

## ■ ЗАРУБІЖНИЙ ДОСВІД

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# The burden of COVID-19 pandemic on tuberculosis detection: a single-center study

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**Conflict of interest:** none

**BACKGROUND.** Despite coronavirus disease 2019 (COVID-19) took over healthcare providers' interest, tuberculosis (TB) is still an important health issue.

**MATERIALS AND METHODS.** Authors analyzed the quarterly reports issued by a TB management unit from 2017 to June 2021. The parameters along 2020 and first half of 2021 were compared with that of the same periods in 2019.

**RESULTS AND DISCUSSION.** Incidence of extrapulmonary TB was higher than pulmonary TB throughout the 4-year study period (7.69 vs. 4.49, 9.44 vs. 4.33, 7.75 vs. 3.58, and 7.82 vs. 2.94/100,000 population, respectively) with a noticeable decline in the incidence of pulmonary TB during 2020. The second quarter of 2020 showed the lowest TB incidence rate with a 41.6 % decline in the total number of diagnosed cases while second quarter of 2021 showed 21.2 % decline. During 2020, only 4 cases of multidrug-resistant TB were reported (compared to an average of 8 cases yearly before the COVID-19 era).

**CONCLUSIONS.** There was a noticeable drop in TB case detection during the COVID-19 pandemic. The lockdown, started in Egypt by the end of March 2020, could contribute to the marked drop in the second quarter. However, a steady partial decline was continued during the first half of 2021, which foretells a growing problem.

**KEY WORDS:** COVID-19, tuberculosis, detection, lockdown.

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## Вплив тягаря пандемії COVID-19 на виявлення туберкульозу: одноцентрове дослідження

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**Конфлікт інтересів:** відсутній

**ОБҐРУНТУВАННЯ.** Незважаючи на те що коронавірусна хвороба (COVID-19) привернула увагу всіх працівників сфери охорони здоров'я, туберкульоз (ТБ) усе ще є важливою проблемою.

**МАТЕРІАЛИ ТА МЕТОДИ.** Автори проаналізували квартальні звіти протитуберкульозної служби з 2017 р. по червень 2021 р., порівнявши параметри за 2020 р. і перше півріччя 2021 р. із показниками за аналогічні періоди 2019 р.

**РЕЗУЛЬТАТИ ТА ЇХ ОБГОВОРЕННЯ.** Захворюваність на позалегеновий ТБ була вищою, ніж захворюваність на ТБ легень, протягом усього 4-річного періоду дослідження (7,69 проти 4,49; 9,44 проти 4,33; 7,75 проти 3,58 та 7,82 проти 2,94/100 тис. населення відповідно) з помітним зниженням захворюваності на ТБ легень протягом 2020 р. У другому кварталі 2020 р. спостерігався найнижчий рівень захворюваності на ТБ зі зниженням загальної кількості виявлених випадків на 41,6 %, тоді як у другому кварталі 2021 р. було зафіксовано зниження на 21,2 %. Протягом 2020 р. було зареєстровано лише 4 випадки мультирезистентного ТБ (порівняно з 8 випадками на рік до пандемії COVID-19).

**ВИСНОВКИ.** Під час пандемії COVID-19 відчутно знизилася виявлення ТБ. Локдаун, розпочатий у Єгипті наприкінці березня 2020 р., міг сприяти помітному падінню показників у другому кварталі цього року. Проте протягом першої половини 2021 р. тривав стабільний частковий спад, що свідчить про потенційне погіршення стану речей.

**КЛЮЧОВІ СЛОВА:** COVID-19, туберкульоз, виявлення, локдаун.

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# Влияние бремени пандемии COVID-19 на выявление туберкулеза: одноцентровое исследование

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**Конфликт интересов:** отсутствует

**ОБОСНОВАНИЕ.** Несмотря на то что коронавирусная болезнь (COVID-19) привлекла внимание всех работников сферы здравоохранения, туберкулез (ТБ) по-прежнему остается важной проблемой.

**МАТЕРИАЛЫ И МЕТОДЫ.** Авторы проанализировали ежеквартальные отчеты противотуберкулезной службы с 2017 г. по июнь 2021 г., сравнив показатели за 2020 г. и первую половину 2021 г. с аналогичными периодами 2019 г.

