Microbes and Infectious Diseases 2020; 2 (2): 189-196

Microbes and Infectious Diseases

Journal homepage: https://mid.journals.ekb.eg/

Case report

Is COVID-19 masking or delaying the diagnosis of active pulmonary tuberculosis? a case report from Bangladesh

Md Reaz Uddin Chowdhury [1]*, Sahedul Islam Bhuiyan [2], Bimal Chandra Das [1], Md Mahfuzur Rahman [1], Fazla Alahi Khan [1]

1- Abdul Malek Ukil Medical College, Noakhali, Bangladesh.
2- Brahmanbaria Medical College, Brahmanbaria, Bangladesh.

CASE REPORT INFO

Case Report history:
Received 24 August 2020
Received in revised form 27 September 2020
Accepted 30 September 2020

Keywords:
COVID-19
Tuberculosis
Pneumonia
Co-infection.

Abbreviations:
COVID-19: Corona virus disease 2019
TB: Tuberculosis
RT-PCR: Real time polymerase chain reaction
AFB: Acid fast bacilli
LTTBi: Latent TB infection
SARS: Severe acute respiratory syndrome
WHO: World Health Organisation
LMICs: Low-and middle-income countries

A B S T R A C T

Background: The pandemic corona virus disease 2019 (COVID-19) impacts a major global health crisis in the whole world including Bangladesh. Bangladesh is one of the world's high tuberculosis (TB) burden countries and TB is a major public health concern in the country. It is also observed that respiratory disease present with similar features of coronavirus disease, unfortunately and regrettably overlooked by the physicians worldwide due to the pandemic crisis. We presented a case of pulmonary TB and COVID-19 co-infection which has not been reported much.

Case report: A 55 years old female presented with acute respiratory symptoms superimposed on chronic respiratory symptoms as she was suffering from bronchial asthma, diagnosed with severe pneumonia. Oropharyngeal and nasal swabs were found positive for coronavirus by real time polymerase chain reaction (RT-PCR) assay. Assessments of the previous history and clinical scenario also suggested investigations for TB. Sputum was positive for acid fast bacilli (AFB) and Gene Xpert detected Mycobacterium tuberculosis complex with rifampicin sensitivity. Patient was treated concomitantly for COVID-19 pneumonia with starting anti-tubercular drugs. So, physicians should suspect COVID-19 co infections with pulmonary TB while treating the patient presented with respiratory and systemic features. It should be kept in consideration for early diagnosis of pulmonary TB to reduce the morbidity and mortality of patients and to prevent transmission in the community from active sputum positive pulmonary TB.

Introduction

The World Health Organisation (WHO) declared the outbreak of novel coronavirus, an international public health emergency on Jan 30,2020 [1]. The pandemic has spread rapidly with clinical severity, high mortality rate, and capacity to overwhelm healthcare systems [2]. The disease is usually characterized by classical respiratory symptoms and signs [3] similar to those of related other viral infections (eg; influenza, SARS, Middle East Respiratory Syndrome (MERS) and TB, although prognosis and complications sometimes differ. Concomitant TB and COVID-19 reports still very limited. Tuberculosis, the leading cause of

DOI: 10.21608/MID.2020.40417.1055
* *Corresponding author:* Md Reaz Uddin Chowdhury
E-mail address: mail2drreaz@gmail.com

death worldwide from a single infectious agent (1.5 million people per year) [4], like COVID-19, is mainly transmitted through the respiratory route and affects the lungs. About one-fourth of world population are estimated to have latent TB infection (LTTB) [4]. A modelling analysis commissioned by the STOP TB Partnership, Geneva, Switzerland, indicates that the COVID-19 pandemic is deeply affecting TB services effort in prevention, case detection and management [5]. As a result, an increase in TB incidence and mortality is expected in the coming future potentially compromising the results achieved so far and delaying the end TB strategy timelines [5]. On the other side risk factors such as advanced age and some co-morbidities, such as diabetes and chronic respiratory diseases, are associated with poor outcomes in both TB and COVID-19 [6]. Convergence of pulmonary TB and COVID-19 pandemic will be more dangerous with propensity to cause sustained community transmission across the countries. To support the ongoing discussion on the association between COVID-19 and TB, we present one case of concomitant co-infection of COVID-19 and pulmonary TB.

