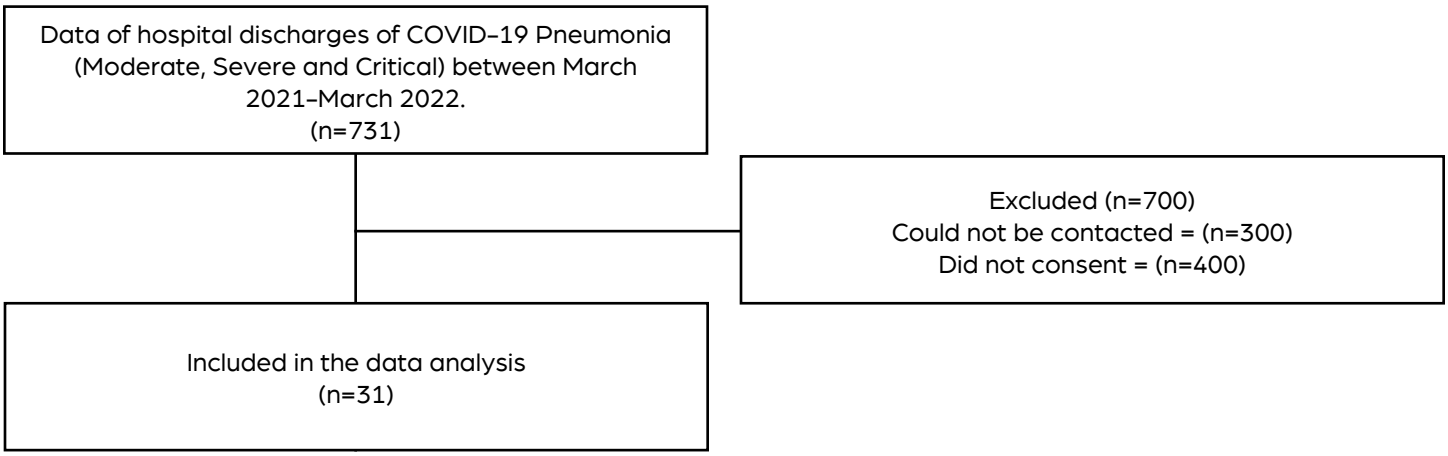


Figure 1. *Flow chart of patients included in the study.*

Baseline Characteristics and Demographic Data

Table 1 presents the clinico-demographic profile of the COVID-19 patients admitted in LCP from March 2021 to March 2022. The median age was 53 years old, range: 25-73 years old. About a quarter were ≥ 60 years old. Most were females. Most common comorbidities were hypertension (48%) and DM (32%). Four patients had other comorbidities, including PCOS (n=1), obesity (n=1), thyroid mass (n=1), and gout (n=1). About a third of the patients had moderate COVID-19, while the rest had severe and critical disease.

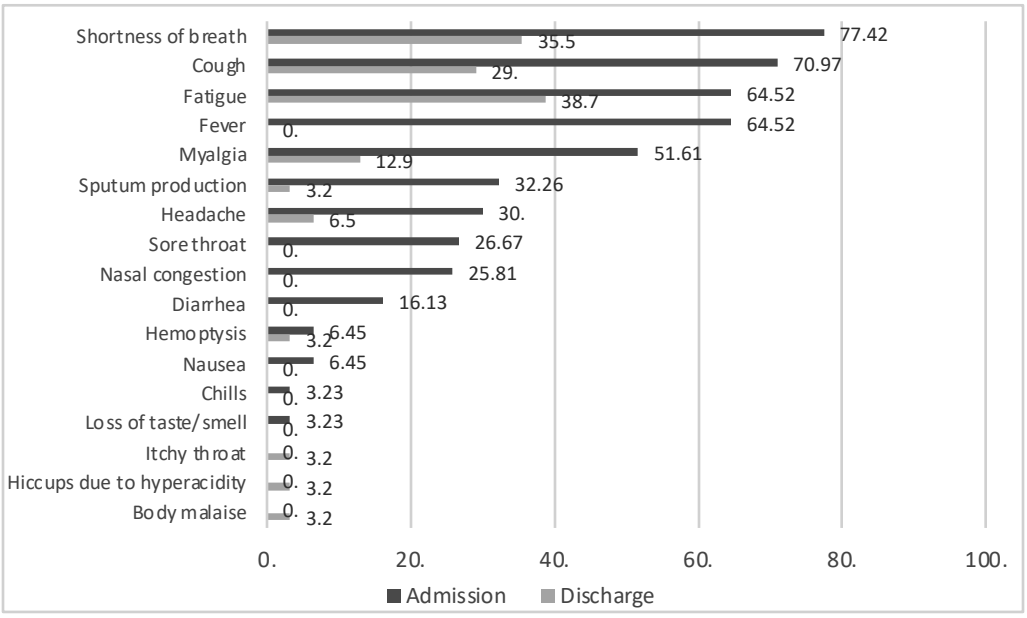
Table 1. *Clinico-Demographic Profile of COVID-19 Patients, Lung Center of the Philippines, March 2021 to March 2022 (n=31)*

CHARACTERISTICS	n (%)
Age (in years), median	53 [IQR: 51-60]
<60 years old	8 (26)
≥60 years old	23 (74)
Sex	
Male	14 (45)
Female	17 (55)
Comorbidities, %yes	
Hypertension	15 (48)
Diabetes Mellitus	10 (32)
Nephrological	3 (10)
Neurological	0
Respiratory	3 (10)
Digestive	1 (3)
Others	4 (13)
Disease severity	
Moderate	10 (32)
Severe	16 (52)
Critical	5 (16)

Symptoms on admission and discharge among COVID-19 patients

On admission, the most common symptoms were shortness of breath (77%), cough (71%), fatigue (65%), fever (65%) and myalgia (52%). Except for new occurrences of itchy throat, hiccups caused by hyperacidity, and body malaise, all symptoms on admission were reduced upon discharge. Fatigue, shortness of breath, and cough were noted to be the most prevalent symptoms upon discharge (Figure 2).

Figure 2. *Symptoms on admission and discharge among COVID-19 Patients, Lung Center of the Philippines, March 2021 to March 2022 (n=31)*



Association between Lung Opacity Score on admission and ancillary chest CT findings on 9-18 months after discharge

All patients

The mean Lung Opacity Score on admission was 8.23±4.16, range: 0-17. Majority were classified under Grade 2 (n=19, 61%), pertaining to a score of 6-15. Table 2 presents the association between the Lung Opacity Score on admission and ancillary chest CT findings 9-18 months after discharge. More than 50% of the patients had the following CT abnormalities: nodule (90%), curvilinear lines (87%), ground-glass opacities (65%), and traction bronchiectasis (58%). None of the patients had bronchocele. No significant association was observed between lung opacity score and any of the chest CT findings.

Table 2. *Association between Lung Opacity Score on admission and ancillary chest CT findings on 9-18 months after discharge.*

	All patients (n=31) n (%)	Lung Opacity Score				P value
		Grade 0 (n=1) n (%)	Grade 1 (n=9) n (%)	Grade 2 (n=19) n (%)	Grade 3 (n=2) n (%)	
Architectural distortion						
With	1 (3)	0	1 (11)	0	0	0.387a
Without	30 (97)	1 (100)	8 (89)	19 (100)	2 (100)	
Bronchocele						
With	0	0	0	0	0	-
Without	31 (100)	1 (100)	9 (100)	19 (100)	2 (100)	
Consolidation						
With	6 (19)	0	3 (33)	2 (11)	1 (50)	0.274a
Without	25 (81)	1 (100)	6 (67)	17 (89)	1 (50)	

Ground-glass opacities						
With	20 (65)	0	7 (78)	12 (63)	1 (50)	0.501a
Without	11 (35)	1 (100)	2 (22)	7 (37)	1 (50)	
Honeycombing						
With	1 (3)	0	0	0	1 (50)	0.097a
Without	30 (97)	1 (100)	9 (100)	19 (100)	1 (50)	
Mosaic attenuation pattern						
With	4 (13)	0	0	4 (21)	0	0.527a
Without	27 (87)	1 (100)	9 (100)	15 (79)	2 (100)	
Nodule						
With	28 (90)	1 (100)	7 (78)	18 (95)	2 (100)	0.442a
Without	3 (10)	0	2 (22)	1 (5)	0	
Perilobular consolidation						
With	1 (3)	0	0	1 (5)	0	1.000a
Without	30 (7)	1 (100)	9 (100)	18 (95)	2 (100)	
Pneumatoceles						
With	3 (10)	0	1 (11)	1 (5)	1 (50)	0.290a
Without	28 (90)	1 (100)	8 (89)	18 (95)	1 (50)	
Reticulations						
With	3 (10)	0	0	3 (16)	0	0.658a
Without	28 (90)	1 (100)	9 (100)	16 (84)	2 (100)	
Curvilinear lines						
With	27 (87)	1 (100)	7 (78)	17 (89)	2 (100)	0.723a
Without	4 (13)	0	2 (22)	2 (11)	0	
Pleural thickening or pleural effusion						
With	7 (23)	0	2 (22)	5 (26)	0	1.000a
Without	24 (77)	1 (100)	7 (78)	14 (74)	2 (100)	
Mucus plugging						
With	3 (10)	0	1 (11)	2 (11)	0	1.000a
Without	28 (90)	1 (100)	8 (89)	17 (89)	2 (100)	
Traction bronchiectasis						
With	18 (58)	0	5 (56)	11 (58)	2 (100)	0.591a
Without	13 (42)	1 (100)	4 (44)	8 (42)	0	

[a] *Fisher's exact test was used*

By disease severity

As seen in Appendix D, the mean lung opacity score showed an increasing trend as COVID-19 severity increases. None of the severe and critical cases were graded as 0, and majority of the severe-to-critical cases were Grade 2. Grade 3 lung opacity score was only reported in two patients, both had critical COVID-19.

Ancillary chest findings by COVID-19 severity were presented in Appendix D. Across all severity, the most common findings were nodule, ground-glass opacities, traction bronchiectasis, and curvilinear lines. Among critical COVID-19 cases, all presented with nodule and curvilinear lines, 80% with traction bronchiectasis, and 60% with ground glass opacities. Similarly, ≥50% of moderate and severe cases (Figures 5 and 6) presented with the mentioned ancillary findings. Honeycombing was only observed in critical cases, affecting 20% of the patients. Meanwhile, only severe cases presented with mucus plugging (19%) and architectural distortion (6%).