**РЕЗУЛЬТАТЫ И ИХ ОБСУЖДЕНИЕ.** Заболеваемость внелегочным ТБ была выше, чем заболеваемость ТБ легких, в течение всего 4-летнего периода исследования (7,69 против 4,49; 9,44 против 4,33; 7,75 против 3,58 и 7,82 против 2,94/100 тыс. населения соответственно) с заметным снижением заболеваемости легочным ТБ в течение 2020 г. Во втором квартале 2020 г. отмечен самый низкий уровень заболеваемости ТБ со снижением общего числа диагностированных случаев на 41,6 %. Во втором квартале 2021 г. данный показатель снизился на 21,2 %. В 2020 г. было зарегистрировано только 4 случая ТБ со множественной лекарственной устойчивостью (по сравнению со средним показателем 8 случаев в год до эпохи COVID-19).

**ВЫВОДЫ.** Во время пандемии COVID-19 произошло заметное снижение выявления ТБ. Локдаун, начавшийся в Египте в конце марта 2020 г., мог способствовать заметному падению показателей во втором квартале этого года. Однако в первой половине 2021 г. продолжилось устойчивое частичное снижение, что свидетельствует о потенциальном ухудшении состояния вещей.

**КЛЮЧЕВЫЕ СЛОВА:** COVID-19, туберкулез, выявление, локдаун.

### Introduction

Since being declared a global pandemic due to its effect on public health and the economy, coronavirus disease 2019 (COVID-19) became the top interest of healthcare providers, scientists, and researchers. However, other epidemic communicable diseases, including tuberculosis (TB), are still a health problem that may grow and drain health facilities [1]. According to the global TB report 2020, an estimated 10 million people are diagnosed with TB, with 1.4 million deaths worldwide [2]. In 2019, the incidence of TB in Egypt was estimated to be 12 cases per 100,000 people [3].

There is growing evidence on the biological, clinical, and epidemiological interaction between TB and COVID-19 [4]. Moreover, patients suffering from comorbid respiratory conditions have impaired lung function and altered immune defense mechanisms putting them at higher risk of developing more severe COVID-19 [5]. A recent meta-analysis indicated that TB was related to a doubled risk of COVID-19 [6]. Unlikely, the response of the COVID-19 pandemic, particularly the transfer of health care equipment and employees and containment measures, affects care initiatives and TB prevention [7, 8]. It was suggested that a lockdown of 3 months followed by an extended recovery of 10 months might result in 1.4 million TB deaths and an additional 6.3 million TB cases from 2020 to 2025. Such statistics would imply a 5-8-year decline in the fight against TB [9]. However, these early modeling investigations depended on assumptions that should be readdressed considering empirical data. Since conducting these analyses, no systematic information has been gathered to quantify the influence of COVID-19 on the burden of TB [10].

The first COVID-19-positive case in Egypt was detected on 3 January 2020, and the lockdown was followed, aiming to limit its spread on 24 March 2020 [11]. To our knowledge, no reports consider the impact of the pandemic and its precautionary measures on healthcare services, including the TB national program in Egypt.

This study aims to estimate the effect of the COVID-19 pandemic on TB case detection in one of the Upper Egypt governorates and evaluate its burden on TB management services.

### Patients and methods

This retrospective chart review study has been conducted by reviewing the records of TB Management Unit in Assiut Chest Hospital. Assiut Chest Hospital was built in 1943 to fight TB in Upper Egypt. Nowadays, the TB Management Unit occupies the old building while the new ones serve other chest diseases. The most recently constructed building, including the emergency room and the respiratory intensive care unit, was transferred to COVID-19 isolation hospital by the beginning of the pandemic. The TB Management Unit collects data of 12 healthcare centers with TB patient management programs all over Assiut Governorate, Egypt. GenXpert (Xpert MTB/RIF assay) was first introduced there in 2015. A total of 2400 samples have been diagnosed with TB and rifampicin resistance.

For the current study, the following data were obtained through the registration system from 2017 to the first two quarters of 2021: new smear-positive and smear-negative cases, retreated cases, treatment failure, defaulters, and new extrapulmonary cases.