Case presentation

A 55 years old female non-diabetic, hypertensive with history of bronchial asthma presented to the hospital with the complaints of recently developing high grade fever for 7 days, cough with expectoration of copious amount of sputum for same duration and respiratory distress for 5 days. On exploration of the previous days, she mentioned that he was suffering from low grade intermittent fever which usually came at the evening and relived by taking antipyretic, paracetamol with profuse sweating. She also complained of cough for last 1 month with expectoration of sputum, but it was increased much in the last 7 days. She said that she expectorated 2 cupful sputum in a day in the recent days. She has decreased appetite in the last 1 month with an eventual weight loss of 3kg.There was no history of pulmonary TB or contact with TB patients or family members suffering from active pulmonary tuberculosis.

Her background history revealed that she was taking anti-hypertensive drug amlodipine 5mg/olmesartan20 mg combination once daily and regular asthma medication sulbutamol /ipratropium bromide metered dose inhaler (MDI) and Beclomethasone metered dose inhaler (MDI), montelukast 10mg and doxophylin200 twice daily. With these medications her asthma was well-controlled in the recent years.

On physical examinations during admission ,the patient was febrile (103®F), pulse was 110/min, regular with normal volume, blood pressure was 150/90 mm of Hg, heart rate was 112 beats/min, respiratory rate of 28 breath /min and oxygen saturation of 86% on room air immediately put on supplemental oxygen therapy by simple face mask. Other general examinations revealed, mild anaemia, emaciated, there was no clubbing, ankle oedema or raised jugular venous pressure. Chest examinations revealed patient was tachypneic, on auscultation there was bilateral coarse crepitation with bronchial breath sound more marked in the right lung. Findings of the remainder systemic examinations were unremarkable.

Routine blood test revealed the following **(Table 1)**: Haemoglobin was 10.15gm/dl, erythrocyte sedimentation rate was 95 mm in 1st hour, Total white blood cell count (WBC) was 14,000/cmm with 82% neutrophils, 11% lymphocytes and 9% eosinophils, platelets count of 182,000/cmm, serum sodium was 134mEq/L, potassium was 3.9mEq/L, blood urea was 42mg/dL, and serum creatinine was 1.2mg/dl. Other remarkable investigations findings included C reactive protein (CRP) was 24mg/l, random blood sugar was 5.5mmol/l, HbA1c was 5.4%, serum ferritin was >1000ng/ml, serum lactate dehydrogenase was 480U/L, Alanine aminotransferase was 24U/L, Aspartate aminotransferase was 38 U/L, Serum lactate dehydrogenase (LDH) was 480, pro-calcitonin was 0.4ng/ml, troponin I was negative, NT-ProBNP (N-terminal brain natriuretic peptide) was 420pg/ml. Electrocardiogram (ECG) and Echocardiography were within normal limit. Serology was negative for hepatitis B and C, dengue, Brucella, Rickettsia, chikungunaya and malaria. Influenza, cytomegalovirus (CMV) and Epstein –Barr virus (EBV) serology were not done. Blood and urine cultures showed no growth.

Chest radiograph posterior-anterior view revealed bilateral extensive pulmonary involvement with a dense homogenous opacity in the right lower zone likely consolidation and small cavitary lesions as shown in **figure (1)**. High resolution computed tomography of chest revealed large areas of consolidations having internal air bronchogram is noted at almost all segments of right lower lobe. Multifocal areas of consolidations surrounded by

ground glass densities with small cavitations were also noted at apical-posterior segments of right upper, lateral segments of right middle and ground glass opacities in the lingual segments of left upper lobe. Multifocal ground glass density areas intermixed with irregular increased attenuated areas and fibrotic bands were also seen at multiple segments of both lungs. The lesions involved approximately 55-60% of the lung volume as shown in **figure (2-A**, **B)** and **figure (3-A, B)**. Provisional diagnosis of community acquired pneumonia was established.

