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Tsunami of Exercisetherapies for COVID-19: A Systematic review and Metanalysis of Qualitative and Quantitative improvement on respiratory parameters

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Abstract

Background: The results of Physiotherapeutic interventions for COVID-19 are less vocal. Also, few studies which have been published have not received the recognition which fall under the category of Physiotherapy. Hence, this systematic review is taken up to derive the significant strategy to deal the current deadliest pandemic.

Objective: To determine the relative effectiveness of Physiotherapeutic regimens on qualitative and quantitative respiratory parameters and compare the qualitative and quantitative measures of the well published physiotherapeutic regimens for COVID-19.

Method: PRISMA was followed for selection of articles for the study. Experimental studies were searched in Pubmed, Google scholar and Cochrane Library using related keywords and advanced option from 2019 to 2021. PEDro scoring was used to assess the Quality of research. Review manager software 5.3 was used to assess Risk of bias and homogeneity. The study followed PRISMA guidelines to the review and Forest plot was developed for the assessment of effectiveness of the treatment. A total of 38 trials were included in the study.

Main results: The schedule of the treatment varied greatly depending on the severity of the subject. Subgroup analysis performed on qualitative and quantitative improvement of COVID after Exercise therapy regimen showed significant statistical difference.

Conclusion: The result of the present study shows strong evidence to support that Exercise therapy regimen works efficiently when used as rehabilitation purpose in COVID-19 subjects by improving by qualitative and quantitative parameters.

Key words: Meta-analysis, Systematic Review, Qualitative, Quantitative, respiratory, cardiac, parameters, COVID

1.1 INTRODUCTION:

Coronavirus disease: a declared global pandemic disease is a viral infection caused by the virus named corona. The recent studies have given the name COVID-19 which means CORONA Virus disease 2019, resulted from an outbreak of corona patients. The defined origin for the outbreak of 2019 is demonstrated to be Bat origin. The disease primarily involves respiratory system with main manifestations in interstitial and alveolar areas of lung and generally causing Severe acute respiratory syndrome (SARS). In chronic cases of COVID-19 the attack is generally on almost on all the organs including kidney, heart, digestive tract, nervous system, vascular system and mainly respiratory system.[1]

World Health Organization (WHO) demonstrated **4 589 526** cases of coronavirus disease 2019 (COVID-19) were reported globally, as of May 20/2020. [2]. Few highest affected countries with the number of positive cases topographically were: Italy, Spain, USA, UK and India. The outbreak of corona varies with various geoghraphical areas. Primary causes can be listed as: high population mobility through air travel and the documented person-to-person transmission, eating Frozen food items, avoiding sickness and terming it as causal sickness etc.[2]

Various therapies are patented and guidelines are copyrighted particularly for treating subjects with COVID.

There exist various types of COVID patients mentioned as follows;

I. **Type L:** usually these patients land up on CPAP or Non-Invasive Ventialation and also have High PEEP (8–10 cmH_2O). Vitals must be mandatorily monitored along with emergency treatment plan.

   Clinical features:

   - Low elastance of the lung
   - Low ventilation to perfusion (VA/Q) ratio
   - Low lung weight
   - Low lung recruitability

II. Type H-

   An early intubation may avert the transition to Type H phenotype and Type H patients should be treated as severe ARDS, including higher PEEP, if compatible with hemodynamics, prone positioning and extracorporeal support.

   Clinical features:

   - High elastance
   - High right-to-left shunt
   - High Lung weight
   - High lung recruitability[3]

Physiotherapy regimens have already been demonstrated which significantly improve both qualitative and quantitative parameters in subjects with pneumonia. Few studies have already been demonstrated in improving the respiratory and cardiac parameters in subjects with COVID as well. According to authors knowledge, there are very few experimental studies defining both the qualitative and quantitative improvement in subjects with COVID. Further, information about change in qualitative and quantitative respiratory and cardiac parameters is limited. Also, type of COVID to which the Physiotherapy regimen is specifically mentioned is limited. Hence it is necessary to know the improvement both qualitatively and quantitatively in cases with COVID after active physiotherapy rehabilitation. Hence this systematic review and meta analysis is undertaken.

