Respiratory symptoms, spirometric, and radiological status of stone-cutting workers in Bangladesh: A cross-sectional study

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Abstract

Background and Aims: Inhalation of respirable silica dust during several stone processing methods can result in several respiratory diseases. However, data are scarce regarding the respiratory health of stone-cutting workers in Bangladesh. We aimed to determine the point prevalence of respiratory symptoms, lung function status and radiological abnormalities among the stone-cutting workers.

Methods: This cross-sectional study was conducted among 200 stone-cutting workers. Adult workers having a job experience of at least 3 years participated in this study. Then inquiry was made regarding respiratory symptoms with the help of a preformed questionnaire. All the participants underwent chest X-ray and spirometry. A respiratory dust sampler was used to measure the dust concentration of the stone-cutting factories.

Results: Among the 200 stone-cutting workers, 89% (178) showed at least one chronic respiratory symptom while they had chest tightness (75.5%), chronic cough (74.5%), and shortness of breath (66.5%) as the most prominent ones. Spirometry findings revealed that the mean forced expiratory volume in 1 s (FEV1) value was 1.42±0.65 L in the obstructive pattern, 1.43 ± 0.73 L in the restrictive pattern. The mean forced vital capacity (FVC) value was 2.53 ± 1.12 L in the obstructive pattern, 1.53 ± 0.75 L in the restrictive pattern. 42.69% of stone-cutting workers who complained of at least one respiratory symptom had abnormal chest X-ray findings. Those with progressive massive fibrosis had the lowest mean FEV1 value (0.75±0.50 L). While measuring workplace dust concentration, we found high particulate matter (PM) 2.5 (979.78 µg/m3) and PM 10 (1298.35 µg/m3) values.

Conclusions: Most of the stone-cutting workers in our study exhibited different respiratory symptoms. These symptoms were associated with abnormal lung function and radiology. Further longitudinal studies are recommended to determine the actual dimension of this problem.

KEYWORDS
pulmonary function test, silica dust, silicosis, stone-cutting workers
1 | INTRODUCTION

Occupational lung diseases have been a significant global health burden since the beginning of civilization. These are the group of diseases that occur in the workers exposed to occupation-related hazards. Persistent exposure to organic dust, inorganic specks of dust, pesticides, and agrochemicals lead to respiratory illness. One such workgroup is stone-cutting workers.

The stone-cutting industry mainly deals with mining, masonry, carving, stone grinding, and mortar making. The main ingredient of this industry is called “Silica” which is the crystalline form of silicon dioxide (SiO₂). Inhalation of respirable silica dust can occur during excavation, disturbance, working, cutting, breaking, crushing, drilling, grinding, or transportation of rock, sand or materials that contain silica. Another dangerous form of exposure to silica is sandblasting or abrasive blasting. Due to exposure to all those processes mentioned above, a disease consists of various respiratory symptoms and radiological abnormalities, known as “Silicosis.”

Silicosis is one of the oldest occupational diseases of civilization. It is a chronic, nodular, exclusively fibrotic disease caused by prolonged inhalation of silica derivatives. When the silica particles accumulate within the airways, they are engulfed and removed into the lymphatic system by lymphocytes and alveolar macrophages. Those who remain in the airways, cause focal aggregation of macrophages, and in due course of time, they convert into fibrosing nodules called “silica nodules” and cause lung inflammation. Silica-induced inflammation can cause pulmonary tissue damage and degeneration of the extracellular matrix, leading to granuloma formation, lung remodeling, and loss of parenchyma. There are different types of manifestations of silicosis, but in a broader headline, they can be classified into acute, subacute and chronic silicosis. The most common respiratory symptoms due to silicosis are dry cough, shortness of breath, and chest tightness. In chest X-ray, there may be multiple nodule sizes ranging from 3 to 5 mm in diameter. These nodules can coalesce and can turn into larger nodules which ultimately leads to progressive massive fibrosis. There may be patchy bilateral lower space consolidation, pleural thickening, and associated hilar lymphadenopathy. Inhalation of particulate matter (PM) 2.5 containing crystalline silica can also increase the likelihood of specific diseases like lung malignancy, mesothelioma, and tuberculosis.