A trial of intravenous antibiotic comprising (ceftriaxone 2gm twice daily, carithromycin 500 twice daily) was initiated. In view of the height of novel SARS-CoV-2 pandemic worldwide, Oropharyngeal and nasal swabs were also sent for RT-PCR and found to be positive. Sputum for AFB stain showed presence of mycobacterium (+++) and Gene X pert of sputum also revealed rifampicin sensitive Mycobacterium TB complex. After that, history of the patient again reviewed but didn't confirm any history of contact with positive COVID-19 patient or contact with known TB patients. After that her treatment was started simultaneously with four standard anti-tubercular drugs (fixed drug combination-FDC) combinations (Rifampicin150mg+Isoniazid 75mg+Pyrazinamide 400mg+Ethumbutol 275mg) -Category 1 regimen (according to her body weight dose adjusted) according to WHO and Bangladesh TB management guideline. Along with antiviral drug Favipiravir 1600mg loading dose on day 1, followed by 600 mg from day 2 to 10 in addition to antibiotic ceftriaxone 2gm twice daily, clarithromycin 500 twice daily for 14 days, low molecular weight heparin, enoxaparin 40mg subcutaneous twice daily for 7 days along with oral methylprednisolone 80 mg daily for 14 days. Her regular medication of metered dose inhalers by spacer chamber, doxophyllin 200 mg, amlodipine5mg/olmesartan20mg, montelukast 10mg also continued along with these medications.

No adverse event was reported within 21 days in hospital stay. During this period in the hospital, she was showing fluctuating oxygen saturation from 88 to 96%, requiring supplemental oxygen (10-15L/min) through a non-rebreather mask. Patient remained in isolation unit with all aseptic precautions to limit transmission according to national guideline of Bangladesh. Written informed consent was obtained from the patient for using clinical records in this study. After 21 days, patient was discharged from hospital as she was clinically stable with some improved laboratory **(Table 2)** parameters, though follow up RT-PCR couldn't be done due to changing discharge criteria in the guideline of Bangladesh. She was advised for taking category 1 anti-TB drugs for six months along with other medications and a follow up visit after 14 days in the outpatient department and with a follow up X-ray after 6 weeks. During follow up, she was clinically improved with increased appetite, she was on good drug compliance without any adverse events and radiological evidence also showed improvement **(Figure 4)**.

Table 1. Initial investigations after admission.

Investigations	Findings with Reference range
Haemoglobin (Hb%)	10.15gm/dl (11.0-16.0gm/dl)
Erythrocyte Sedimentation rate (ESR)	95 mm in 1st hour (0-20mm in 1st hour)
Total White blood Cell Count (WBC)	14,000/cmm (4000-11000/cmm)
Neutrophils (Differentials)	82% (40-75%)
Lymphocytes (Differentials)	11% (20-35%)
Eosinophils (Differentials)	09% (01-06%)
Platelet count	182,000/cmm (150,000-400,000/cmm)
C reactive protein (CRP)	24mg/L (<7 mg/L)
Alanine Aminotransferase (ALT)	24U/L (Up to 32U/L)
Aspartate Aminotransferase (AST)	38U/L (UP to 40U/L)
Serum Creatinine	1.2mg/dl (0.5-1.3mg/dl)
Blood urea	42mg/dl (10-50mg/dl)
Mantoux test (MT)	Not significant. (Normal induration<10mm)

