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IMPORTANT TAKEAWAY FROM COVID-19 TRIAL ON NEBULIZATION AND INHALER USE TO DIRECT FUTURE DEVELOPMENTS IN RESPIRATORY DISORDERS

Physiology

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ABSTRACT

Introduction: Despite a lack of published evidence, clinicians are questioning whether nebulizers, an open medication reservoir, should be avoided in favor of MDIs, an enclosed portable inhaler, due to potentially lower risk of viral transmission, since COVID-19 spreads primarily through aerosolization of the virus. Aerosol generating medication delivery has been theorized to increase infection transmission. **Aims:** To evaluate the clinical relationship between effectiveness of use of inhalers, and nebulisation from qRT-PCR positive patients admitted in hospital. **Materials And Method:** The present study was a cross-sectional observational hospital-based study in West-Bengal, India. Total 436 patients were included in this study. **Result:** In Case, 6 (2.8%) patients had Inhalers. In Control, 14 (6.4%) patients had Inhalers. Association of Inhalers with Group was not statistically significant (p=0.0670). In Case, 6 (2.8%) patients had Nebulisation. In Control, 57 (26.1%) patients had Nebulisation. Our study showed that, most of patients had Nebulisation in Control Group compared to Case Group but this was statistically significant (p<0.0001). **Conclusion:** There is little information on whether nebulized treatment increases the risk of SARS-CoV-2 infection. Conclusively this research offers important new understandings of the interactions between two aerosol-based treatment modalities and will suggest a suitable device that is customized to the individual needs and clinical circumstances of each patient. The COVID-19 pandemic has provided important insights into the long-term pharmacological treatments for respiratory infectious illnesses.The potential for augmenting the expertise of healthcare practitioners through the use of AI to improve patient outcomes and respiratory care practices in conjunction with experimental data could result in more precise diagnosis and efficacious treatment plans.

KEYWORDS

COVID-19, nebulization, inhaler, respiratory illness, artificial intelligence

INTRODUCTION

The World Health Organization (WHO) declared the outbreak of novel coronavirus disease (COVID-19) as a public health emergency of international concern on 30 January 2020. The first case in Turkey was detected on 11 March 2020. According to the Turkish Ministry of Health data, 3,297,509 tests had been performed and 198,284 laboratory-confirmed cases reported by 30 June 2020.

In order to prevent unintentional inhalation of fugitive emissions during therapy, caregivers and healthcare professionals were concerned about practical ways for a safe and effective delivery of aerosolized drugs to patients with COVID-19. The goal of this study is to reiterate the importance of patient safety and the useful lessons learned from the pandemic scenario regarding treatment methods that can be used to future respiratory infections, given the paucity of information in this area of clinical practice**.**

MATERIALS AND METHODS

Study Area

A cross-sectional observational hospital-based study in West-Bengal, India

Study Population

Participants of the present study are in-house patients with COVID-19 symptoms who are diagnosed with COVID-19 based on clinical respiratory symptoms and radiological images and confirmed to be infected with SARS- CoV-2 by qRT-PCR using nasopharyngeal specimens during the study period. Also age matched control group qRT-PCR negative for COVID-19 but having the non- communicable diseases or pre-existing comorbidities are selected.

Study Design

- A cross-sectional observational hospital- based study in West Bengal, India.
- During admission, clinical assessment data were collected.
- The nasopharyngeal and oropharyngeal swab samples were collected during the three peak periods of the COVID-19 epidemic using standard procedures.
- Clinical and other support measures required during admission and hospital stay were collected.
- Data were double checked and entered in excel data sheet. Descriptive statistics were applied. According to need necessary inferential statistics were applied. Software Microsoft Office (10.0) and Statistical Package for the Social Sciences (SPSS), version 18.0 for windows (SPSS Inc., Chicago, IL, USA) was used for final data management and analysis.

Sample Collection

The tertiary care hospital has been identified as a designated COVID laboratory to diagnose COVID-19 in the state of West Bengal.

A pretested questionnaire is applied following the standard questionnaire of the Department of Health and Family Welfare, Government of West Bengal as per guidelines (WHO.,2020). Socio-demographic data like age, sex, residence, and data for clinical assessment and treatment modalities were collected from in-house admissions in person and medical records section of the designated hospital or through telephonic conversations with permission.

