COVID-19 and tuberculosis co-infection: a neglected paradigm

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Abstract

COVID-19 pandemic has posed a serious threat to global healthcare and economy. India has one of the highest burden of COVID-19 disease in the world. Presentation of the disease is highly variable. Tuberculosis, one of the top ten causes of mortality has a presentation conspicuously similar to the current SARS-CoV-2 infection. Co-infections of Tuberculosis with past corona virus epidemics like SARS and MERS-CoV had posed a major threat in spread of the disease. We suggest proper tuberculosis screening, isolation of patient, remote tracking of suspected patients for symptoms during the current pandemic.

Introduction

COVID-19 has been declared a Public Health Emergency of International Concern on 30th of January, 2020 by World Health Organisation (WHO) [1]. The presentation of disease ranges from a mild cough, fever and sore throat to pneumonia, acute respiratory distress syndrome and death. Patients with associated comorbidities are usually more vulnerable for a severe disease. As of 15th June 2020, 78 million people have been infected in 216 countries with case fatality rate of 5.52%. India has reported 13.7 million cases with 9520 deaths during the same time [2].

Tuberculosis (TB) is a chronic persistent bacterial disease with a high burden in developing countries like India. TB is of high concern during this pandemic as it presents with symptoms similar to COVID-19. WHO estimates that every year, around 10 million people fall sick with TB infection. It is one of the top ten causes of mortality globally. The disease manifests mostly in adults with male/female ratio of 2:1. It is estimated that worldwide, 1.7 billion people are infected with Mycobacterium tuberculosis and are hence at risk of developing the disease. In 2018, most TB cases were in the WHO regions of South-East Asia (44%), Africa (24%) and Western Pacific (18%), with smaller shares in Eastern Mediterranean (8%), Americas (3%) and Europe (3%) [3].

In this review, we strive to provide evidence from published literature regarding coronavirus related infections (SARS and MERS-CoV) and inapparent/sub-clinical TB co-infection and formulate measures to prevent this global dual burden.

Lessons from SARS and MERS-CoV

It is a well-established fact that corona viruses have caused global concerns in the past with Severe Acute Respiratory Syndrome (SARS) in 2002 and Middle East Respiratory Syndrome (MERS-CoV) in 2013. Genetic composition of the SARS-CoV-2 is very similar to SARS-CoV according to a study [4]. Hence, we have conducted a search with keywords SARS, Tuberculosis and MERS-CoV. Few case studies assessing the risk and burden of co-infection with TB were retrieved using the search engine.

In 2003, a healthcare worker (HCW) in Taipei, Taiwan, was screened for SARS symptoms. He was found to have pleural effusion and later tested positive for TB. In the same hospital, a total of 60 cases of TB among HCs were diagnosed indicating nosocomial transmission [5]. Two patients amongst 236 probable SARS cases in Singapore presented with persistent respiratory symptoms and/or worsening chest radiography findings. They were later found to be co-infected with pulmonary TB. As infection with SARS coronavirus causes a temporary suppression of cellular immunity, these patients were predisposed to aggravated reactivation or new infection with TB [6]. In Beijing, it was seen that 3 patients were co-infected with TB and SARS. Two of them were known cases of TB and had contracted SARS as they shared...
same hospital ward surroundings. One of the patients developed TB after being cured for SARS, which might again be a result of sharing same surroundings with TB patients [7]. In China, another case was reported where a young girl suffering from pulmonary TB was falsely diagnosed as SARS. The patient later on developed SARS as she was isolated with other SARS patients. The treatment of SARS and TB resulted in liver dysfunction. Although the patient recovered uneventfully, it imposes the risk of mis-diagnosis and burden on the patient [8].

Similarly, in Riyadh, 2 cases of TB co-infection were reported from patients of MERS-CoV. Both of them had long-lasting symptoms which predict their chances of being infected with TB prior and with MERS-CoV later. This study highlighted the importance of detailed evaluation of suspected MERS-CoV patients for the presence of other infectious diseases, such as TB and avoid nosocomial transmission in turn [9].

**Infection prevention and control practices – growing concern for communicable diseases**

A review by Migliori et al. [31] reinforced the vital need for IPC practices at the level of patients, family members, health care personnel and hospital surroundings to prevent the communicability of tuberculosis infection. As the main mode of spread is through droplets, IPC plays a predominant role to curb the spread of tuberculosis. Administrative control in proper segregation of high-risk patients and minimising risk of exposure, environmental control in the form of adequate mechanical and natural ventilation and provision of personal protective equipment to health care workers constitute the mainstay of IPC. Even in COVID-19, WHO has advocated to follow similar IPC practices and spatial distancing of at least 1 metre between two suspected patients [32].