Sodium (Na^+)	134mEq/L (135-145mEq/L)
Potassium(K^+)	3.9mEq/L(3.5-5.5mEq/L)
D-dimer	0.44mg/l(<0.50mg/l)
N-terminal Pro Bain Natriuretic peptide (NT-ProBNP)	420Pg/ml (<300Pg/ml HF unlikely)
Serum Lactate dehydrogenase (LDH)	480U/L(200-400U/L)
ICT for dengue	Negative
ICT for malarial parasite	negative
Serum ferritin	>1000ng/ml(20-250ng/ml)
Sero immunological test for Brucella Group	Not significant
Weil-Felix Test	Not significant
Sputum for AFB	Positive (+++)
Gene Xpert for Mycobacterium complex and rifampicin sensitivity	Positive with rifampicin sensitive
Random Blood Sugar	5.5mmol/l (Up to 7.8mmol/l)
HbA1c	5.4% (4.5-6.5%)
Pro-calcitonin	0.04ng/ml (<0.1 ng/ml)
Electrocardiogram (ECG)	Within normal limit
Trans thoracic Echocardiography	Normal with good Left ventricular function (EF 65%)

Table2. Investigations before discharge from hospital.

Investigations	Findings with Reference Range
Haemoglobin (Hb%)	11.4gm/dl (11.0-16.9gm/dl)
Total White Blood cell count (WBC)	15,100/cmm(4000-11000/cmm)
Neutrophils (Differentials)	76% (40-75%)
Lymphocytes (Differential)	16% (20-35%)
Erythrocyte Sedimentation Rate (ESR)	62mm in 1st hour (0-20 mm in 1st hour)
Platelet count	213,000/cmm (150,000-400,000/cmm)
C reactive protein (CRP)	26mg/L (<7mg//L)
Serum Creatinine	1.1mg/dl (0.5-1.3mg/dl)
Alanine Aminotransferase (ALT)	36(Up to 32U/L)
Serum ferritin	632ng/ml (20-250ng.ml)
Random Blood Sugar	6.2mmol/l (<7.8mmol/l)
Sodium (Na^+)	144mEq/L(135-145mEq/L)
Potassium(K^+)	5.1MEq/L(3.5-5.5mEq/L)

Serum urea	48mg/dl(10-50mg/dl)
Blood urea nitrogen (BUN)	22.4mg/dl (6.0-21mg/dl)

Figure 1. Bilateral extensive pulmonary involvement with a dense homogenous opacity in the right lower zone likely consolidations with some cavitary lesions in both lungs. White arrows: lesions of COVID-19. Black arrows: lesions of TB.

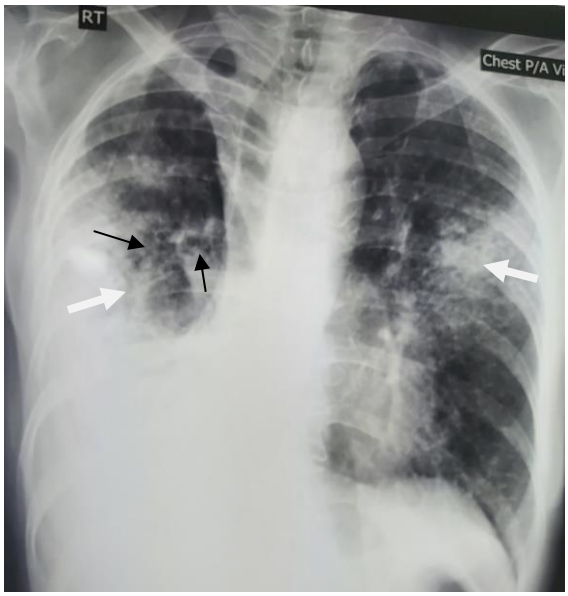
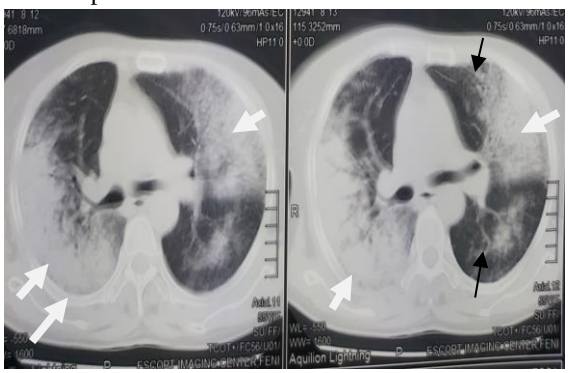


Figure 2 (A, B). Axial view of CT chest showing large areas of consolidation having air bronchogram at almost all segments of right lower lobe. Multifocal areas of consolidations surrounded by ground glass densities are noted. Some ill-defined cavitary lesions also noted in the apical region of left lung. White arrows: lesions of COVID-19. Black arrows: probable lesions of TB.