Nasopharyngeal and oropharyngeal swab samples suspected of COVID-19 from Kolkata and the adjacent areas of the state of West Bengal were provided during the 3 peaks of the COVID-19 epidemic in the state. The samples were collected according to standard procedures and transported using viral transport medium, and accompanied with minimal relevant details such as contact number of the suspected individual, date, and site of sample collection.

Sample Analysis

The tests were done by the real time RT PCR using standard protocol given by the manufacturer under Principles and Procedure used in laboratory. The nasopharyngeal and oropharyngeal swab samples were collected in 15 ml conical tubes in VTM (viral transport media) using disposable sterile plastic swabsticks for qRT-PCR and analyzed using Tru- NAAT Gene Xpert RT- PCR system(Molbio Diagnostics, Goa,India; WHO approved) for SARS-CoV-2. The SARS CoV 2 primer and probe set(s) was designed to detect RNA from the SARS CoV 2 in the samples. The real time fluorescent RT PCR Kit selects a specific target region in the ORF1ab region, E gene, N gene of SARS CoV 2 genome. Further, human housekeeping gene β Actin was worked as the target gene for the internal control.

Clinical Data Collection And Analysis

Background clinical data and other support measures required during admission and hospital stay were collected from the cases and control groups by trained nursing staffs under the supervision of a clinician.

Analysis of other support needed like the use of inhalers and nebulization required for this study was compiled following the standard rules and regulations. All tests and studies were done following the COVID-19 protocol and clinical protocol.

Ethical clearance has been initiated from the University Ethics Committee and the clearance from the Tertiary Care Hospital management.

Data Management And Analysis

Data were recorded on specially designed pre-tested schedule and managed in Microsoft Excel spreadsheet (Software: Microsoft Office 10.0). All entries were double checked for any possible error.

Necessary statistical tests including descriptive and inferential statistics were done using SPSS (Statistical Package for the Social Sciences, version 18.0 for Windows) as per necessity.

Statistical Analysis:

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples.

Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.

Explicit expressions that can be used to carry out various t-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a t-distribution under the null hypothesis is given.

Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

Once a t value is determined, a p-value can be found using a table of values from Student's t-distribution. If the calculated p-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favour of the alternative hypothesis. p-value ≤ 0.05 was considered for statistically significant.

RESULT AND ANALYSIS

Table 1: Association between Age in group: Group

Group			
Age in group	**Case**	**Control**	**Total**
<20	3	0	3
Row %	100.0	0.0	100.0
Col %	1.4	0.0	0.7
21-30	10	8	18
Row %	55.6	44.4	100.0
Col %	4.6	3.7	4.1
31-40	7	8	15
Row %	46.7	53.3	100.0
Col %	3.2	3.7	3.4
41-50	43	28	71
Row %	60.6	39.4	100.0
Col %	19.7	12.8	16.3
51-60	34	44	78
Row %	43.6	56.4	100.0
Col %	15.6	20.2	17.9
61-70	73	86	159
Row %	45.9	54.1	100.0
Col %	33.5	39.4	36.5
71-80	48	30	78
Row %	61.5	38.5	100.0
Col %	22.0	13.8	17.9
81-90	0	14	14
Row %	0.0	100.0	100.0
Col %	0.0	6.4	3.2
Total	218	218	436
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

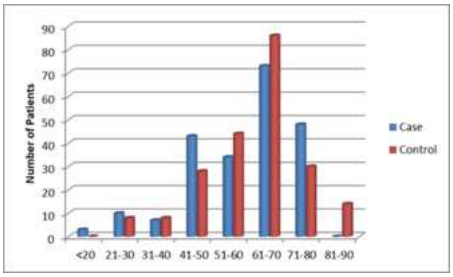


Figure 1: Distribution of the studied population depending on age group

Chi-square value: 26.9567**; df: 7 p-value:** 0.0003

In Case, 3 (1.4%) patients were ≤20 years of age, 10 (4.6%) patients were 21-30 years of age, 7 (3.2%) patients were 31-40 years of age, 43 (19.7%) patients were 41-50 years of age, 34 (15.6%) patients were 51-60 years of age, 73 (33.5%) patients were 61-70 years of age and 48 (22.0%) patients were 71-80 years of age.