**Action points – need for focus**

Following are few measures which could be followed in practice to overcome the dual burden of TB and COVID-19:

i) Immunity to TB in developing countries might be the leading reason of less cases of COVID-19. Although, demographic profile, number of samples tested and socio-demographic determinants might be a serious factor of concern, this needs to be explored further.

ii) Few measures can be taken in the ongoing pandemic to improve effective screening of patients for TB. History of the patient regarding duration of symptoms and past history or family history of active TB can be taken to categorise potential suspects for TB and provide remedial measures as needed.

iii) Patients who seem to be strong suspects (with classical symptoms of TB) ought to be tested for corona virus and mycobacterium tuberculosis to avoid unforeseen burden in the coming times.

iv) Practices like segregation of cases if symptomatic for TB have to be followed without fail to avoid spread to other suspected patients of COVID-19.

v) Cohorting of patients co-infected with COVID-19 and TB has to be done with utmost care in isolation wards to protect patients of COVID-19 from contracting TB as was seen in the past with SARS and MERS-CoV infections.

vi) Newly registered patients of TB should be tested for corona virus to avoid potential mis-diagnosis.
Table 1. Similarities and differences between tuberculosis and COVID-19.

<table>
<thead>
<tr>
<th>No</th>
<th>Characteristic</th>
<th>Tuberculosis</th>
<th>COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Agent</td>
<td>Mycobacterium tuberculosis</td>
<td>Novel Coronavirus (SARS COV-2)</td>
</tr>
<tr>
<td>4</td>
<td>Age group</td>
<td>Mostly affects adults in productive age group (15-34 years). People with HIV/AIDS are at higher risk of infection [3]</td>
<td>Older adults and people who have severe underlying medical conditions like heart or lung disease or diabetes seem to be at higher risk for developing more serious complications from COVID-19 illness [15]</td>
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<td>5</td>
<td>Incubation period</td>
<td>Variable, symptoms develop weeks to years after exposure [16]</td>
<td>2-14 days [17]</td>
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<td>6</td>
<td>Mode of spread</td>
<td>Respiratory droplets produced when an infected person coughs, sneezes, or talks - Virus can also spread from touching a surface or object that has virus on it and then touching their own mouth, nose, or possibly their eyes (less common route) [19]</td>
<td>Fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea [17]</td>
</tr>
<tr>
<td>7</td>
<td>Clinical features</td>
<td>Cough with sputum and blood at times, weight loss, fever and night sweats, chest pain, weakness [20]</td>
<td>Fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea [17]</td>
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<tr>
<td>8</td>
<td>Laboratory features</td>
<td>High erythrocyte sedimentation rate, leukopenia, lymphopenia, high thrombocytopenia, anemia [21]</td>
<td>Decreased albumin, high C-reactive protein, high aspartate amino transferase, high alanine amino transferase, high creatinine kinase, leukocytosis, high bilirubin, high creatinine [23]</td>
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<td>9</td>
<td>Chest X-ray features</td>
<td>Consolidation, thick walled cavity, cavities with air-fluid levels, clustered and military nodules and pleural effusion [24]</td>
<td>Bilateral lower lobe consolidations, peripheral air space opacities, ground glass opacities, diffuse lung opacities and pleural effusion [25]</td>
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<td>10</td>
<td>Diagnostic tests</td>
<td>Sputum smear microscopy, culture test, TB interferon gamma release assays, chest X-rays, serological tests, tuberculin skin tests, molecular assays as Genexpert and Truenat [26]</td>
<td>Viral load detection (RT-PCR), serological-antibody tests (IgM and IgG) [27]TrueNat Beta CoV is used as a screening tool in India [28]</td>
</tr>
<tr>
<td>11</td>
<td>Treatment</td>
<td>Specific treatment guidelines available (isoniazid, rifampicin, ethambutol, pyrazinamide, streptomycin, etc.)</td>
<td>Many trials are underway. Hydroxychloroquine and corticosteroids are currently in place</td>
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<td>12</td>
<td>Case fatality</td>
<td>1.4 million deaths (in 2018) [3]</td>
<td>0.5 million deaths and counting (case fatality rate is 4.9%) [2]</td>
</tr>
<tr>
<td>13</td>
<td>Health sector expenditure</td>
<td>USD 6.8 billion (in 2018) [3]</td>
<td>Unknown, but would be huge leading to global recession</td>
</tr>
<tr>
<td>15</td>
<td>Social impact - stigma</td>
<td>Yes [29]</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Data sharing platform</td>
<td>Lack of organised data sharing platform [29]</td>
<td></td>
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<tr>
<td>17</td>
<td>International surveillance system</td>
<td>Lack of finances [29]</td>
<td>Appropriate surveillance systems in place to track the spread [29]</td>
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<td>18</td>
<td>Knowledge on individual susceptibility</td>
<td>Absent [29]</td>
<td></td>
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<tr>
<td>21</td>
<td>Contact tracing</td>
<td>Helpful in case detection [30]</td>
<td></td>
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<tr>
<td>22</td>
<td>Preventive measures</td>
<td>Following respiratory hygiene and cough etiquettes [30]</td>
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Conclusions

This review provides an insight into the neglected paradigm of a long-standing infectious disease, tuberculosis amidst the ongoing COVID-19 pandemic. Though multi-faceted approaches are in place to deal with the pandemic, few other measures taken at this time might enhance to contain COVID-19 and prevent the ill-effects of missing potential suspects of Tuberculosis.

References