Silica-based ceramic industries have the potential to become the third-largest contributors to Bangladesh's economy within the next 5 years. The most abundant stone processing industries are located in Lalmonirhat, Panchagrah, and Sylhet regions. Most stone-cutting factories (26) are in the Burimari union, Patgram Upazila, Lalmonirhat. As Bangladesh is transforming from an agro-based country to an industrial powerhouse, the prevalence of occupation-related lung diseases is also increasing rapidly. Silicosis is not an uncommon disease in Bangladesh, as many people are exposed to silica dust in their workplaces.

From an epidemiological point of view, data are scarce regarding the respiratory health of stone-cutting workers in Bangladesh. We conducted an epidemiological study to determine respiratory symptoms' prevalence, lung function status, and radiological abnormalities among stone-cutting workers in Lalmonirhat district, Bangladesh. We also measured the dust levels at the workplace by using respiratory dust sampler.

2 | METHODS

2.1 | Study participants and data collection

This cross-sectional study was conducted in Burimari union under Patgram upazila of Lalmonirhat district of Bangladesh. A standardized field questionnaire was formulated in consonance with the British Medical Research Council (BMRC) questionnaire on Respiratory symptoms. As the subjects of this study were from rural communities, the research questionnaire was slightly modified as per the study objectives and local needs and then translated into Bangla for the convenience of data collection from the respondents. Thirteen stone-cutting mills were selected purposively for the convenience of data collection. Before the commencement of actual data collection, the nature and intent of the study were explained to the participants in their vernacular language with the help of local collaborators. A total of 200 stone-cutting workers were selected as the study population. Data were collected by face-to-face interviews taken one by one using a predesigned, pretested questionnaire.

2.2 | Instruments

Our questionnaire-based interview had four parts. The first part was based on the participant's sociodemographic profile, including name, age, sex, religion, marital status, educational status, and monthly income. The second part included work-related history, including questions comprising all the details of present and past employment, including working time, working section, duration of employment, and use of personal protective equipment. The third part contained detail of smoking history, pack-years of smoking and passive smoking, biomass fuel usage during cooking, and mosquito coil or aerosol usage. The final part covered different respiratory symptoms such as chronic cough, chronic phlegm, and chest tightness, shortness of breath, and runny nose. Chronic cough and phlegm were defined as cough and phlegm that persisted for more than 8 weeks. Chest tightness and runny nose were defined as the presence of those symptoms more than twice a month in a year. Shortness of breath was defined as difficulty in breathing while hurrying or walking up a slight hill (MRC grade 2). Physical measurements including height, weight, and body mass index (BMI) of each participant were recorded.

2.3 | Pulmonary function test

After finishing the interview, spirometry was done among the stone-cutting workers. Each subject performed three blows. Forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) measurements were obtained on all subjects in the same sitting
position and manner according to the guidance of "The American Thoracic Society (ATS)" using MIR-Spirolab II spirometer.

2.4 | Chest radiograph

All the stone-cutting workers in this study underwent chest radiographs in a local health facility nearby the stone-cutting factories. After obtaining the radiographs, the films were checked and reviewed by a qualified radiologist.

2.5 | Measurement of dust concentration

Dust concentrations such as PM 2.5 and PM 10 were measured in different areas of the factories by a portable respiratory dust sampler named "Temtop air quality detector." Air quality was checked for 2 days on different occasions. The maximum value recorded among all the readings displayed on the monitor was taken.

PM 2.5 health parameters standards:
- Good: PM 2.5 < 35 µg/m³
- Moderate: 35 ≤ PM 2.5 ≤ 100 µg/m³
- Unhealthy: 100 < PM 2.5 ≤ 250 µg/m³
- Hazardous: PM 2.5 > 250 µg/m³

PM 10 health parameter standards:
- Low: up to 50 µg/m³
- Moderate: up to 75 µg/m³
- High: up to 100 µg/m³
- Very high: >100 µg/m³

2.6 | Data analysis

Data were collected in a preformed questionnaire. After collecting data, all data were checked, tabulated, and coded. Then the data were entered into the computer and statistical analysis was done using the software IBM-SPSS (Statistical Package for the Social Science) version 23. After compilation, data were presented in tables, pie charts and bar diagrams as necessary. Frequency was expressed in percentage. Unpaired t-test, χ² test, scattered plots, and analysis of variance (ANOVA) test were used to find out the differences of different variables as per requirement. A p value of less than 0.05 was considered statistically significant.