In Control, 8 (3.7%) patients were 21-30 years of age, 8 (3.7%) patients were 31-40 years of age, 28 (12.8%) patients were 41-50 years of age, 44 (20.2%) patients were 51-60 years of age, 86 (39.4%) patients were 61-70 years of age, 30 (13.8%) patients were 71-80 years of age and 14 (6.4%) patients were 81-90 years of age.

Association of Age in Group with Group was statistically significant (p=0.0003).

In our study, out of 436 patients most of the patients were 61-70 years old but this was statistically significant.

Table 2: Association between Sex: Group

Group			
Sex	**Case**	**Control**	**Total**
Female	85	95	180
Row %	47.2	52.8	100.0
Col %	39.0	43.6	41.3
Male	133	123	256
Row %	52.0	48.0	100.0
Col %	61.0	56.4	58.7
Total	218	218	436
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

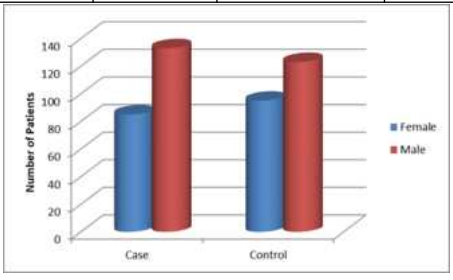


Figure 2: Distribution of the studied population depending on Sex

Chi-square value: 0.9462**; p-value:** 0.3306

Odds ratio: 0.8275 **(**0.5649**,** 1.2121**)**

In Case, 85 (39.0%) patients were Female and 133 (61.0%) patients were Male.

In Control, 95 (43.6%) patients were Female and 123 (56.4%) patients were Male.

Association of Sex with Group was not statistically significant (p=0.3306).

We found that, male population was higher than the female population. Male: Female ratio was 1.4:1 but this was not statistically significant.

Table 3: Association between Area: Group

Group			
Area	**Case**	**Control**	**Total**
Rural	61	82	143
Row %	42.7	57.3	100.0
Col %	28.0	37.6	32.8
Urban	157	136	293
Row %	53.6	46.4	100.0
Col %	72.0	62.4	67.2
Total	218	218	436
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

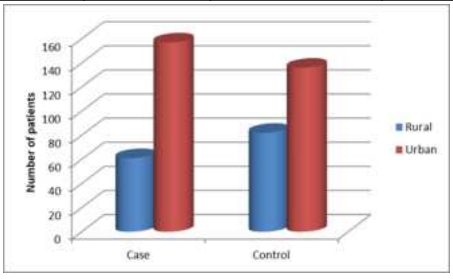


Figure 3: Distribution of the studied population depending on area of habitation
Chi-square value: 4.5890**; p-value:** 0.0321
Odds ratio: 0.6444 **(**0.4306**,** 0.9644**)**

In Case, 61 (28.0%) patients were rural area and 157 (72.0%) patients were urban area.

In Control, 82 (37.6%) patients were rural area and 136 (62.4%) patients were urban area.

Association of urban to rural population was statistically significant (p=0.0321).

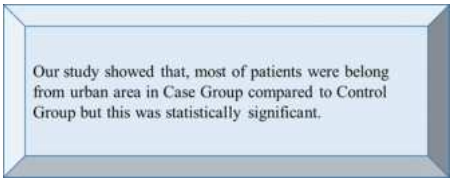


Table 4: Association between Nebulisation: Group

GROUP			
Nebulisation	**Case**	**Control**	**TOTAL**
No	212	161	373
Row %	56.8	43.2	100.0
Col %	97.2	73.9	85.6
Yes	6	57	63
Row %	30.0	100.0	100.0
Col %	2.8	26.1	14.5
TOTAL	218	218	436
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

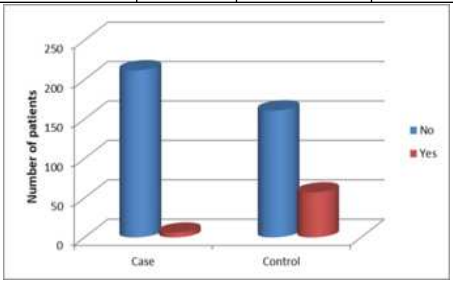


Figure 4: Distribution of the studied population depending on Nebulisation as therapy
Chi-square value: 53.1732; **df**: 2 **p-value:** <0.0001

In Case, 6 (2.8%) patients had Nebulisation. In Control, 57 (26.1%) patients had Nebulisation.