Appendix E presents the cross-tabulation of lung opacity score and chest CT finding by disease severity. The lone moderate COVID-19 patient with Grade 0 LOS presented with nodule and curvilinear lines on chest CT 9-18 months after discharge. Similarly, all moderate COVID-19 cases with Grade 2 LOS presented with nodule (Figure 3), curvilinear

lines. Majority of cases with Grade 1 LOS exhibited ground-glass opacities (67%), nodule (67%), curvilinear lines (67%), and traction bronchiectasis (67%). Among severe COVID-19 patients with Grade 1 and 2 LOS, most presented with ground-glass opacities, nodules, curvilinear lines (Figure 6) and traction bronchiectasis (Figure 4). In critical COVID-19 patients, Grade 2 and 3 LOS were noted, with ground-glass opacities (Figure 4), nodule, curvilinear lines and traction bronchiectasis being the most observed ancillary CT scan finding.

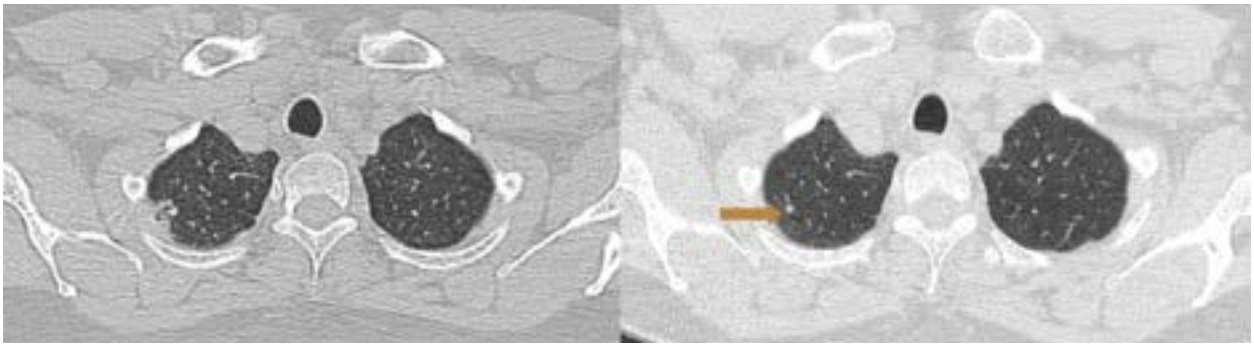


Figure 3. *Axial chest CT image in lung window setting of a 54-year-old female moderate COVID-19 patient. Image upon admission (left) demonstrates a sub centimeter nodule in the apical segment of the right upper lobe with unchanged appearance in the follow-up CT examination done after 13 months (right).*

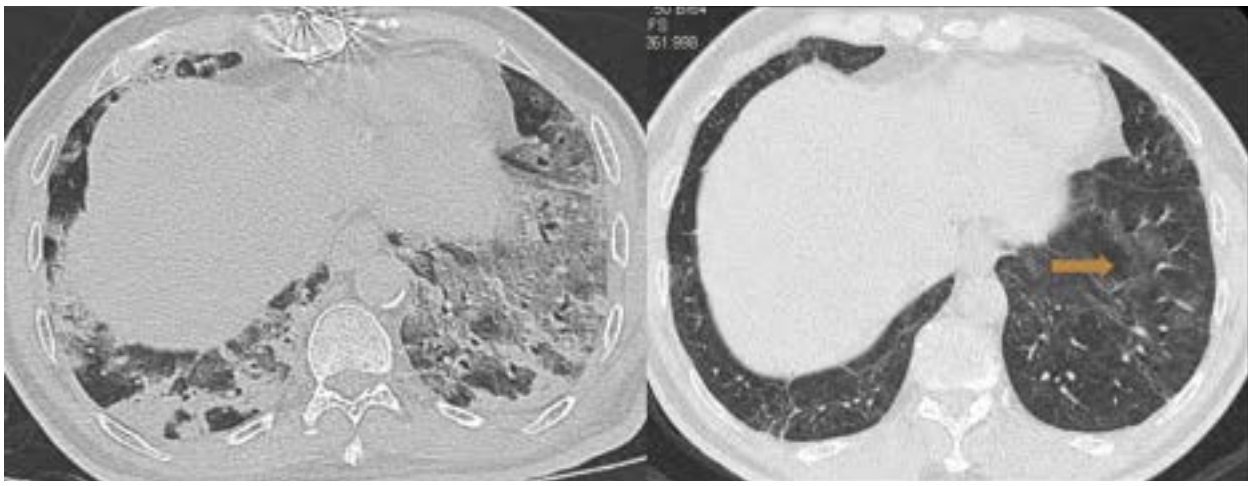


Figure 4. *Axial chest CT image in lung window setting of a 64-year-old male critical COVID-19 patient. Upon admission, CT image exhibits extensive areas of consolidation (left). Areas of ground glass opacities remain in both lungs in the following CT study done 13 months after (right).*

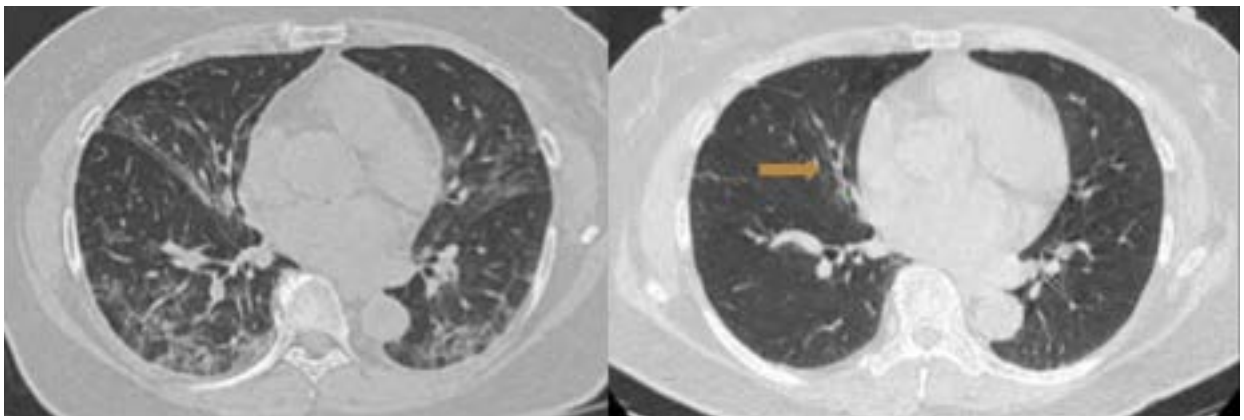


Figure 5. *Axial chest CT image in lung window setting of a 67-year-old female severe COVID-19 patient. Initial admission study shows traction bronchiectasis in the medial segment of the right middle lobe (left). Follow-up CT done 18 months later reveals stable traction bronchiectasis in the middle lobe (right).*

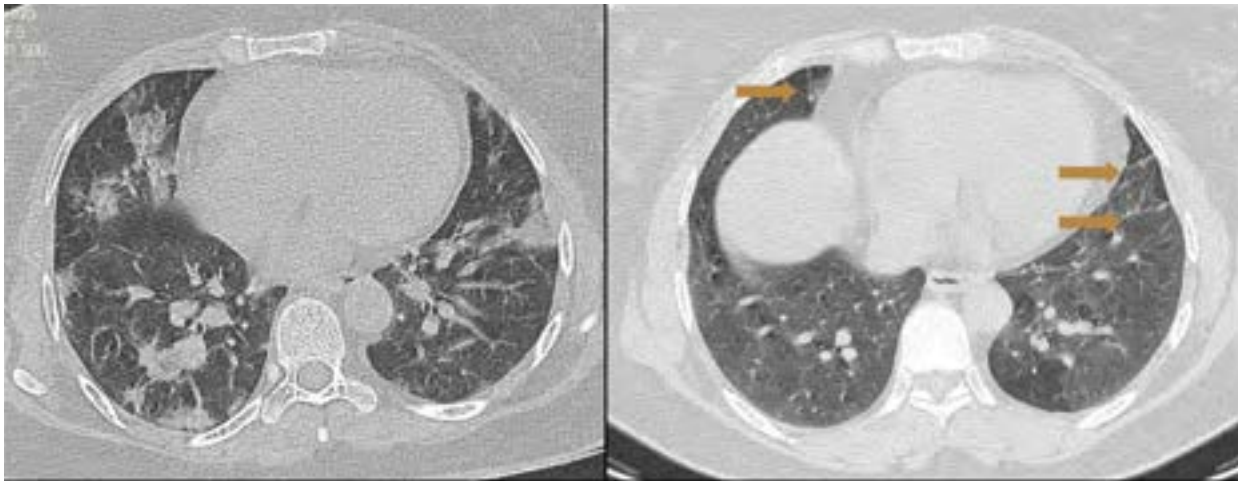


Figure 6. *Axial chest CT images in lung window setting of a 47-year-old female severe COVID-19 patient. Initial (left) and follow-up chest CT studies done 18 months after (right) exhibiting stationary curvilinear densities in the medial segment of the right middle lobe and lingula.*

Post-COVID-19 Functional Scale 1 month before admission and 9 to 18 months after discharge

Before admission due to COVID-19, 27 (87%) of patients rated their PCFS as Grade 0. Of these patients, only 41% remained Grade 0 9-18 months after discharge. Meanwhile, of the four patients with Grade 1 on admission, only one patient (25%) remained Grade 1 9-18 months post-discharge.

By disease severity

When analyzed by disease severity (Appendix F), the majority (80%) rated their PCFS as Grade 0 prior to their admission due to COVID-19. Among these patients, 38% of moderate COVID-19 patients and ≥ 40% of both severe and critical patients remained Grade 0 9-18 months post discharge. Based on our data, patients who rated their PCFS from Grade 0 prior to their COVID-19 admission to Grade 3 9-18 months post-discharge were only noted among severe and critical COVID-19, 7% and 20% respectively. None rated their PCFS as Grade 4 on both PCFS before admission and 9-18 months after discharge.

Table 3. *PCFS 1 month before admission and 9-18 months after discharge (n=31)*

1 month before admission	9-18 months post-discharge				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Grade 0 (n=27)	11 (41)	9 (33)	5 (19)	2 (7)	0
Grade 1 (n=4)	0	1 (25)	2 (50)	1 (25)	0
Grade 2 (n=0)	-	-	-	-	-
Grade 3 (n=0)	-	-	-	-	-
Grade 4 (n=0)	-	-	-	-	-

Grade 1: negligible limitations with persistent symptoms but with no effect on everyday life; grade 2: limitations in everyday life, with occasional need to avoid or reduce usual activities; grade 3: limitations in everyday life and the patient was not able to perform all usual activities; and grade 4: severe functional limitations requiring assistance with activities of daily living

Association between Lung Opacity Score on admission and PCFS 9–18 months after discharge

All patients

Majority of the patients have Lung Opacity Score (LOS) of Grade 1 and 2 on admission. Among the patients with grade 1 LOS on admission, 3 (33%) rated their PCFS 9–18 months after discharge as Grade 0 while 6 (67%) rated their PCFS as Grade 1–4. In contrast to those 2 patients whose LOS are Grade 3 on admission, both rated their PCFS 9–18 months after discharge as with functional limitations. No significant association between lung opacity score on admission and PCFS 9–18 months post-discharge (Table 4).