3 | RESULTS

3.1 | Baseline characteristics

The mean age of the stone-cutting workers was 42.45 ± 12.46 years. The majority of the workers were male (81.5%). Mean BMI was 22.67 ± 3.06. The mean working experience was 9.5 ± 6.63 years. Ninety-six percent of the workers did not wear masks (Table 1).

3.2 | Respiratory symptoms

We observed that 89% (178 workers out of 200) of the stone-cutting workers complained of at least one chronic respiratory symptom. Chest tightness was the predominant symptom (76%) followed by shortness of breath (74.5%) and chronic cough (66.5%). 54.5% of workers complained of wheeze. 45.5% reported phlegm and 29.5% about runny nose (Figure 1). Higher frequency of respiratory symptoms among nonsmokers (64.6%). Twenty-three percent stone-cutting workers who were smokers complained of at least one respiratory symptom.

3.3 | Lung function and radiology

Mean FEV₁ value was 1.74 ± 0.79 L (range: 0.29–3.6) and FVC value was 2.14 ± 0.97 L (range: 0.29–4.93). The mean FEV₁/FVC ratio was 82.76 ± 16.93 among the stone-cutting workers (Table 2). We observed a decline in FEV₁ and FVC with age (Figure 2). This finding was statistically significant (p < 0.001). Thirty-eight of stone-cutting workers had abnormal X-ray findings. Among them, 27% had bilateral multiple nodular opacity, and 5% showed progressive massive fibrosis. Three percent had eggshell calcification and another 3% showed unilateral patchy opacity. Sixty-two had normal chest X-ray findings (Table 3). 42.69% of stone-cutting workers who exhibited at least one chronic respiratory symptom had restrictive abnormality and 29.77% had an obstructive abnormality. 27.54% of workers had

| Characteristics | n (%) |
|-----------------|-------|
| Mean (±SD)      | 42.45 ± 12.46 years |
| Gender          |       |
| Male            | 163 (81.5%) |
| Female          | 37 (18.5%)  |
| Mean BMI (±SD)  | 22.67 ± 3.06 |
| Mean working experience in years (±SD) | 9.5 ± 6.63 years |
| Use of mask     |       |
| Yes             | 8 (4%)  |
| No              | 192 (96%) |
| Smoking status  |       |
| Nonsmoker       | 131 (65%) |
| Smoker          |         |
| Current         | 43 (21.5%) |
| Ex              | 26 (13%)  |
| Pack year: <10  | 35 (50.7%), |
| 10–20          | 16 (23.2%), |
| >20:           | 18 (26.1%) |

Abbreviations: BMI, body mass index; SD, standard deviation.
normal spirometry findings. The mean FEV₁ value was 1.42 ± 0.65 L in the obstructive pattern, 1.43 ± 0.73 L in the restrictive pattern and 2.29 ± 0.62 L in the normal pattern of spirometry. The mean FVC value was 2.53 ± 1.12 L in the obstructive pattern, 1.53 ± 0.75 L in the restrictive pattern and 2.59 ± 0.71 L in the normal pattern of spirometry. These findings were statistically significant (p < 0.001) (Table 4). 42.69% of stone-cutting workers (76 workers out of 200) who complained of at least one chronic respiratory symptom had abnormal chest X-ray findings. These data were statistically significant (p < 0.05) (Table 5). The mean FEV₁ was 1.24 ± 0.63 L in...
TABLE 5  Frequency of respiratory symptoms according to X-ray findings among stone-cutting workers (N = 200)

| X-ray findings | Respiratory symptoms|
|----------------|---------------------|
|                | Positive (n = 178) n (%) | Negative (n = 22) n (%) | \( \chi^2, df \) | \( p \) value |
| Normal         | 102 (57.3)         | 22 (12.9)          | 3.179, 4 | <0.05 |
| Abnormal (bilateral multiple nodular opacity + unilateral patchy opacity + eggshell calcification + progressive massive fibrosis) | 76 (42.69) | 0 (0) | \( \chi^2 \) test was done. |

Note: A \( \chi^2 \) test was done.