2.0 METHODS:

Literature Search:

The reviewer searched the following computerized bibliographic English language databases: Google Scholar and PubMed from 2019 to 2021. The highly sensitive Cochrane collaboration strategy was used which targeted only interventional studies.

Literature selection:

Studies were included on the basis of inclusion criteria. Inclusion criteria: 1) Interventional study of active Physiotherapy/Exercise therapy in subjects with COVID, 2) Active Physiotherapy/Exercise therapy intervention 3) Subjects with Immediate Physiotherapy/Exercise therapy referral, 3) Interventional studies having Respiratory and cardiac parameters, 4) Interventional studies having any one of the dyspnoea scale disability, 5) Interventional studies which can be downloaded and 6) Interventional studies published in and after 2019. Exclusion Criteria: 1) Severe Co-morbidities, 2) Unstable vitals of subjects with COVID and Passive Physiotherapeutic Regimen.

Quality assessment:

Quality of the studies recruited in this study was assessed by quality list from Cochrane Back Review Group [4]. Data were extracted Independently and checked for accuracy for the purpose of methodological quality.

2.1.1 *Ethical Clearance:* was obtained from Institutional ethical committee DSU Bangalore, Karnataka.

2.1.1 Sample Size:

Effective direct sample size would be number of patients in study A versus C/ that in study B versus C;

The sample size and power calculations were performed with a local software. The calculations were based on: Hedge Metanalysis sample deduction method[5];

Sample of one study (A)[6] + Sample of study (B)[7] / Sample of study (B)[7] + Sample of study C[8] = 419+15/15+43≈7.

These assumptions generated a sample size of at least 7.