By disease severity

As seen in Appendix G, the predominant LOS grade among moderate and severe COVID-19 patients are Grade 1 and Grade 2. In moderate COVID-19 patients with LOS Grades of 1 and 2, none has rated their PCFS 9–18 months after discharge as Grade 3. Meanwhile, no LOS Grade of 0 or 1 was noted among critical COVID-19 patients.

Table 4. *Association between Lung Opacity Score on admission and PCFS 9–18 months after discharge*

Lung Opacity Score	PFCS		P-VALUE
	Grade 0	Grade 1–4	
Grade 0	0	1 (100)	0.819a
Grade 1	3 (33)	6 (67)	
Grade 2	8 (42)	11 (58)	
Grade 3	0	2 (100)	

[a] Fisher's exact test was used. Post-COVID-19 Functional Scale (PCFS) Grade. Grade 0, no functional limitation; Grade 1–4, with functional limitation. Lung Opacity Score (LOS) Grade. Grade 0: total lung opacity score of 0; Grade 1: total lung opacity score of 1–5; Grade 2: total lung opacity score of 6–15; Grade 3: total lung opacity score of 16–20.

DISCUSSION

As the global COVID-19 pandemic has progressed, evidence has emerged that some patients are experiencing prolonged multi-organ symptoms after COVID-19 infection. Understanding the changes in chest CT scan and the functional capacity was the first step in the accurate and effective way of designing effective intervention for post COVID-19 cases. The study sought to provide the needed data such as chest CT scan changes and functional status of COVID-19 patients to fully understand the nature of the disease and how it affects their functional status.

Clinico-Demographic Profile

In our study, the median age was 53 years old, and the most common comorbidities were hypertension and diabetes mellitus, similar to the findings of Zhang, S et al.[12] According to studies, the most frequent symptoms after 6 months were fatigue, post-exertional malaise, and cognitive dysfunction[4]. Similarly in our study, the most common symptoms 9–18 months after discharge were fatigue, followed by shortness of breath, cough and myalgia.

Lung Opacity Score and Ancillary Chest CT Findings

Previous evidence suggests that Lung Opacity Score correlated positively with COVID-19 disease severity resulting in poor clinical outcomes, including patients with severe and critical illness, history of ICU admission, respiratory failure and prolonged hospital stay.[13] We noted that as the LOS grade increases, there was a corresponding increase in the patient's disease severity.

In a prospective, longitudinal, cohort study by Xiaojun Wu, wherein residual changes seen at 9 months after discharge of recovered severe COVID-19 patients, ground-glass opacity, interlobular septal thickening, reticular opacity, mosaic attenuation and subpleural curvilinear opacity were the most common CT features found.[14] In the study done by Parry et al, the dominant pulmonary opacities observed on follow-up CT included GGO, curvilinear opacity, interlobular septal thickening, and bronchiectasis.[15] However, our study noted a predominance of nodule (90%) in more than 50% of the patients. This was followed by the presence of curvilinear lines (87%), ground-glass opacities (65%) and traction bronchiectasis (58%), which was consistent with the findings of Xiaojun Wu and Parry, et al. The studies of Zhichao Feng and Huanyuan Luo showed that a higher CT opacity score correlates with a higher proportion of lobes involved and a higher disease severity, supporting the findings of our study.

In our overall analysis, we found out that there were no significant association between lung opacity score and any of the chest CT findings. While there was a dearth of study which correlates the lung opacity score and chest CT findings, however, in the study by Parry et. al, they noted a positive correlation between presence of residual lung opacities on follow-up CT and initial CT severity score.[15] The low sample size in our study could have led to a low statistical power in our study; thus, explaining the lack of association.

Functional Capacity

Some patients reported a reduction in function post-COVID-19. In our study, we noted that among patients who initially rated their PCFS as Grade 0 1 month prior to admission, majority were noted to have a regression in their functional capacity as 59% rated their PCFS from Grade 1 to 3 after discharge across all disease severity. Congruent with the other studies, the functional status of post-COVID-19 patients was found to be affected by disease severity and the presence of post-COVID-19 symptoms.[16] The reduction in the functional status among post-COVID-19 patients may be due to the persistence of post-COVID-19 symptoms. Our findings are consistent with that of Gamal et al, which found that COVID-19 has shown a negative impact on post-COVID-19 patients' PCFS.[16] Our study was one of the few to assess the functional status among post-COVID-19 patients using PCFS, a validated, specific, and easy-to-use tool that can be applied to the patients.

Lung Opacity Score and Functional Capacity

We observed that while most severe cases of COVID-19 presented with an LOS of Grade 1-2, and critical patients had an LOS of Grade 2-3, their PCFS were noted to be at Grade 1-3. There is, however, a lone case of a critical COVID-19 patient who had an LOS of Grade 2 but with a PCFS of Grade 0 post-discharge. Whereas a moderate COVID-19 patient presented with an LOS of Grade 0 but with a PCFS of Grade 1 after discharge.

We have analyzed that there were no significant association between lung opacity score on admission and PCFS 9 to 18 months post-discharge. This was compatible with other studies that observed no correlation between PCFS and lung opacity score, suggesting that symptom burden has no correlation with the initial severity or existence of lung abnormalities.[17,18] Again, a possible reason for non-significant association is the low sample size. Furthermore, owing to this low sample size, we were unable to control for possible confounders, and sub-analysis by disease severity was not performed.

CONCLUSION

In this study, most of our patients are middle-aged, female, hypertensive and diabetic, with severe COVID-19 infection, with the most common presenting symptoms of shortness of breath, cough, fatigue, fever, and myalgia. Majority were classified with a lung opacity score of Grade 2. More than half of the patients were noted to have nodules, curvilinear lines, ground-glass opacities, and traction bronchiectasis on chest CT scan. However, no significant association was observed between lung opacity score and any of the chest CT findings. Prior to admission due to COVID-19, most of the patients rated their PCFS as having no functional limitation. This further reduced to less than half 9-18 months after discharge. After discharge, about a third of patients rated their functional capacity as having slight or moderate functional limitation. There were no noted significant association between lung opacity score on admission and PCFS 9-18 months post-discharge.

LIMITATIONS

This study has its limitations. As one of the referral centers for COVID-19, LCP caters to mostly severe to critically ill patients, which was why more than two-thirds of the patients included in the study belonged to the severe and critical disease severity. These characteristics of patients admitted in LCP may be different from other institutions. Moreover, management of COVID in LCP compared with other institutions may also differ, which may lead to differences in the residual lung changes and physiologic or functional impairment of patients. The result of this study may therefore have limited generalizability. Furthermore, the non-participation rate was 95%. Those who failed to return for the repeat CT scan were mostly older patients and have higher disease severity which may have affected their means to consult at this institution. There were also cases where patients can no longer be contacted. Moreover, those who agreed to participate are those with persistent symptoms. These factors could contribute to the selection bias.

While medical charts and the result of the previous chest CT scan done during admission were sources of information for this study, to minimize bias, we have retrieved again the chest CT scan images and have two radiologists review these. The repeat chest CT scans were also performed and reviewed by the same radiologists and blinding was performed to minimize information bias.

Initially, we have planned to perform regression analysis to control for the effects of confounding variables. However, due to the low sample size attained, this was no longer feasible. Subgroup analysis by disease severity was also no longer feasible. The low sample size could have led to the low statistical power, which may explain the lack of association observed in the study.

RECOMMENDATIONS

While there has not been an established optimal time for follow-up imaging to assess for radiologic sequelae of COVID-19, we echo the recommendation provided in the study of Parry et al, wherein follow-up CT was not recommended if patients do not present with pneumonia during the initial phase of the disease or those with noted resolution of lung findings based on the chest X-ray upon discharge. Chest CT scan can be done for patients with significant lung findings on chest X-ray or those with persistent symptoms or functional impairment.

The researchers propose that a follow-up study be done that will include a larger sample size of patients admitted and managed as COVID-19. This can be achieved by including patients admitted at other institutions, while also ensuring a longer period for data collection. To improve recruitment and participation of patients, follow-up on discharge and early enrollment at LCP's post-COVID-19 Clinic can be explored. This will improve the statistical power of the study, controlling for the confounding bias, and aid in establishing a significant finding in terms of the association between lung opacity score and the functional capacity of patients after discharge. The development of a post-COVID-19 clinic can aid in maximizing medical management, based on the patient's symptoms, comorbidities and treatment goals. The inclusion of PCFS on follow up could also be explored, to determine the functional capacity of patients after discharge, which can also be the basis for early pulmonary rehabilitation.

Furthermore, the differences in results by disease severity on admission can also be examined. Review of ancillary findings of chest CT scan of patients on admission can also be included in the study to compare with the CT scan findings on follow-up, to establish whether the ancillary findings on follow-up were related to COVID-19 infection or attributable to other lung diseases. In addition, performance of pulmonary function tests on follow-up could provide information on the impairment of the lungs.

ACKNOWLEDGEMENTS

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FUNDING

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CONFLICT OF INTEREST

None declared.