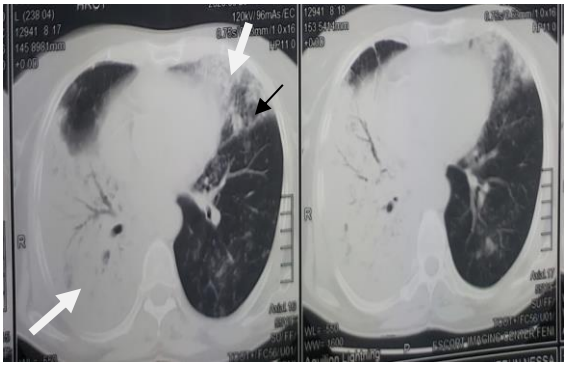


Figure 3 (A, B). Coronal view of CT Chest showing large areas of consolidation having air bronchogram at almost all segments of right lower lobe. Multifocal areas of consolidations surrounded by ground glass densities are noted. Small cavitary lesions also noted in the apical region of both lungs. White arrows: lesions of COVID-19. Black arrows: probable lesions of TB.

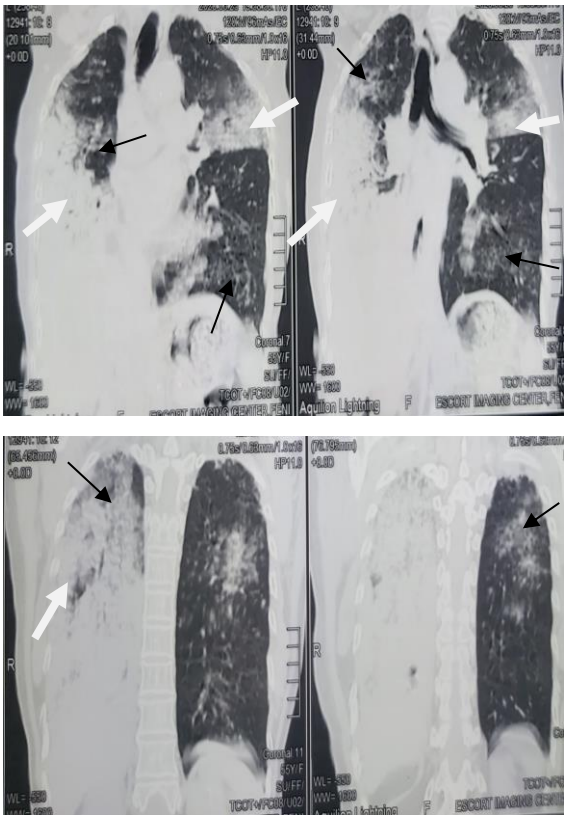
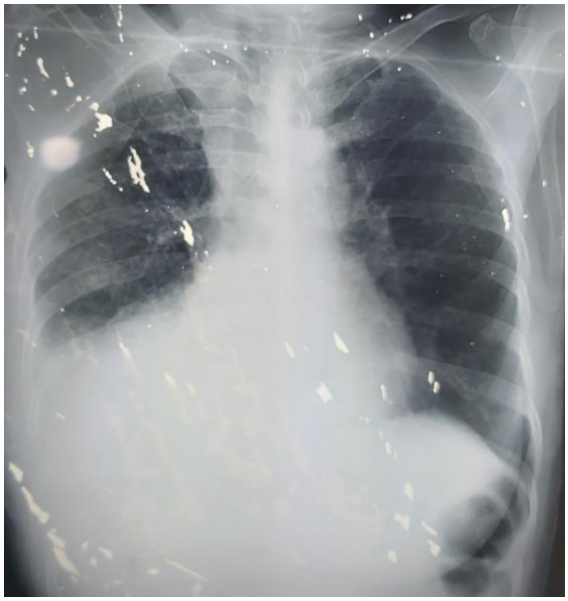


Figure 4. Chest X ray posterior anterior view at follow up after 6 weeks, showing resolving pneumonia.