2.1.3 *Search strategy:*

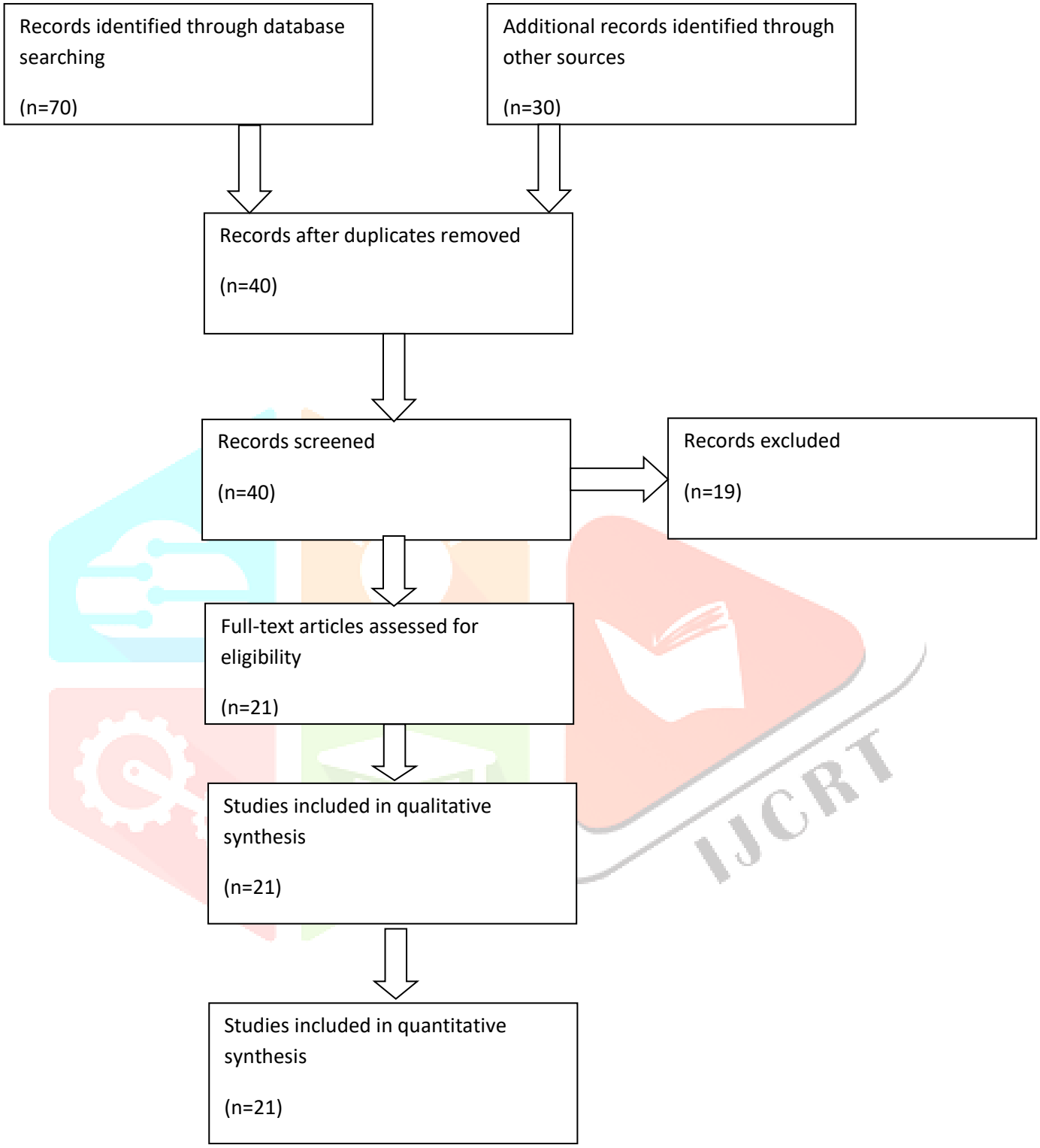
The author underwent searches of Google scholar, PubMed, Embase, Cochrane Library, Web of Science and CINAHL (Cumulative Index to Nursing and Allied Health Literature). **English database was strictly followed for recruitment of the articles in the study.**

Study selection: Reviewer independently selected the articles and downloaded the articles from Google scholar and PubMed. Inclusion criteria: experimental studies indentifying physiotherapy treatment that improve respiratory and cardiac parameters both qualitative and quantitatively in subjects with COVID.

2.1.5 *Data Extraction:*

Information was extracted from each included study on: Demographic data, Journal name, study setting, published year, Title, sample size, sample characteristics, Type of physiotherapy treatment. Prisma flow chart was used to process the study selection.[9]

PRISMA FLOWCHART



2.1.6 *Data Synthesis and statistical methods*:

The above mentioned data was collected from the published interventional studies.

Effect size was calculated of the changes in outcome measure after therapies. Analysis was performed using comprehensive Meta-analysis V.2 software. Effect size interpretation: interpretation of statistical information is based on Cohen's criteria for evaluation [small(≥0.20), medium (≥.50) and large (≥.80)] using d metrics. Negative effects were used indicating to smaller outcomes and positive effects indicated larger outcomes. For one group research study, negative effects represented larger pretest score whereas positive effect determined the post test score.[10]

Error modeling: random effects model was pre-mentioned for the present investigation due to the expected variability between studies.

The quality of the study included using physiotherapy evidence database (PEDro) scale and Cochrane risk of bias tool. The methodological quality was assessed using PEDro scale by 8 items; random allocation, blinding procedures, and the drop-out rate. Two items related to statistical reporting. Aggregate scores ranged from 0 to 10 points; where higher score indicated better quality. Quality was classified as; high: 6-10, fair: 4 or 5 and poor: ≤3. Using Cochrane risk of bias tool, we assessed seven domains of bias and stratified the risk of bias into low, high and unclear risk.[10]

Exploration of PaO_2/FiO_2 ratio, FiO_2, 6 minute walk test, dyspnea, oxygen index, SPO_2, Anxiety, Depression, Health related questions, Fatigue quantitative and/ qualitative parameters related to cardio-respiratory system and CNS etc was performed before selecting the studies.