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APPENDIX A. DATA COLLECTION TOOL

Study Code	
Date of admission (mm/dd/yyyy)	
Date of discharge (mm/dd/yyyy)	Date of follow up (mm/dd/yyyy)
Age on admission	____ years old
Sex	☐ Male ☐ Female
Comorbidities Check all that applies	☐ Hypertension ☐ Diabetes Mellitus ☐ Nephrological (e.g., chronic kidney disease) ☐ Neurological (e.g., Stroke) ☐ Digestive (e.g., Hepatitis) ☐ Others, specify: _____
Symptoms on admission Check all that applies	☐ Fever ☐ Headache ☐ Cough ☐ Fatigue ☐ Hemoptysis ☐ Nausea ☐ Vomiting ☐ Myalgia ☐ Conjunctival congestion ☐ Nasal congestion ☐ Sore throat ☐ Sputum production ☐ Shortness of breath ☐ Diarrhea
Symptoms on discharge Check all that applies	☐ Fever ☐ Headache ☐ Cough ☐ Fatigue ☐ Hemoptysis ☐ Nausea ☐ Vomiting ☐ Myalgia ☐ Conjunctival congestion ☐ Nasal congestion ☐ Sore throat ☐ Sputum production ☐ Shortness of breath ☐ Diarrhea
Disease severity	☐ Moderate ☐ Severe ☐ Critical
CT opacity score: CT on admission	

Ancillary Findings: CT on follow-up (Mark if PRESENT or ABSENT)	PRESENT	ABSENT
1. Consolidation		
2. Ground-glass opacities: (focal, multifocal, diffuse)		
3. Mosaic attenuation pattern (hypoattenuating areas, hyperattenuating areas)		
4. Perilobular consolidation (organizing pneumonia-like pattern		
5. Reticulations		
6. Architectural distortion		
7. Honeycombing		
8. Traction bronchiectasis		
9. Pneumatoceles		
10. Curvilinear lines		
11. Nodules		
12. Pleural thickening or pleural effusion		
13. Mucus plugging		

APPENDIX B. Post-COVID-19 Functional Status Scale (PCFS)

How much are you currently affected in your everyday life by COVID-19? **Please indicate which one of the following statements applies to you most.** *Please tick only one box at a time.*		**Corresponding PCFS scale grade if the box is ticked**
I have no limitations in my everyday life and no symptoms, pain, depression or anxiety.	☐	0
I have negligible limitations in my everyday life as I can perform all usual duties/activities, although I still have persistent symptoms, pain, depression or anxiety.	☐	1
I suffer from limitations in my everyday life as I occasionally need to avoid or reduce usual duties/activities or need to spread these over time due to symptoms, pain, depression or anxiety. I am, however, able to perform all activities without any assistance.	☐	2
I suffer from limitations in my everyday life as I am not able to perform all usual duties/activities due to symptoms, pain, depression or anxiety. I am, however, able to take care of myself without any assistance.	☐	3
I suffer from severe limitations in my everyday life: I am not able to take care of myself and therefore I am dependent on nursing care and/or assistance from another person due to symptoms, pain, depression or anxiety.	☐	4

Siegerink, B., Boon, D., Barco, S., Klok, E., & Le, J. (2022, July 12). The Post-COVID-19 Functional Status (PCFS) Scale: a tool to measure functional status over time after COVID-19. https://doi.org/10.17605/OSF.IO/QGPDV

ANNEX C. Outcome Measures

Independent variables

- Lung Opacity Score (LOS) based on the CT pneumonia analysis of the chest CT images at the time of COVID-19 admission retrieved from the Radiology Department.
- Functional capacity based on the post-COVID-19 Functional Status (PCFS) Scale at 1 month before their COVID-19 admission.

Dependent variables

- Chest CT scan findings presence of the following ancillary findings on repeat chest CT scan at the time of study participation [8]. Categorized as with or without.
    - Architectural distortion – Distorted appearance of the lung anatomy usually associated with pulmonary fibrosis and accompanied by volume loss.
    - Bronchocele – A bronchocele is a tubular or branching Y- or V-shaped structure that may resemble a gloved finger, representing dilated bronchioles due to retained secretions (mucoid impaction or mucus plugging).
    - Consolidation – homogeneous increase in pulmonary parenchymal attenuation that obscures the margins of vessels and airway walls. An air bronchogram may be present.
    - Ground-glass opacities – hazy increased opacity of lung, with preservation of bronchial and vascular margins, caused by partial filling of airspaces, interstitial thickening, increased capillary blood volume, or a combination of these; the common factor being the

partial displacement of air. Ground-glass opacity is less opaque than consolidation, in which bronchovascular margins are obscured. Ground-glass opacities may be focal (seen in one lobe), multifocal (in multiple lobes), or diffuse.

- Honeycombing – Clustered cystic air spaces of comparable diameters ranging from 3–10 mm but occasionally as large as 2.5 cm. Honeycombing is usually subpleural and is characterized by well-defined walls. It is a CT feature of established pulmonary fibrosis.
- Mosaic attenuation pattern – A CT pattern that appears as a patchwork of regions of decreased or increased attenuation that may represent (a) patchy interstitial disease, (b) obliterative small airways disease, or (c) occlusive vascular disease. Mosaic attenuation patterns can be produced by air trapping secondary to bronchial or bronchiolar obstruction, which are seen as focal zones of decreased attenuation. Mosaic attenuation patterns can also be produced by interstitial lung disease characterized by ground-glass opacity, where areas of higher attenuation represent the interstitial process and areas of lower attenuation represent the normal lung.
- Nodule – A rounded opacity, well or poorly defined, measuring up to 3 cm in diameter.
- Perilobular consolidation – Consolidations that are seen along the structures that border the pulmonary lobules (i.e., interlobular septa, visceral pleura, and vessels). The term is most frequently used in the context of diseases that are distributed mainly around the inner surface of the secondary pulmonary lobule (such as organizing pneumonia).
- Pneumatoceles – A pneumatocele appears as an approximately round, thin-walled airspace in the lung.
- Reticulations – Innumerable small linear opacities that, by summation, produce an appearance resembling a net. On CT scan, the constituents of a reticular pattern are more clearly seen, whether they are interlobular septal thickening, intralobular lines, or the cyst walls of honeycombing.
- Traction bronchiectasis or bronchiolectasis – Traction bronchiectasis and traction bronchiolectasis respectively represent irregular bronchial and bronchiolar dilatation caused by surrounding retractile pulmonary fibrosis. Dilated airways may be seen as cysts (bronchi) or microcysts (bronchioles in the lung periphery).

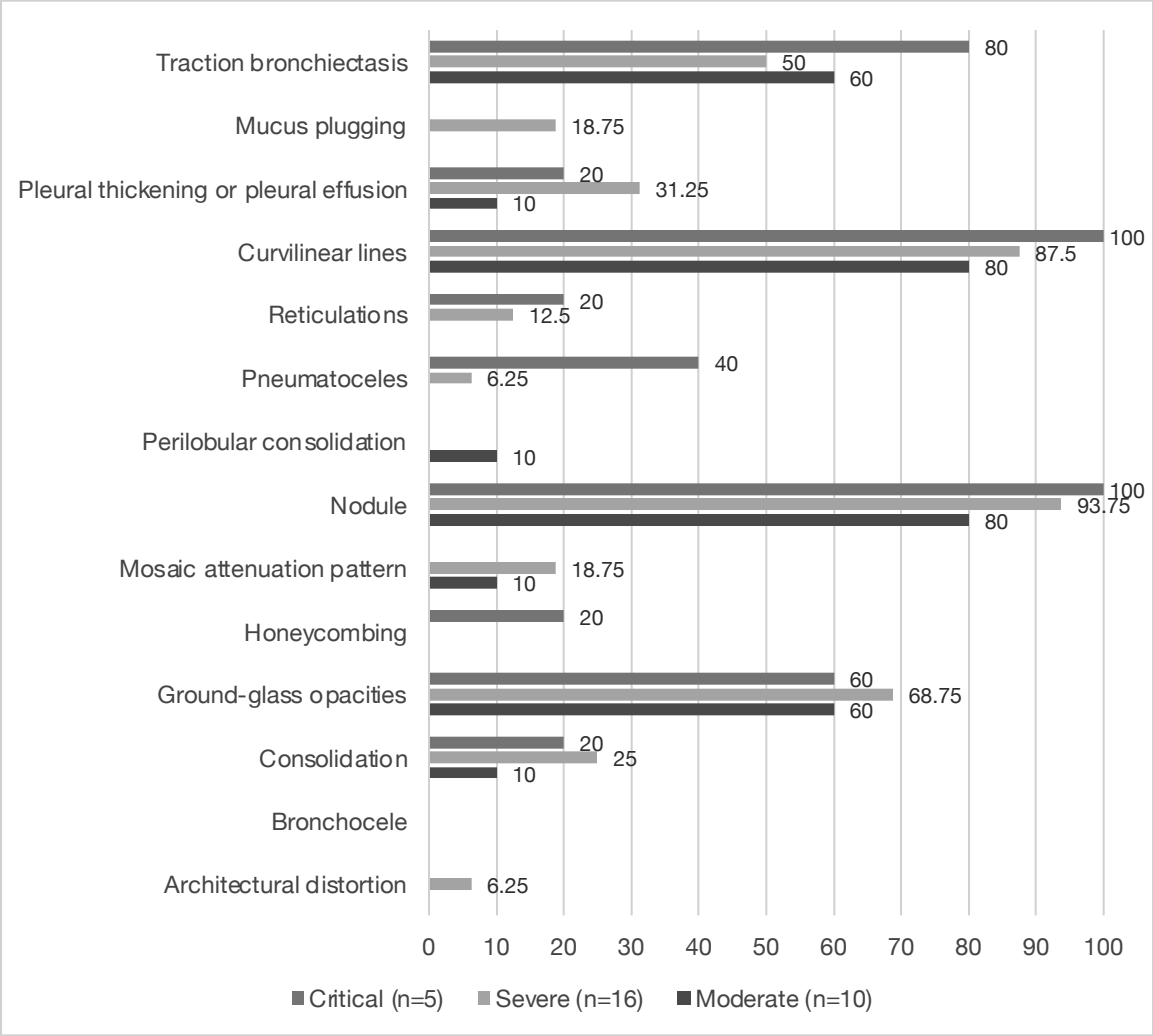
Other variables obtained from medical charts.

- Age (in years) at the time of hospital admission. Categorized as <60 and ≥60 years old.
- Sex of patient. Categorized as male or female.
- Comorbidities are based on patient's self-reported pre-existing conditions on admission: hypertension, diabetes mellitus, nephrological (i.e., chronic kidney disease), neurological (i.e., stroke), digestive (i.e., hepatitis) and others. Categorized as with and without. Multiple answers possible.
- Symptoms of COVID-19 on admission and discharge: fever, headache, cough, fatigue, hemoptysis, nausea, vomiting, myalgia, conjunctival congestion, nasal congestion, sore throat, sputum production, diarrhea, and shortness of breath. Categorized as with and without. Multiple answers possible.
- Disease severity of COVID 19 on admission based on the WHO definition. Categorized as:
  - COVID-19 moderate – clinical signs of pneumonia but with an oxygen saturation greater than 90% at room air.
  - COVID-19 severe – signs of pneumonia with respiratory rate greater than 30 breaths per minute, severe respiratory distress, or an oxygen saturation less than 90% at room air.
  - COVID-19 critical – acute respiratory distress syndrome, sepsis, or septic shock.