Discussion:

We have presented the case with particular interest that co-infection of SARS-CoV-2 and pulmonary TB still rare. Few studies have reported co infection of TB and SARS-CoV-1 and middle East Respiratory Syndrome (MERS-CoV) during outbreaks in 2003 and 2012, respectively [7, 8]. Most of the cases were having pulmonary TB initially followed by viral super infection [9] or contacted TB after recovery from viral infection [10]. In our case, the patient seems to have pulmonary TB before and infected with COVID-19 later. The differentiation between TB and COVID-19 is difficult as both manifest with similar respiratory symptoms like fever, cough, breathlessness and generalized weakness. So, it not only can create diagnostic confusion but could also worsen the stigmatisation of TB patients especially in LMICs, given the fear of COVID-19 [11]. But in our case, it was not difficult for us as because the patient had chronic respiratory symptoms in the last 1 month, profuse expectoration of sputum and documented weight loss but she was not presented to the health care systems (Physicians) on the early onset of symptoms ,rather took treatment from the local traditional healer in the fear of COVID-19 and due to lock down in her area. COVID-19 delayed the diagnosis of pulmonary TB according to suggestive clinical presentation of the patient.

With viruses like influenza and SAR-CoV-1, it has been postulated that there is augmentation of dual infection as both cause a transient suppression of cellular immunity predisposing to new infection or exaggerated reactivation of latent infections, both inhibit immune responses mediated by interferon –gamma leading to flare up of TB infection [12]. However, a recent study observed that SARS-CoV-2 did not significantly induce any types of interferons and only upregulated few pro inflammatory cytokines or chemokines unlike SARS-CoV-1[13]. These findings are also similar to our patient.

One study of COVID-19 in 3 cases of TB patients, laboratory test showed leucocytosis, elevated ESR, low lymphocyte count, increased levels of CRP, Ferritin and LDH [14] which is also similar to our findings.

According to the WHO 2017 Global TB report, 38% of drug sensitive and approximately 84% of drug resistant patients are undiagnosed or unreported [15]. In addition to the COVID-19 pandemic, the situation may be going worse though still no data were published. The case we reported also indicates the worse scenario during this pandemic period regarding diagnosis of TB.

As the COVID-19 pandemic spreads into high TB burden settings, countries must put in place strategies to ease pressure on health systems and to mitigate disruption in routine health services [16]. The current social distancing and staying at home measures make it particularly challenging for TB programme to provide diagnosis, treatment and care for communities affected by TB [16]. During the diagnosis and management of the patient, we also felt the same.

Conclusion

This report guided the importance of strict isolation of COVID-19 patients, aggressive contact tracing, careful consideration of previous respiratory symptoms during diagnosis of COVID-19, careful investigations to find out concomitant respiratory disease particularly pulmonary TB because most infectious TB patients are these missing cases. Undiagnosed TB patients often transmit the disease in patient wards, infecting health care workers, patient attendance and other patients like COVID-19. Careful use of steroids or other immunosuppressive drugs need to be evaluated with these subsets of patients to avoid severity or complications. The clinical features and treatment of pulmonary TB with COVID-19 is still unclear and understudied. So, it is essential to make an interim guideline for the management of pulmonary TB with concomitant COVID-19 infection.

Acknowledgements

The authors would like to thank Medinova specialized hospital, Feni, Bangladesh, SARS-CoV-2 managing director Mr Humayun kabir, Chairman of the hospital Mr Abdul Quddus Sumon , medical assistant team ,nursing team and all other stuffs that are fighting against this pandemic disease.

Consent: Written informed consent was obtained from the patient for publication of this case report.

Declaration of competing interest: The authors have no conflict of interest relevant to this case.