A random-effect model was used, and a point estimate with a 95% confidence interval (CI) was presented. Heterogeneity across studies was tested using the I2 test. I2 values of 25%, 50%, and 75% were considered low, moderate, and high, respectively. The meta-analysis was performed using Review Manager Software 5.3.

TABLE: The detailed elaboration of the studies recruited in this systematic review. Attached separately.

Results:

Electronic searches identified 100 records, after removal of duplicates, screening the titles and abstracts of 40 was recorded. Full-text articles were assessed for 40 studies and 21 eligible studies were taken into consideration. The studies involved a total of 1902 subjects.

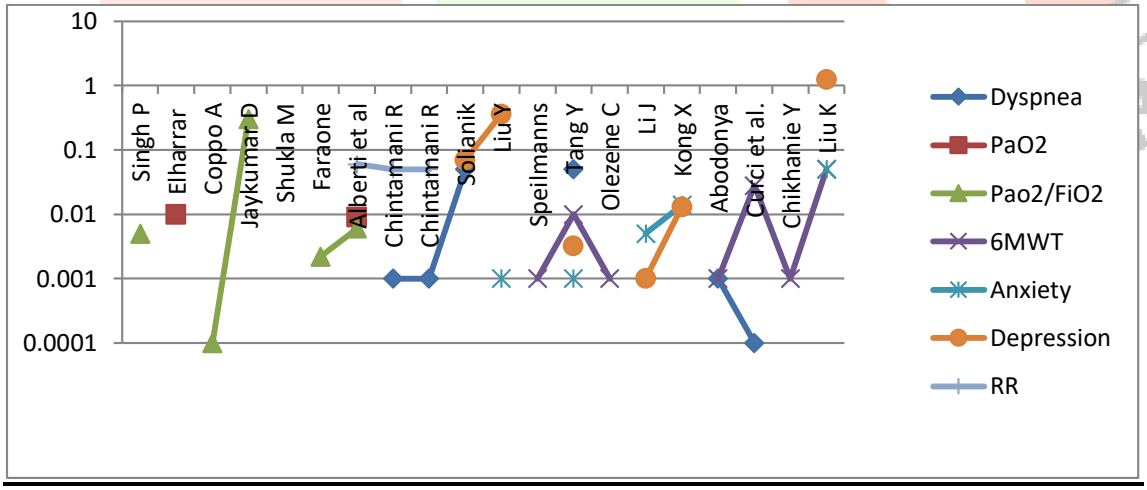
Quality Assessment:

The studies included in the present study were ranked medium to high on PEDro scoring. One study scored 11, one study scored 10 and 3 studies scored 8 and the rest scored 7.[10]

Effect size of changes in outcome measures:

Studies included in the present analysis showed heterogenic distribution, however the variance between the study (τ^2) and overlap of Confidence Intervals ($I^{2)}$ were inconsistent demonstrating small and large variability in the scores.

Forest plots for qualitative measures:



Outcome analysis:

Outcome measures changed from positive values for PaO_2/FiO_2, Dyspnea, 6minute walk test, and Anxiety to negative values for depression, respiratory rate and PaO_2.