APPENDIX D. Lung Opacity Score by disease severity

	Moderate (n=10)	Severe (n=16)	Critical (n=5)
Mean ± SD [Range]	5.5 ± 3.27 [Range: 0–11]	8.31 ± 3.14 [Range: 4–15]	13.40 ± 4.10 [Range: 7–17]
Grade 0	1 (10)	0	0
Grade 1	6 (60)	3 (19)	0
Grade 2	3 (30)	13 (81)	3 (60)
Grade 3	0	0	2 (40)

APPENDIX E. Ancillary chest CT findings on 9–18 months after discharge



APPENDIX F. Lung Opacity Score on admission and ancillary chest CT findings on 9–18 months after discharge

	Lung Opacity Score			
	Grade 0 (n=1) n (%)	Grade 1 (n=6) n (%)	Grade 2 (n=3) n (%)	Grade 3 (n=0) n (%)
Moderate COVID-19				
Architectural distortion, % yes	0	0	0	–
Bronchocele, %yes	0	0	0	–
Consolidation, %yes	0	1 (17)	0	–
Ground-glass opacities, %yes	0	4 (67)	2 (67)	–
Honeycombing, %yes	0	0	0	–
Mosaic attenuation pattern, %yes	0	0	1 (33)	–
Nodule, %yes	1 (100)	4 (67)	3 (100)	–
Perilobular consolidation, %yes	0	0	1 (33)	–
Pneumatoceles, %yes	0	0	0	–
Reticulations, %yes	0	0	0	–

Curvilinear lines, %yes	1 (100)	4 (67)	3 (100)	–
Pleural thickening or pleural effusion, %yes	0	1 (17)	0	–
Mucus plugging, %yes	0	0	0	–
Traction bronchiectasis, %yes	0	4 (67)	2 (67)	–
Severe COVID–19				
Architectural distortion, % yes	–	1 (33)	0	–
Bronchocele, %yes	–	0	0	–
Consolidation, %yes	–	2 (67)	2 (15)	–
Ground–glass opacities, %yes	–	3 (100)	8 (62)	–
Honeycombing, %yes	–	0	0	–
Mosaic attenuation pattern, %yes	–	0	3 (23)	–
Nodule, %yes	–	3 (100)	12 (92)	–
Perilobular consolidation, %yes	–	0	0	–
Pneumatoceles, %yes	–	1 (33)	0	–
Reticulations, %yes	–	0	2 (15)	–
Curvilinear lines, %yes	–	3 (100)	11 (85)	–
Pleural thickening or pleural effusion, %yes	–	1 (33)	4 (31)	–
Mucus plugging, %yes	–	1 (33)	2 (15)	–
Traction bronchiectasis, %yes	–	1 (33)	7 (54)	–
Critical COVID–19				
Architectural distortion, % yes	–	–	0	0
Bronchocele, %yes	–	–	0	0
Consolidation, %yes	–	–	0	1 (50)
Ground–glass opacities, %yes	–	–	2 (67)	1 (50)
Honeycombing, %yes	–	–	0	1 (50)
Mosaic attenuation pattern, %yes	–	–	0	0
Nodule, %yes	–	–	3 (100)	2 (100)
Perilobular consolidation, %yes	–	–	0	0
Pneumatoceles, %yes	–	–	1 (33)	1 (50)
Reticulations, %yes	–	–	1 (33)	0
Curvilinear lines, %yes	–	–	3 (100)	2 (100)
Pleural thickening or pleural effusion, %yes	–	–	1 (33)	0
Mucus plugging, %yes	–	–	0	0
Traction bronchiectasis, %yes	–	–	2 (67)	2 (100)

APPENDIX G. PCFS 1 month before admission and 9–18 months after discharge by disease severity (n=31)

1 month before admission	9–18 months post-discharge				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Moderate COVID-19					
Grade 0 (n=8) n (%)	3 (38)	4 (50)	1 (13)	0	0
Grade 1 (n=2) n (%)	0	0	2 (100)	0	0
Grade 2 (n=0) n (%)	–	–	–	–	–
Grade 3 (n=0) n (%)	–	–	–	–	–
Grade 4 (n=0) n (%)	–	–	–	–	–
Grade 1: negligible limitations with persistent symptoms but with no effect on everyday life; grade 2: limitations in everyday life, with occasional need to avoid or reduce usual activities; grade 3: limitations in everyday life and the patient is not able to perform all usual activities; and grade 4: severe functional limitations requiring assistance with activities of daily living					
Severe COVID-19					
Grade 0 (n=14) n (%)	6 (43)	4 (29)	3 (21)	1 (7)	0
Grade 1 (n=2) n (%)	0	1 (50)	0	1 (50)	0
Grade 2 (n=0) n (%)	–	–	–	–	–
Grade 3 (n=0) n (%)	–	–	–	–	–
Grade 4 (n=0)	–	–	–	–	–
Grade 1: negligible limitations with persistent symptoms but with no effect on everyday life; grade 2: limitations in everyday life, with occasional need to avoid or reduce usual activities; grade 3: limitations in everyday life and the patient is not able to perform all usual activities; and grade 4: severe functional limitations requiring assistance with activities of daily living.					
Critical COVID-19					
Grade 0 (n=5) n (%)	2 (40)	1 (20)	1 (20)	1 (20)	0
Grade 1 (n=0) n (%)	–	–	–	–	–
Grade 2 (n=0) n (%)	–	–	–	–	–

Grade 3 (n=0) n (%)	–	–	–	–	–
Grade 4 (n=0) n (%)	–	–	–	–	–
Grade 1: negligible limitations with persistent symptoms but with no effect on everyday life; grade 2: limitations in everyday life, with occasional need to avoid or reduce usual activities; grade 3: limitations in everyday life and the patient is not able to perform all usual activities; and grade 4: severe functional limitations requiring assistance with activities of daily living.					

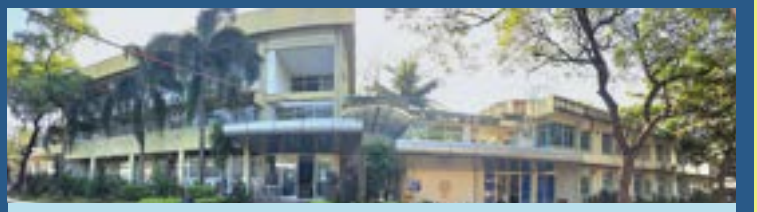
APPENDIX H. Lung Opacity Score on admission and PCFS 9–18 months after discharge

Lung Opacity Score	PCFS				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Moderate COVID–19					
Grade 0 (n=1) n (%)	0	1 (100)	0	0	0
Grade 1 (n=6) n (%)	2 (33)	2 (33)	2 (33)	0	0
Grade 2 (n=3) n (%)	1 (33)	1 (33)	1 (33)	0	0
Grade 3 (n=0) n (%)	–	–	–	–	–
Post–COVID–19 Functional Scale (PCFS) Grade. Grade 1: negligible limitations with persistent symptoms but with no effect on everyday life; grade 2: limitations in everyday life, with occasional need to avoid or reduce usual activities; grade 3: limitations in everyday life and the patient is not able to perform all usual activities; and grade 4: severe functional limitations requiring assistance with activities of daily living. Lung Opacity Score (LOS) Grade. Grade 0: total lung opacity score of 0; Grade 1: total lung opacity score of 1–5; Grade 2: total lung opacity score of 6–15; Grade 3: total lung opacity score of 16–20.					
Severe COVID–19					
Grade 0 (n=0) n (%)	–	–	–	–	–
Grade 1 (n=3) n (%)	1 (33)	0	1 (33)	1 (33)	0
Grade 2 (n=13) n (%)	5 (38)	5 (38)	2 (15)	1 (8)	0
Grade 3 (n=0) n (%)	–	–	–	–	–
Post–COVID–19 Functional Scale (PCFS) Grade. Grade 1: negligible limitations with persistent symptoms but with no effect on everyday life; grade 2: limitations in everyday life, with occasional need to avoid or reduce usual activities; grade 3: limitations in everyday life and the patient is not able to perform all usual activities; and grade 4: severe functional limitations requiring assistance with activities of daily living. Lung Opacity Score (LOS) Grade. Grade 0: total lung opacity score of 0; Grade 1: total lung opacity score of 1–5; Grade 2: total lung opacity score of 6–15; Grade 3: total lung opacity score of 16–20.					

Critical COVID–19					
Grade 0 (n=0) n (%)	–	–	–	–	–
Grade 1 (n=0) n (%)	–	–	–	–	–
Grade 2 (n=3) n (%)	2 (67)	0	0	1 (33)	0
Grade 3 (n=2) n (%)	0	1 (50)	1 (50)	0	0

Post–COVID–19 Functional Scale (PCFS) Grade. Grade 1: negligible limitations with persistent symptoms but with no effect on everyday life; grade 2: limitations in everyday life, with occasional need to avoid or reduce usual activities; grade 3: limitations in everyday life and the patient is not able to perform all usual activities; and grade 4: severe functional limitations requiring assistance with activities of daily living. Lung Opacity Score (LOS) Grade. Grade 0: total lung opacity score of 0; Grade 1: total lung opacity score of 1–5; Grade 2: total lung opacity score of 6–15; Grade 3: total lung opacity score of 16–20.

PUBLIC HEALTH AND DOMICILIARY DIVISION



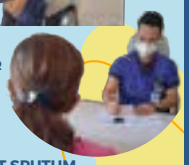
This is a program that caters to adult afflicted with TB since early 2000 and children with TB in 2007. The Lung Center of the Philippines DOTS clinic is the first public health facility engaged implementing Programmatic Management for Drug resistant TB in 2005 as a satellite treatment center under the Green Light Committee. In 2008, it became one of the ten (10) treatment centers implementing the DOH guidelines on PMDT as issued by DOH Administrative Order 2008-0018.

SERVICES OFFERED

- CONTACT TRACING

- DSTB/DRTB SCREENING (GENEXPERT)

- HIV COUNSELING AND TESTING FOR ENROLLED TB PATIENTS (15 YEARS OLD AND ABOVE)



- PROVISION OF ANTI TB MEDICATIONS (DSTB/DRTB) FOR ADULT AND CHILDREN FOR FREE

- DIRECT SPUTUM SMEAR MICROSCOPY TEST FOR ENROLLED PATIENTS

OTHER SERVICES PROVIDED

- CONDUCTS TB EDUCATION
- REFERRING AND PROVIDING CENTER FOR PRESUMPTIVE DSTB/DRTB PATIENTS
- ACT AS TREATMENT PARTNER
- FOLLOW UP CASES WHO FAILED TO REPORT FOR TREATMENT
- SUBMITS ACCOMPLISHMENT REPORTS TO LCP/NTP/QCHD

OUR OBJECTIVES

TB-FREE PHILIPPINES

ENSURE THAT TB DOTS SERVICES ARE AVAILABLE, ACCESSIBLE, AND AFFORDABLE IN COLLABORATION WITH THE LGUS AND OTHER PARTNERS.