TABLE 6  Association of FEV\(_1\) and FVC with chest X-ray findings with spirometry findings (N = 200)

| Respiratory symptoms | Normal | Bilateral multiple nodular opacity | Unilateral patchy opacity | Eggshell calcification | Progressive massive fibrosis | \( p \) value |
|---------------------|--------|-----------------------------------|---------------------------|-----------------------|-----------------------------|------------|
| FEV\(_1\)           | 2.1 ± 0.68 | 1.24 ± 0.63                      | 1.07 ± 0.27               | 1.29 ± 0.12             | 0.75 ± 0.5                   | <0.001     |
| FVC                 | 2.58 ± 0.76 | 1.49 ± 0.94                      | 1.82 ± 0.26               | 1.48 ± 0.17             | 0.82 ± 0.61                   | <0.001     |

Note: An unpaired t-test was done.

Abbreviations: FEV\(_1\), forced expiratory volume in 1 s; FVC, forced vital capacity.

stone-cutting workers with bilateral multiple nodular opacities on chest X-ray. Those who had progressive massive fibrosis had the lowest mean FEV\(_1\) (0.75 ± 0.5 L) and FVC (0.82 ± 0.61 L) values. This value was much lower than the value found in stone-cutting workers with a normal chest X-ray. All these findings were statistically significant (\( p < 0.001 \)) (Table 6). Workplace dust concentration was measured by a respiratory dust sampler and we found that PM 2.5 and PM 10 levels were higher than the normal safety range. The average PM 2.5 value was 979.78 µg/m\(^3\) and the average PM 10 value was 1298.35 µg/m\(^3\).

4  | DISCUSSION

4.1  | Key findings of the study

This cross-sectional study was conducted at Burimari union under Patgram upazila of Lalmonirhat district, Bangladesh, to measure the point prevalence of respiratory symptoms due to silica dust exposure, lung function status, and radiological abnormalities among the 200 stone-cutting workers of 13 different stone-cutting factories. In this study, we observed that 89% of the stone-cutting workers (178 workers out of 200) had at least one respiratory symptom. This finding is much higher than the other studies. The possible reasons for the higher prevalence in our study may be the usage of outdated pieces of machinery which generated more dust, poor ventilation systems due to lack of proper exhausting fans, overcrowded workers working in a confined space, lack usage of personal protective equipment by the workers and lack of awareness of the workers about the dangers of exposure to silica dust. These airborne pollutants enter the lungs bypassing the upper airway defense mechanism (those with particle size less than 10 µm) and induce an inflammatory response resulting in diverse respiratory symptoms. The reaction is dose-dependent and if the exposure persists, then chronic inflammatory response leads to distortion of lung parenchyma and alteration of pulmonary elasticity. As a consequence, functional impairment of the lungs ensues. A Thai study found that the prevalence of respiratory symptoms among stone-cutting workers was 55.2%. A Nigerian study found that 70.5% of the stone-cutting workers developed respiratory symptoms. These variations of the results may be due to different populations, ethnicity, and machinery setup.

This study found that chest tightness was the predominant symptom (76%), followed by shortness of breath (74.5%) and chronic cough (66.5%), wheeze (54.5%), phlegm (45.5%), and runny nose (29.5%). Similar findings were observed in an Ethiopian study. They observed that chest tightness was the prime symptom (76.8%) followed by shortness of breath (71%), cough (60%), and phlegm (45.8%). A previous study conducted among the stone-cutting workers in our country found that 28.33% of the workers suffered from cough, 4.58% from shortness of breath, 2.29% from wheezing and 1.68% from tightness of the chest. A study in Congo found cough 52.5%, phlegm 45%, and shortness of breath 18.3%. On the other hand, a Thai study found phlegm 24% and cough 17%. The possible lower prevalence of respiratory symptoms due to improved ventilation systems and increased use of personal protective equipment in those countries.

In our study, we tried to observe the association of the frequency of respiratory symptoms with age. We found that the mean age of exhibiting respiratory symptoms was 42.66 ± 12.38 years. Similarly, a Nigerian study found the mean age of exhibiting respiratory symptoms was 40 years.