	Effect size statistics			Null test	Heterogeniety statistics			Publication bias
	K	**g**	**s^2**	**Z**	**Q**	**(τ^2)**	**($I^{2)}$**	Fail-Safe N
Random effects model	**28**	**0.09**	**0.002**	**-1.35***	**42.01**	**0.002**	**30.31**	**0**
PaO_2/FiO_2	2	0.5	0.014	0.23	3.08	0.01	38.23	**0**
Dyspnea	7	0.2	0.003	-0.34	21.05	0.03	2.69	**0**
6MWT	6	0.4	0.005	-0.20	8.55	0.05	40.25	**0**
Anxiety	2	0.03	0.0004	-0.27	29.29*	0.05	43.52	**0**
PaO_2	7	0.9	0.288	-0.57	12.16	0.04	60.52	**0**
Depression	14	0.9	0.236	-0.81*	29.29*	0.295	78.59	**0**
Respiratory rate	12	0.7	3.333	-1.65	1932*	0.224	69.28	**0**

Significant level= *p<0.05, †Total Q-value used to determine heterogeneity, g, effect size (Hedges g); I2, total variance explained by moderator; k, number of effect sizes; s2, variance; Z, test of null hypothesis; τ2, between-study variance in random effects model.

Subgroup Analysis:

	Effect size statistics			Null test	Heterogeniety statistics			Publication bias
	K	**G**	**s^2**	**Z**	**Q**	**(τ^2)**	**($I^{2)}$**	Fail-Safe N
Random effects model	**28**	**0.09**	**0.002**	**-1.35***	**42.01**	**0.002**	**30.31**	**0**
Sample Characteristics								
Female	10	0.01	0.007	0.09	3.51	0.004	17.21	**0**
Male	14	0.07	0.011	-0.72	6.30	0.086	20.57	**0**
Age								
65+	5	0.5	0.011	-0.99	0.38	0.066	25.34	**0**
55-65	5	0.2	0.034	0.50	0.368	0.012	22.32	**0**
45-55	2	0.4	0.005	-1.16	0.412	0.015	25.12	**0**
Study Characteristics								
Subjective and Objective	2	0.3	0.002	-0.97	19.33	0.020	29.08	**0**
Objective	4	0.5	0.004	-1.70	16.45	0.029	30.12	**0**

Significant level= *p<0.05, †Total Q-value used to determine heterogeneity, g, effect size (Hedges g); I2, total variance explained by moderator; k, number of effect sizes; s2, variance; Z, test of null hypothesis; τ2, between-study variance in random effects model.

3.0 DISCUSSION:

General Discussion:

As far as the authors knowledge the present study is the first metanalytical systematic review of evidence based COVID 19 Exercise therapy regimen. The study concludes that there is no conclusive evidence that exercise therapy is associated with adverse effects specifically on Dyspnea, PaO2/FiO2, PaO2, 6 minute walk test, Anxiety and Depression. In the present study; the authors demonstrated the significance of treatment in

reduction of Dyspnea, PaO2/FiO2, 6 minute walk test and Anxiety whereas the least significance was seen with PaO2, Depression and Respiratory Rate. However, this effect of least significance was based on only few studies and did not control for conclusion, therefore the interpretation limited. Though exercise therapy well known in another obstructive and restrictive conditions of the chest, due to less publications on COVID19 subjects the result becomes indecisive.

CONCLUSION: In addition to this a meta-analysis, the study also demonstrated that, Physiotherapy treatment for subjects with COVID should focus on occurred low pulmonary compliance and concordant changes in lung and cardiovascular function with hypoxemia and repercussions. Also, the Physiotherapy must consider the musculoskeletal changes that have occurred in the ICU admitted subjects with COVID. The need for further updates to this document is anticipated as changes in functionality for Physiotherapy are better known

STRENGTHS AND LIMITATION:

Strengths: Strengths of the study were: No publication bias was noted, the present study clarifies the current state of the literature with regard to this topic, the present study was carried out on COVID positive patients admitted in Hospital,

Limitations: Less number of studies hence conclusion becomes indecisive, wide variety of the age and gender was seen, insufficient data is mentioned in many studies which led to recruitment of smaller inclusion number due to restriction by PRISMA guidelines.

FUTURE SCOPE:

A. Publication of more number of randomized controlled trial
B. Implementation of cognitive behavioral therapy in COVID 19 therapies
C. Implementation of Virtual reality in COVID19 therapies

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CONFLICTS OF INTEREST: No conflicts of interest.

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