TO REDUCE PREVALENCE AND MORTALITY FROM TB.

CONTACT INFORMATION AND SCHEDULE

SCHEDULE:
MONDAY TO FRIDAY, 8AM-5PM

CONTACT US AT:
8924-6101 LOC 1856-57

EMAIL US AT:
PHDD@lcp.gov.ph

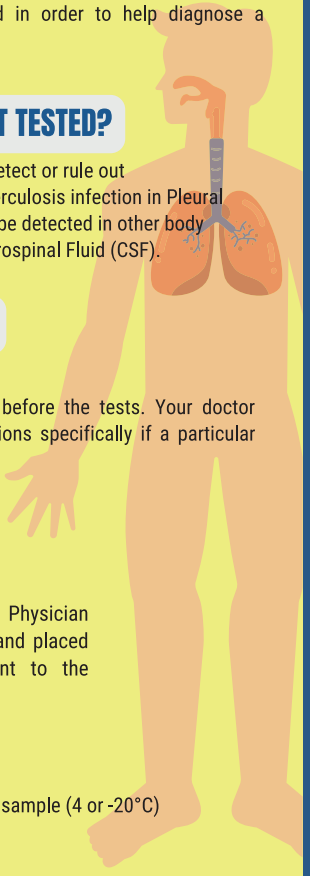
LUNG CENTER OF THE PHILIPPINES
NATIONAL REFERENCE LABORATORY FOR CLINICAL CHEMISTRY

ADENOSINE DEAMINASE (ADA)

Is a protein that is produced by cells throughout the body and is associated with the activation of lymphocytes, a type of white blood cell that plays a role in the immune response to infections. Conditions that trigger the immune system, such as an infection by Mycobacterium tuberculosis, the bacteria that causes tuberculosis (TB), may cause increased amounts of ADA to be produced in the areas where the bacteria are present. This test measures the amount of adenosine deaminase present in pleural fluid in order to help diagnose a tuberculosis infection of the pleurae.

1 WHY GET TESTED?

ADA tests helps to detect or rule out Mycobacterium Tuberculosis infection in Pleural Fluid. This may also be detected in other body fluids such as Cerebrospinal Fluid (CSF).



2 WHEN TO GET TESTED?

- Upon doctor's request
- Consult your Attending Physician before the tests. Your doctor may guide you for further instructions specifically if a particular medication might need to stop.

3 SAMPLE COLLECTION

Required sample: **PLEURAL FLUID**
A volume of Pleural Fluid is collected by a Physician using a procedure called THORACENTESIS and placed on a sterile container. This shall be sent to the laboratory as soon as possible without delay.

Volume: At least 5-10 mL in sterile container
Sample Handling: Room temperature
Sample Processing: Freshly collected or frozen sample (4 or -20°C)

LABORATORY GUIDELINES

Sample Preparation / Receiving of Samples:
1. Freshly collected samples: must be sent to the laboratory within 2 hours at room temperature
2. For send in referrals: call the LCP Patient Laboratory Service (02-89246101 loc. 1196) for more details
   : specimen preferably frozen or kept at controlled temperature 4 or -20°C

Time of collection is indicated on the request form

Processing Day: Mondays, Wednesdays and Fridays
Cut off Time: 10:00AM
Releasing of result: Same day, 4:00PM

Price: Php 2,700.00

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Scientific Proceedings

ORIGINAL ARTICLE

OUTCOMES OF ADULT FILIPINO SMOKERS ENROLLED IN THE QUITLINE AND COMPASSIONATE USE OF NICOTINE PATCH IN A TERTIARY GOVERNMENT HOSPITAL

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ABSTRACT

Background. The National Quitline Smoking Cessation Program was started by the Department of Health with the Lung Center of the Philippines in June 2017. The addition of the compassionate use of Nicotine Patches started in June 2021. Objectives. The study aimed to determine the outcomes among Adult Filipino Smokers enrolled in the Quitline Program and the Compassionate Use of Nicotine Patch from June 2021 to June 2022, in terms of self-reported continuous abstinence for 6 months and secondary outcomes (adherence to counseling program and compassionate use of Nicotine Replacement Therapy [NRT] and its adverse events), and to determine the quit rate, relapse rate, reasons for staying quit, level of Nicotine dependence, and stage of change.

Methodology. This is a retrospective cohort study among participants of Quitline program in a tertiary government hospital from June 2021 to June 2022.

Results. A total of 50 participants were enrolled in the study. 35 (70%) were successful quitters while 15 (30%) went into relapse. Most of the participants who stayed quit were males (80%), between 42-57 years old (40%), married (74%), employed (36%) and without comorbidities (50%). Majority were smokers for more than 10 pack-years (76%). While 76% of participants who used Nicotine Patch had adverse events, 97% of these were non-serious.

Conclusion. The Quitline behavioral counselling along with the use of Nicotine Patches in a tertiary government hospital is a useful strategy in smoking cessation. The combination of Quitline Counseling and NRT increases the success of smoking cessation.

Keywords. *Quitline, nicotine replacement therapy, smoking cessation*

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INTRODUCTION

The tobacco epidemic is one of the biggest public health problems. It approximately kills more than 8 million people per year. More than 7 million deaths are due to first hand smoking while 1.2 million deaths are due to second hand smoking.[1] Cigarette smoking and secondhand tobacco smoke are link to diseases of all the organs in the body and with ill effects on infants and children as well.[2]

The Department of Health, in partnership with the Lung Center of the Philippines (LCP) launched the National Quitline program last June 2017 (165-364) in the Philippines. The Quitline program is a telephone-based counseling service, which smokers in the country can call once they are ready to quit or if ever, they are considering to quit.[3] The program aims to provide counseling to smokers and facilitate their potential of becoming free of Nicotine in the future. It also aims to make callers across the country become more aware of the bad effects of smoking, thereby promoting prevention of smoking-related respiratory diseases.

In 2020, Cantela, M., and Ong-Cabrera, G., conducted a one-year follow up study of patients enrolled in the DOH-LCP Quitline Program using the behavioral approach. A total of 118 participants were included in this study. Most participants who enrolled in the program belongs to the 25- to 44-year-old age group (50.1%), males (83.1%) married (51.7%), college graduate (41.5%), employed (65.2%), without comorbidities (75.4%) and at least 10 pack-year smokers (60.2%). As of 2020, the quit rate is 58.8% while the relapse rate is 41.2%. The main reason for staying quit was health-related (69%) while the main reason for relapse was due to cravings and withdrawal symptoms (56.8%) followed by emotional stress, and peer influence and relationships. Among those with relapse, the majority are in the preparation stage (72.7%).[4]

Nicotine, the main active ingredient in tobacco products, is an addictive substance that makes it difficult for people to quit.5 Hence, since Nicotine dependence is identified as the main obstacle in the process of smoking cessation, Nicotine replacement therapy on top of behavioral intervention was found to improve quit rates and decrease relapse rates.

The therapeutic use of Nicotine containing medications is the most widely studied and used pharmacotherapy for managing Nicotine dependence and withdrawal.[6] NRT products take several forms: gum, transdermal Patch, nasal spray, oral inhaler, and tablet. Transdermal Patch is a slow sustained release form of Nicotine delivery. Other products like gum, nasal spray, oral inhaler, and tablets are acute dosing forms of Nicotine. They provide craving relief and breakthrough craving relief with immediate release of Nicotine. All these products have different levels of efficacy. They are most effective when the consumer also receives simultaneous cessation-counseling. NRT aims to reduce motivation to consume tobacco and the physiological and psychomotor withdrawal symptoms through delivery of Nicotine.[5]

In June 25, 2021, the NRT Program, as well the Toll-Free Quitline 1558 were launched by the Lung Center of the Philippines in collaboration with the World Health Organization and the Department of Health. This was to facilitate the improvement of the national quit rate by improving the accessibility of the Quitline service by providing a toll-free number as well as providing pharmacotherapy for free for 2 months using 16 Hour-Nicotine Patches of 25mg, 15mg and 10mg Patch formulation.

METHODOLOGY

Study Population and Sampling Design

Using non-probability purposive sampling, we included all adult Filipino patients 18 years old and above, enrolled in a tertiary government hospital Quitline Program from June 2021 to June 2022, and prescribed with Nicotine Patches. We excluded enrolled patients who have either withdrawn from the program, have not started at least 1 counseling session with the tertiary government hospital Quitline Program, or have not used at least 1 Nicotine Patch as prescribed.

Study Design and Site

This is a retrospective cohort study using chart review of those enrolled in the National Quitline Program from June 2021 to June 2022 located in a tertiary government hospital in Metro Manila.

In the Quitline program, calls were received by counselors through telephone lines. The program is briefly introduced to interested participants who plan to quit smoking. Once with informed consent and enrolled in the program, participants were asked to set a quit date. They received a series of calls and are followed-up 24 hours after their first call, then regularly after 48 hours, 72 hours, weekly until the 4th week of the month, then monthly until 12 months. The 5 A's (Ask, Advise, Assess, Assist and Arrange) or Brief Tobacco Intervention as well as Motivational Interviewing strategies were employed in conducting the behavioral approach in providing smoking cessation services to the participants. Smokers are being asked regarding their cigarette use, including the difficulties or challenges of quitting, benefits, or positive changes when quitting was started, withdrawal symptoms, and triggers. Smoking Cessation Specialists or quit coaches gives advices on how to prepare for the quit date and how to manage withdrawal symptoms. Participants assisted in formulating a quit plan and were advised techniques on how to manage withdrawal symptoms. Series of follow-up calls were arranged by the quit coaches for monitoring and reassessment for 6 months. Participants enrolled were prescribed 16 Hour-Nicotine Patches with 25mg, 15mg, and 10mg formulation.

Baseline Demographic Profile, such as age, gender, civil status, occupation, medical and smoking profile were obtained. The level of Nicotine dependence using the Fagerstrom Test and Stage of Change were also documented in the Quitline Questionnaire. Outcome data were reported as recorded in the patient database retrieved from tertiary government hospital Quitline Program. Descriptive statistics was done to summarize the continuous and categorical data.