Association of Nebulisation with Group was statistically significant (p<0.0001).

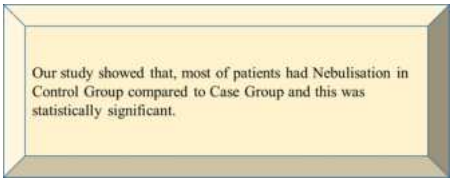


Table 5: Association between Inhalers: Group

GROUP			
Inhalers	**Case**	**Control**	**TOTAL**
No	212	204	416
Row %	51.0	49.0	100.0
Col %	97.2	93.6	95.4
Yes	6	14	20
Row %	30.0	70.0	100.0
Col %	2.8	6.4	4.6
TOTAL	218	218	436
Row %	50.0	50.0	100.0
Col %	100.0	100.0	100.0

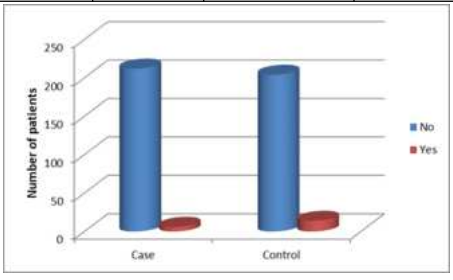
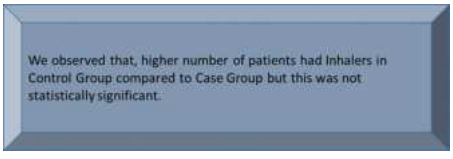


Figure 5: Distribution of the studied population depending on Inhalational therapy
Chi-square value: 3.3538; **p-value:** 0.0670
Odds ratio: 2.4248 (0.9142, 6.4319)

In Case, 6 (2.8%) patients had Inhalers. In Control, 14 (6.4%) patients had Inhalers.

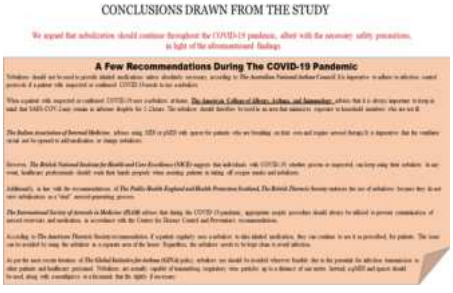
Association of Inhalers with Group was not statistically significant (p=0.0670).



Limitations Of The Study

In spite of every sincere effort this study has lacunae.
The notable short comings of this study are:

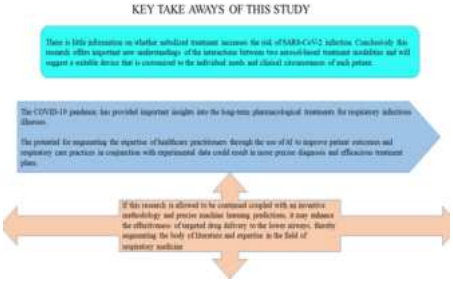
- The sample size was small. Only 436 cases are not sufficient for this kind of study.
- The study has been done in a single centre.
- The study was carried out in a tertiary care hospital, so hospital bias cannot be ruled out.



DISCUSSION

We argued that nebulization should continue throughout the COVID-19 pandemic, albeit with the necessary safety precautions, in light of the aforementioned findings The mainstay of treatment for obstructive airway illnesses is inhaled medication.The primary computational issue in the health risk evaluation of aerosol transit and deposition to the lower airways is this. This aerosol transport prediction model is

able to forecast atmospheric aerosol transport and deposition to human lung airways with high accuracy, which is necessary for medicine delivery and health assessment. If this research is coupled with an inventive methodology and precise machine learning predictions, it may enhance the effectiveness of targeted drug delivery to the lower airways, thereby augmenting the body of literature and expertise in the field of respiratory medicine.



Declarations

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Conflict Of Interest

The author hereby declares no conflict of interest

Ethical Guidelines

Ethical clearance has been initiated from the University Ethics Committee and the clearance from the Tertiary Care Hospital management was obtained on 05.01.2023.

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