In our study, we observed that 71.3% workers who worked 10 years or less exhibited at least one respiratory symptom. Only 4.5% who worked for more than 20 years complained of respiratory symptoms. This finding may be due to the toxic effect of silica dust exposure causing early quitting from the job or death of the workers. Very few (only eight) workers in our study could work more than 10 years.
20 years. The mean working duration in years related to the exhibition of at least one respiratory symptom was 9.74 ± 6.73 years. We observed that 23% stone-cutting workers who were smokers complained of at least one chronic respiratory symptom in our study. Tobacco has an additive effect on the respiratory health of the workers in different occupations exposed to dust. However, in our study, we found higher frequency of respiratory symptoms among nonsmokers (64.6%). Also 52.4% of stone-cutting workers who complained of at least one respiratory symptom smoked below 10 pack year. These data were not statistically significant (p > 0.05). It indicates that exposure to silica dust can cause respiratory symptoms or disease independently irrespective of the smoking status of the individuals. A Nigerian study19 found a similar finding.

4.2 | Respiratory symptoms and lung function status

We performed spirometry to observe the lung function status of our study subjects. We observed that the mean FEV1 value in obstructive pattern and restrictive pattern was lower than in standard pattern. The mean FVC value was in obstructive pattern and in restrictive pattern was also lower than in normal pattern of spirometry. These findings were statistically significant (p < 0.05). An Indian study24 found similar findings.

The silica nodules coalesce to form larger nodules which ultimately lead to progressive massive fibrosis and cause restrictive abnormality. On the other hand, silica particles <0.2 µm, diffuse in terminal respiratory units and contact epithelium.25 Thus in this way deposited silica causes irritation of respiratory mucosa which results in hypersecretion of mucus along with hypertrophy of submucosal glands in the trachea and bronchi. Neutrophil also releases proteases which stimulate mucus hypersecretion. Also there is an increase in goblet cells of small airways which leads to excessive mucus production25 which obstructs the airway lumen. We also found an inverse relationship between FEV1 and FVC with age. As the age of the stone-cutting workers increased, the FEV1 and FVC values decreased.

4.3 | Frequency of respiratory symptoms and chest X-ray abnormality

We observed in our study that 42.69% of stone-cutting workers who complaint of at least one respiratory symptom had abnormal chest X-ray findings. These data were statistically significant (p < 0.05). Among them, most had bilateral multiple nodular opacity, few showed progressive massive fibrosis, eggshell calcification and unilateral patchy opacity. An Iranian study26 found 16.4% abnormalities in chest X-ray which was lower than our findings. This finding may be due to improved working conditions and increased workplace hygiene by the workers of that country. Also the application of the “wet treatment system” to the silica dust might have resulted decreased dust emission and therefore reduced dust exposure.27 Wet dusts are relatively heavy and less able to remain airborne. In Bangladesh, this system has not been implemented yet.

4.4 | Association between spirometry findings and chest X-ray findings

We also observed the association between spirometry findings and radiographic abnormalities. We found that among the stone-cutting workers with obstructive pattern in spirometry, 18.2% had bilateral multiple nodular opacities, and 13.6% had unilateral patchy opacities. Among the stone-cutting workers with restrictive spirometry patterns, most had bilateral multiple nodular opacities followed by eggshell calcification and progressive massive calcification. Among the stone-cutting workers with standard spirometry patterns, 94.6% had normal chest X-ray and 5.4% had bilateral multiple nodular opacities. These findings were statistically significant.

We also observed that mean FEV1 was 1.24 ± 0.63 L in stone-cutting workers who had bilateral multiple nodular opacities on chest X-ray. Those with progressive massive fibrosis had the lowest mean FEV1 value (0.75 ± 0.50 L). The mean FVC value was also lower in those with progressive massive fibrosis on chest-ray. These values were much lower than those found in the stone-cutting workers with normal chest X-ray. These findings were statistically significant (p < 0.05).

4.5 | Dust concentration in the stone-cutting factories

During the inspection of the stone-cutting factories, we observed that inside of those factories was filled with visible dust, which looked dense and cloudy. This finding is probably due to increased airborne particulate matter from silica dust contaminated with other dust and emissions from machines during grinding, particularly from the outdated and poorly maintained machines. We found average PM 2.5 concentration was 979.78 µg/m3 and the PM 10 concentration was 1298.35 µg/m3 which was much higher than the safety range.