Ethical considerations

This study followed the National Ethical Guidelines for Health and Health Related Research and follows the principles of the Data Privacy Act. It was also approved by the Institutional Ethics and Review Board (IERB). Confidentiality was maintained by the investigators. Only the primary investigator and co-authors had access to the data. Participants did not receive any payment or compensation in this research, since this research investigation only involved review of records gathered.

RESULTS

There was a total of 323 participants enrolled in the program who underwent counseling and were prescribed with Nicotine Patches under the Quitline program. About 273 participants were excluded, 50% of them dropped out, while 48% underwent solely behavioral counseling and 2% had only used Nicotine Replacement Therapy. A total of 50 participants were included in this study. Furthermore, 35 (70%) participants stayed quit for at least 6 months while 15 (30%) participants had relapses. Among those who stayed quit, the quit rate and reasons for quitting were identified. On the other hand, among those with relapse, the relapse rate, reasons for relapse and stage of change were identified.

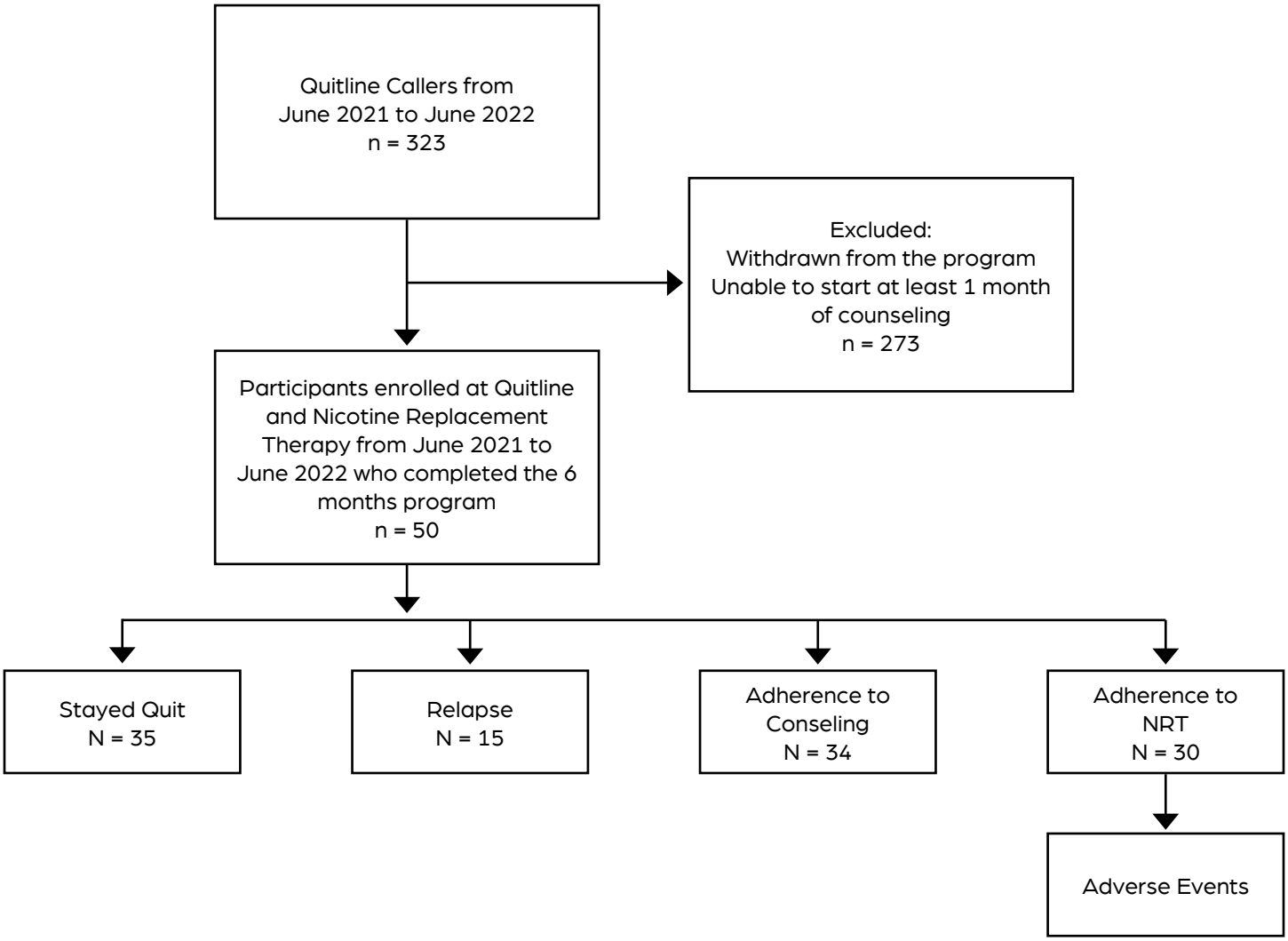

Figure 1. *Study Flow*

Table 1. *Demographic Profile of Quitline Participants*

Characteristic		No. of Participants (n = 50)	%
Sex	Male Female	40 10	80.0 20.0
Age (years)	18–25 26–41 42–57 58 and above	1 16 20 13	2.0 32.0 40.0 26.0
Civil Status	Married Single Widow Separated	37 9 1 1	74.0 18.0 2.0 2.0
Occupation	Employed Self Employed Unemployed	18 5 5	36.0 10.0 10.0

Table 1 shows the baseline characteristics of participants of the Quitline Program who both underwent counseling and took Nicotine replacement therapy Majority of the participants were males (80%), between ages 42–57 years old (40%), married (74%) and employed (36%).

Table 2. *Comorbidities and Smoking Profile of Quitline Participants*

		No. of Participants (n = 50)	%
Co-morbidities	No known comorbidities Hypertension Diabetes Dyslipidemia Asthma COPD	25 10 5 3 2 1	50.0 20.0 10.0 6.0 4.0 2.0
Pack-years Smoking	Less than 10 years More than 10 years	12 38	24.0 76.0
Uses e – cigarettes	No Yes	43 7	86.0 14.0
Level of Nicotine Dependence	Low Low to Moderate Moderate High No data	17 3 18 4 8	34.0 6.0 36.0 8.0 16.0
Stages of Change	Pre contemplation Contemplation Preparation Action Maintenance	0 25 18 5 0	0 50.0 36.0 10.0 0

50% of participants had no comorbidities, however, among those with comorbidities, hypertension was the most common. Most of the participants had a smoking history of more than 10 pack years (76%) and there were at least 7 participants who were users of electronic cigarettes.

Table 3. *Adherence to counseling session according to demographic, medical and smoking profile of Quitline participants*

			Adherence to Counseling		
		Total (n=50)	No. (n=34)	%	P – value
Sex	Male Female	40 10	30 4	75.0 40.0	NS
Age (years)	18–41 42–57 58 and above	17 20 13	10 15 8	58.8 75.0 61.5	NS
Civil Status	Married Other	37 11	25 7	67.6 63.6	NS
Occupation	Employed Self Employed Unemployed	18 5 5	12 3 5	66.7 60 100	NS
Co-morbidities	Absent Present	25 21	15 14	60.0 66.7	NS
Pack years of smoking	10 years or less More than 10 years	12 38	8 26	66.7 68.4	NS
Level of Nicotine dependence	Low to Moderate Moderate to High	20 22	16 14	80.0 63.6	NS
Stages of Change	Contemplation Preparation Action	25 18 5	19 10 5	76.0 55.0 100	NS

Among participants who adhered to the counseling session of the Quitline program, most participants were male, ages 42–57%, married, employed, smoked for more than 10 pack years, and had a low level of Nicotine dependence. Majority were in the contemplation stage. Post hoc analysis was done and baseline characteristics had no significant impact on adherence to counseling.

Table 4. *Adherence to NRT according to demographic, medical and smoking profile of Quitline participants*

			Adherence to NRT		
		Total (n=50)	No. (n=30)	%	P – value
Sex	Male Female	40 10	26 4	65.0 40.0	NS
Age (years)	18–41 42–57 58 and above	17 20 13	10 14 6	58.8 70.0 46.2	NS
Civil Status	Married Other	37 11	25 4	67.6 36.5	NS
Occupation	Employed Self Employed Unemployed	18 6 7	24 4 4	77.8 66.7 57.1	NS
Co-morbidities	Absent Present	25 21	15 12	60.0 57.1	NS
Pack years of smoking	10 years or less More than 10 years	12 38	6 24	50.0 63.2	NS
Level of Nicotine dependence	Low to Moderate Moderate to High	20 22	12 16	60.0 72.7	NS
Stages of Change	Contemplation Preparation	25 18	8 12	72.0 67.0	NS

Among participants who adhered to compassionate use of Nicotine Patches in the Quitline program, most participants were male, ages 42–57%, married, employed, no comorbidities, smoked for more than 10 pack years and had moderate to high levels of Nicotine dependence. Majority were in the contemplation stage. A post hoc analysis was done and these baseline characteristics had no significant impact on adherence to NRT use.

Table 5. *Continuous Abstinence for 6 months according to demographic, medical and smoking profile of Quitline participants*

			Continuous Abstinence for 6 months		
		Total (n=50)	No. (n=35)	%	P – value
Sex	Male Female	40 10	29 6	72.5 60.0	NS
Age (years)	18–41 42–57 58 and above	17 20 13	14 14 7	82.3 70.0 53.8	NS
Civil Status	Married Other	37 11	27 7	72.9 63.6	NS
Occupation	Employed Self Employed Unemployed	18 6 7	14 5 5	77.8 83.3 71.4	NS
Co-morbidities	Absent Present	25 25	18 17	72.0 68.0	NS
Pack years of smoking	10 years or less More than 10 years	12 38	8 26	66.7 68.4	NS
Level of Nicotine dependence	Low to Moderate Moderate to High	20 22	7 28	58.3 73.6	NS
Stages of Change	Contemplation Preparation	25 18	18 14	72.0 77.7	NS

Among participants who continuously abstained from smoking for 6 months, majority of participants were male, ages 42–57%, married, employed, no comorbidities, smoked for more than 10 pack years and have moderate to high levels of Nicotine dependence. Majority were in the contemplation stage. A post hoc analysis was done and these baseline characteristics had no significant impact on the 6 months continuous abstinence.

Table 6. *Incidence of Adverse Events in participants of Quitline program receiving Nicotine Replacement Therapy*

Adverse Event	Total Participants (n=50)	%
Itchiness	19	38
Dizziness	5	10
Drowsiness	4	8
Difficulty in sleeping	3	6
Rashes or redness	2	4
Vivid dreams	2	4
Palpitation	2	4
Difficulty in breathing	1	2

Table 6 shows that among participants of the Quitline program who received Nicotine Patch, the incidence of adverse events was at least 76%. Majority had non-serious adverse events, and the most common non-serious adverse events were due to itchiness (38%), followed by drowsiness (10%). On the other hand, only 2% experienced a serious adverse event, exemplified by difficulty in breathing.