Financial disclosure: none declared

References

1- **World Health Organization**. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus(2019-nCoV).2020. Available at: https://www.who.int/news-room/detail/30-01-2020-statement-on the-second meeting of the international –health programme-(2005)-emergency committee-regarding the outbreak-of novel coronavirus. Accessed Feb 15, 2020

2- **Worldometers**. COVID-19 coronavirus pandemic. Available at: https://www.worldometers.info/coronavirus. Accessed June 13, 2020.

3- **Guan WJ, Ni ZY, Hu Yu, Liang WH, Ou CQ, He JX, et al.** Clinical Characteristics of Coronavirus Disease 2019 in China. N Eng J Med 2020; 382(18):1708-20.

4- **World Health organisation**. Global TB Report 2019. Geneva: World Health Organisation 2019. Available at: https://www.who.int/tb/publications/global_report/en/.

5- **Stop TB Partnership, Imperial College, Avenir Health, Johns Hopkins University, and USAID**. The Potential Impact of the COVID-19 Response on Tuberculosis in High-Burden Countries: A Modelling Analysis. Available at: www.stoptb.org/assets/documents/news/Modeling%20Report_1%20May%202020_FINAL.pdf Date last updated: May 1 2020. Accessed May 21, 2020.

6- **Onder G, Rezza G, Brusaferri S.** Case-Fatality Rate and Characteristics of patients Dying in Relation to COVID-19 in Italy. Jama. 2020; 323(18): 1775-6.

7- **Wong CY, Wong KY, Law TSG, Shun TT, Li YK, Pang WK.** Tuberculosis in a SARS outbreak. J Chin Med Assoc 2004; 67: 579-582.

8- **Alfaraj SH, Al-Tawfiq JA, Altuwaijri TA, Memish ZA.** Middle East Respiratory Syndrome Coronavirus and Pulmonary Tuberculosis Co infection: Implications for Infection Control. Intervirology 2017; 60: 53-55.

9- **Liu W, Fontanet A, Zhang PH, Zhan L, Xin ZT, Tang F,** et al. Pulmonary tuberculosis and SARS, China. Emerg Infect Dis 2006; 12:707-709.

10- **Low JGH, Lee CC, Leo YS, Guek-Hong Low J, Lee CC, Leo YS**. Severe acute respiratory syndrome and pulmonary tuberculosis. Clin Infect Dis 2004; 38: e123-e125.

11- **Togun T, Kampmann, B, Stoker NG, Lipman M.** Anticipating the impact of the COVID-19 pandemic on TB patients and TB control programmes. Annals of Clinical Microbiology and Antimicrobials 2020; 19(1): 1-6.

12- **de Paus RA, van Crevel R, van Beek R, Sahiratmadja E, Alisjahbana B, Maruzuki S**, **et al.** The influence of influenza virus infections on the development of tuberculosis. Tuberculosis 2013; 93: 338-342.

13- **Chu H, Fuk-Woo Chan J, Wang Y, Yuen TTT, Chai Y, Hou Y, et al.** Comparative replication and immune activation profiles of SARS-CoV -2 and SARS-CoV in human lungs: an ex vivo study with implications for

the pathogenesis of COVID-19 (2020). Clin Infect Dis 2020; 71(6): 1400-1409.

14-**He G, Wu J, Shi J, Dai J, Gamber M, Jiang X, Sun W, Cai J. COVID-19 in Tuberculosis patients: a report of three cases. Journal of Medical Virology. 2020. Doi:** doi:10.1002/jmv.25943

15-Global Tuberculosis Report. .30 Oct 2017. Available at: https://www.who.int/tb/publications/global_report/en/.

16-**Zumla A, Marais BJ, McHugh TD, Maeurer M, Zumla A, Kapata N, et al.** COVID-19 and tuberculosis—threats and opportunities. The International Journal of Tuberculosis and Lung Disease 2020; 24(8): 757-60.

Chowdhury MRU, Bhuiyan SI, Das BC, Rahman MM, Khan FA. A case report of nosocomial infection with SARS CoV-2 in a one-year old meningoencephalitis patient in a tertiary hospital of Bangladesh. Microbes Infect Dis 2020; 2 (2): 189-196.