4.6 | Implications of the study

The stone-cutting workers in our country belong to a particular occupational group, one of the significant contributors to our flourishing economy. So, their occupation-related respiratory problems demand special attention. In our study, we have observed that most of the stone-cutting workers had respiratory symptoms. We also have observed lower FEV1 and FVC values in those workers. We have observed in our study that the scenario of the respiratory health status of the stone-cutting workers is not propitious. From our study point of view, we can draw inferences that increased indoor air
pollution is mainly responsible for this deleterious respiratory health status. Lack of latest technologies, excess dust emission from the outdated machines, improper exhausting system and periodic cleaning of the facilities are the prime reasons for excessive indoor air pollution. Another critical observation is the lack of usage of personal protective equipment by the workers, which has led to the higher frequency of chronic respiratory symptoms in this group.

4.7 | Strengths and limitations of the study

Very few studies in our country have been conducted regarding the frequency of respiratory symptoms, spirometric and radiological abnormalities among the stone-cutting workers in Bangladesh. We measured workplace dust concentration that provided valuable information regarding the impact of dust concentration on the respiratory health of the stone-cutting workers.

As it was a cross-sectional study, data were collected at only a single point in time. The study subjects could not be followed up. We could not measure the toxin level, including Mycoflora mixed with silica dust. The study population was selected from one upazila of Lalmonirhat district, so the results of the study may not reflect the whole picture of the country. Randomization could not be done which might result in selection bias. Designed as cross-sectional, this study could give a clue about possible associations. Actual causation can be perceived based on assumption only. The lack of control group was one of the few limitations of our study.

4.8 | Recommendations

Pre-employment and periodic clinical examination, chest radiography, and pulmonary function tests of the stone-cutting workers should be done. Application of ergonomics should be applied to improve the workplace environment. The use of protective devices such as respiratory masks and goggles by the workers must be implemented to reduce occupational exposure to dust. Although we did not investigate for tuberculosis in those stone-cutting workers exposed to silica dusts, the relationship between silica dust exposure and the occurrence of tuberculosis has been well established. So, we recommend that all employees with cough for more than 2 weeks should be counseled to undergo sputum testing for tuberculosis. Encouragement of the workers should be done to reduce or stop smoking to prevent the development of harmful effects of smoking to themselves and others. Regular cleaning of the floor after work should be encouraged. Health education and rationalization of the work methods to improve the workers’ health and safety must be provided. Workers showing increased respiratory symptoms should be relocated to other profession where dust concentration is low. Collaboration with the government to formulate proper guidelines regarding the ecofriendly establishment of stone-cutting factories and surveillance of the working condition. We also need a proper legal framework to ensure the health safety of our workers. Old and outdated machines must be replaced as they emit an excessive amount of dust. Longitudinal or Intervention studies should be conducted in the future to find out the temporal association between respiratory symptoms and various characteristics, enrich the knowledge and awareness among workers on health hazards based on observations.

5 | CONCLUSION

In conclusion, most of the stone-cutting workers in our study exhibited different respiratory symptoms. These symptoms were associated with abnormal lung function and radiology. Further longitudinal studies are recommended to find out the actual dimension of this problem.

AUTHOR CONTRIBUTIONS
Shamim Ahmed: Conceptualization; formal analysis; methodology; project administration; supervision; validation; visualization; writing—review & editing. Shah Ashiqur Rahman Ashiq Choudhury: Conceptualization; data curation; formal analysis; investigation; methodology; visualization; writing—original draft; writing—review & editing. Abir Hasan Dip: Data curation; investigation. Taposh Bose: Supervision. Ashis Kumar Sarkar: Investigation. Mohammed Atiqur Rahman: Project administration; supervision. Jannatul Ferdous: Supervision. All authors have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST
The authors declare no conflict of interest.

TRANSPARENCY STATEMENT
The lead author Dr. Shamim Ahmed affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted, and that any discrepancies from the study as planned have been explained.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The corresponding author had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

ETHICS STATEMENT
The proposal of this study was approved at the 223rd meeting of IRB (Institutional Review Board) of BSMMU (Bangabandhu Sheikh Mujib Medical University), Bangladesh (NO. BSMMU/2021/4631). Informed written consent was taken from every patient before enrollment.
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