Overall, among 50 participants enrolled in the Quitline program and were prescribed Nicotine Patch, 35 participants self-reported non-use of any tobacco or any Nicotine-containing devices for the past 6 months with a computed continuous abstinence rate for 6 months or Quit Rate of 70%. 15 participants (30%) went into relapse.

DISCUSSION

This study shows a higher quit rate (70%) when Quitline behavioral counseling and Nicotine Replacement Therapy were adopted as compared to Quitline behavioral alone which is 62.7% quit rate.[4] The relapse rate with Quitline Counselling Program with compassionate use of Nicotine Replacement therapy is 50%. The reasons for staying quit were medical and health-related reasons while the reasons for relapse were due to withdrawal symptoms and cravings because of non-adherence to the Nicotine Patch.

The sociodemographic factors including age, gender, civil status, socio economic status, education, and smoking history impact successful and unsuccessful quitters.[8] The successful quit attempt was seen mostly in older male, good socioeconomic status and fewer sticks smoked. A study by Wilcox et. al. (2007) showed that people on higher income groups and higher educational status are likely to reattempt quitting after a relapse. In a study conducted by Youngmee and Won-Kyung (2014), successful quitters also belong to those who are employed and have higher income. There is no difference between the age of starting smoking, the duration of cigarette consumption and the age of quitting smoking. This study shows the importance of sociodemographic status in the success of quitting smoking. Majority of the participants were in the middle age group, married and employed. Hence, Quitline aims to augment the smoking cessation program of the Department of Health in all subgroups by way of a free behavioral counselling / consult and Nicotine replacement therapy roll out.

Moreover, this study investigated the status of Nicotine dependence and the success of quitting smoking. In a study by Koks, G. et al. (2019) majority of the smokers had moderate dependence in the Fagerstrom Test for Nicotine Dependence. The high Nicotine dependence emphasizes the need for supportive counselling and Nicotine Patch replacement therapy for successful smoking cessation.[9] As shown in this study, with the implementation of the Quitline program through counseling and NRT, there was a high quit rate of 70%. On the other hand, relapse was also seen in those participants non-adherent to the NRT.

This study looks at the Stages of Change in smoking cessation, majority of the participants who successfully quit smoking belonged to the "stage of contemplation". This tells us that 50% of the subjects considered the idea of quitting. Hence, Quitline behavioral counselling and NRT impacts the success rate of smoking cessation.

Only 76% of the participants had adverse events while on Nicotine replacement therapy and the majority were non-serious adverse events (97%). As clinicians, who are members of Quitline, it is important to discuss with the patients the NRT including its potential side effects to increase its adherence to the Nicotine replacement therapy hence, reducing the relapse rate and increasing the quit rate.

Lastly, a study conducted by Batungbacal et al. last 2018 in a tertiary institution in the Philippines showed a quit rate of 18% and a relapse rate of 82% during the Quitline's first year of implementation of behavioral therapy. Another study of patients enrolled in Quitline Program using the behavioral approach in the same tertiary institution in 2020 by Cantela M., and Ong-Cabrera G. showed an increase of quit rate of 67.2% and a relapse rate of 37%. Hence, with this current study on smoking cessation program by Quitline's behavioral counselling together with Nicotine Replacement Therapy showed a spike of quit rate of 70% and a relapse rate of 30%.[4] This study is comparable to an international study which states a 35 % quit rate for and Nicotine Replacement Therapy combined with behavioral therapy.[10]

LIMITATIONS OF THE STUDY

The smoking abstinence of participants enrolled in the program are self-reported, which may lead to outcome bias. The smoking cessation program ends at 6 months from the start of enrollment that among the successful quitters, follow-ups are only limited. Hence, this study did not further evaluate whether these quitters continued to abstain from smoking or had relapsed beyond the completion of the program.

RECOMMENDATION

For the participants, it is recommended that follow-ups beyond the 6-month enrollment for better monitoring and prevent relapse. Among those who did not complete the 6-month program and did not adhere with the Nicotine Replacement Therapy, a more proactive counselling, improved communication, and modification of strategies including a face-to-face counseling and increasing the frequency of calls should be made. Inclusion of family members during the counseling to improve the support system of participants is also recommended.

For future research, the researchers recommend a longer study period to increase the study population hence, further increase representativeness of the program and make further improvement as necessary.

CONCLUSION

In this study, there are a total of 50 subjects enrolled in the Quitline program who participated in both behavioral counseling and Compassionate Use of Nicotine Replacement Therapy in a tertiary government hospital from June 2021 to June 2022. A total of 35 (70%) participants were successful quitters while 15 (30%) participants went into relapse. Most of the participants (40%) were between ages 42–57 years old. Majority of the participants were males (80%). A relatively higher proportion of participants who stayed quit for at least 6 months were married (77%) and employed (40%). About 50% of participants had no comorbidities. Majority of the participants had a smoking history of more than 10 pack years (76%).

The addition of Nicotine Replacement Therapy to the Quitline counseling program was an effective strategy to achieve abstinence of smoking for 6 months or achieve a state of being "quit" as the quit rate was 70% as compared to solely behavioral therapy which was 62.7%. Also, proactive counseling and through discussion with Nicotine Replacement Therapy improve adherence to the said therapies, hence increases the success of smoking cessation.

In addition, it was also necessary for more individuals to become more aware of this program by increasing its accessibility through various forms of advertisements.

Quitline smoking cessation programs must always consider the personal, emotional, behavioral, and social aspects of smokers for a successful quit rate. Individualized approach should also be observed through an understanding of the different factors of quitting and relapse; level of Nicotine dependence, adverse effects of Nicotine Patches and the stage of change. Lastly, a well-informed participant regarding Nicotine Replacement Therapy increases its adherence. Therefore, Quitline's Cessation Program, which comprises counseling and Compassionate use of NRT, increases the success of smoking cessation.

FUNDING

The transdermal Nicotine Patches used by the Quitline were donated by the World Health Organization to the Department of Health in 2021.

CONFLICT OF INTEREST

None declared.

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APPENDIX

Outcome Measures and Definition

Baseline and outcome data was reported as recorded in the patient database retrieved from DOH-LCP Quitline patient database. Formulas used for reporting of outcomes are stated below:

1. **6 months Quit Rate**
   a. Measured at 6 months after enrolment, self-reported non-use of any tobacco or any Nicotine containing devices for the past 6 months (Tertiary government hospital Quitline definition)
   b. Formula for 6 months Quit Rate
      i. Numerator represents the number of participants who continuously abstained from smoking for 6 months
      ii. Denominator represents the number of participants who are enrolled in the Tertiary government hospital Quitline program and was prescribed Nicotine Patch and has used it at least once during the study period
2. **Adherence to counseling program by the National Quitline**
   a. Measured at 6 months after enrolment in the counselling program, patients who has attended the counseling sessions as scheduled by Tertiary government hospital Quitline (100% of the schedule) (Tertiary government hospital Quitline definition)
   b. Formula for % counseling adherence
      i. Numerator represents the number of participants adhered to the counseling program by the Quitline
      ii. Denominator represents the number of participants who are enrolled in the Tertiary government hospital Quitline program and was prescribed Nicotine Patch and has used it at least once during the study period
3. **Adherence to prescribed compassionate use of Nicotine Patch**
   a. Measured at 8 weeks after enrolment in the Nicotine Patch program, patients who has used the Patch for 8 weeks (100% of the time) (Tertiary government hospital Quitline definition)
   b. Formula for % adherence to Nicotine Patch
      i. Numerator represents the number of participants who adhered to the prescribed compassionate use of Nicotine
      ii. Denominator represents the number of participants who are enrolled in the Tertiary government hospital Quitline program and was prescribed Nicotine Patch and has used it at least once during the study period
4. **Adverse events**
   a. Qualitative description of adverse events regardless of causality as noted by patient, listed as reported by patient (Tertiary government hospital Quitline definition)
      i. Classified as:
         1. Non-serious - not leading to hospitalization, disability, or mortality
         2. Serious - leading to hospitalization, disability, or mortality
   b. Formula for % adverse events
      i. Numerator represents the number of participants who had non-serious and serious adverse events
      ii. Denominator represents the number of participants who are enrolled in the Quitline program and was prescribed Nicotine Patch during the study period
5. **Quitter** - participant of the Quitline program who decides to quit or stop smoking for at least 6 months
6. **Relapse** - participant of the Quitline program who initially stops smoking for at least 1 month but returned to their regular smoking habit
7. **Contemplation stage** - one of the stages of change from the Transtheoretical model of intentional behavior change, current smokers who are considering quitting within the next six (6) months and have not tried in the last year (Tertiary government hospital Quitline definition)

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  Meltzer PS, Kallioniemi A, Trent JM, Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

  Book

  Murray, PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

  Gilstrap LC 3rd, Cunningham FG, VanDorsten JP, editors. Operative obstetrics. 2nd ed. New York: McGraw-Hill; 2002.

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  World Health Organization. Hospital infection control guidelines for severe acute respiratory syndrome. April 16, 2003: http://who.int/csr/sars/infectioncontrol/en (accessed April 24, 2003).

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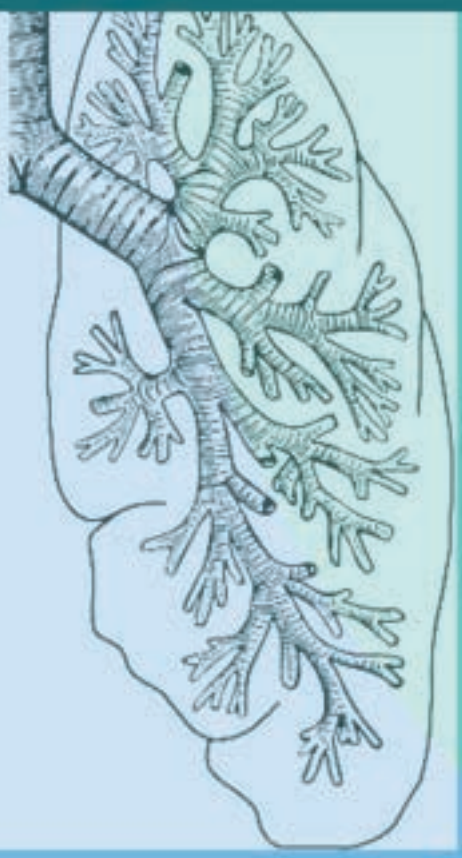

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