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For each quarter, the incidence rates (IR) were calculated. Pulmonary TB was estimated by dividing new and relapsed pulmonary cases over 100,000 population. Moreover, extrapulmonary TB was measured by dividing new and relapsed extrapulmonary cases over 100,000 population. The overall IR for both pulmonary and extrapulmonary cases was also calculated. Comparison between incidence rates was done using Medcalc software based on chi square statistics and P value < 0.05 considered as significant. Besides, the yearly incidence was calculated from 2017 to 2020. For incidence rate calculations and plotting of line graphs, MS Excel was used. The quarterly percentage change in TB cases numbers was calculated by dividing the difference between new and old cases by the old cases multiplied by 100 (2020 relative to 2019 and 2021 to 2019).

$$\text{Percentage change} = \frac{\text{New cases} - \text{Old cases}}{\text{Old cases}} \times 100$$

The study was approved by the institutional review board and ethical committee in compliance with the Helsinki Declaration (IRB: 17300480).

### Results

A total 2256 TB cases were diagnosed in Assiut Chest Hospital from 2017 to 2020 and 237 cases in the first 6 months of 2021. Extrapulmonary cases were more than pulmonary during the study period. There was a gradual decline in the incidence of TB from 12.18 case / 100,000 population in 2017 to 10.75 case / 100,000 population in 2020 and this difference is statistically significant (P value = 0.044) (fig. 1).

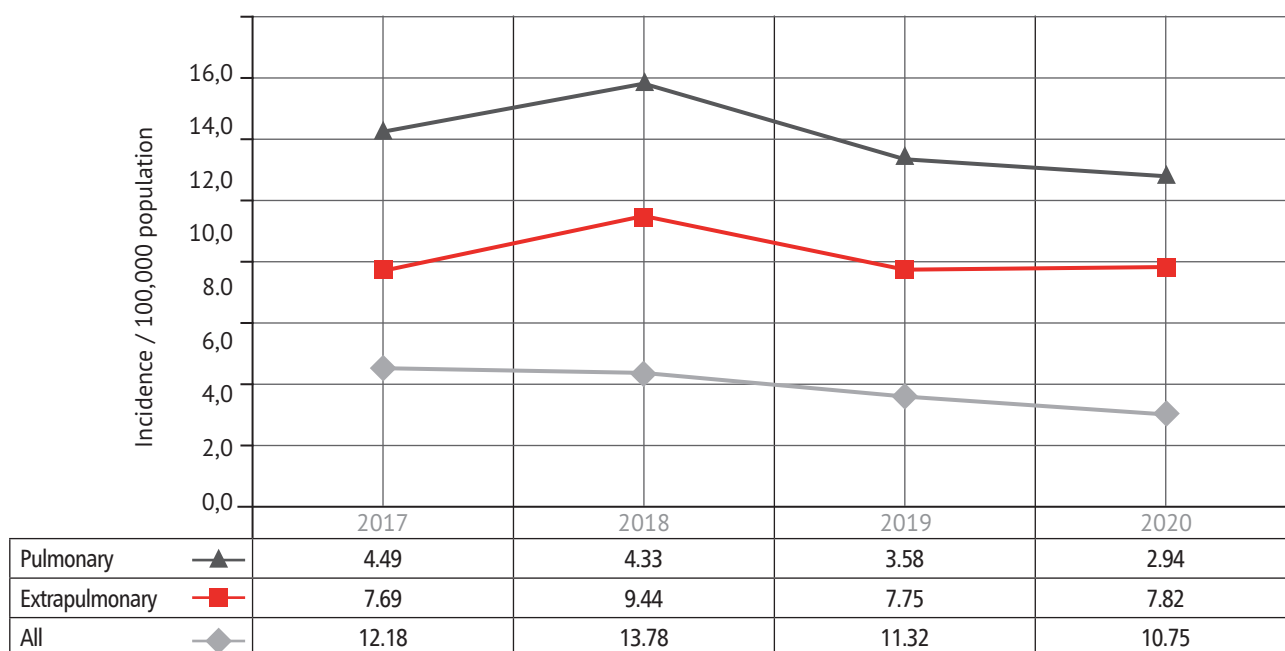
The TB case notification has been markedly declined at the second quarter of 2020 (incidence rate difference for 2020 first quarter vs. second quarter = -1.39/100,000 population,

P value < 0.001) and then rose to its previous levels, then steadily decreased in the first and second quarters in 2021. These patterns of change were observed in all TB cases, either pulmonary or extrapulmonary (fig. 2). Figure 3 demonstrated the incidence trend of all TB cases, pulmonary and extrapulmonary, in different quarters of years 2017-2021. As illustrated, the second quarter of 2020 showed a deep decline in all cases. Incidence rate difference of different years is presented in table.

**Table.** TB incidence rate difference in Assiut Chest Hospital for different years (2017-2020)

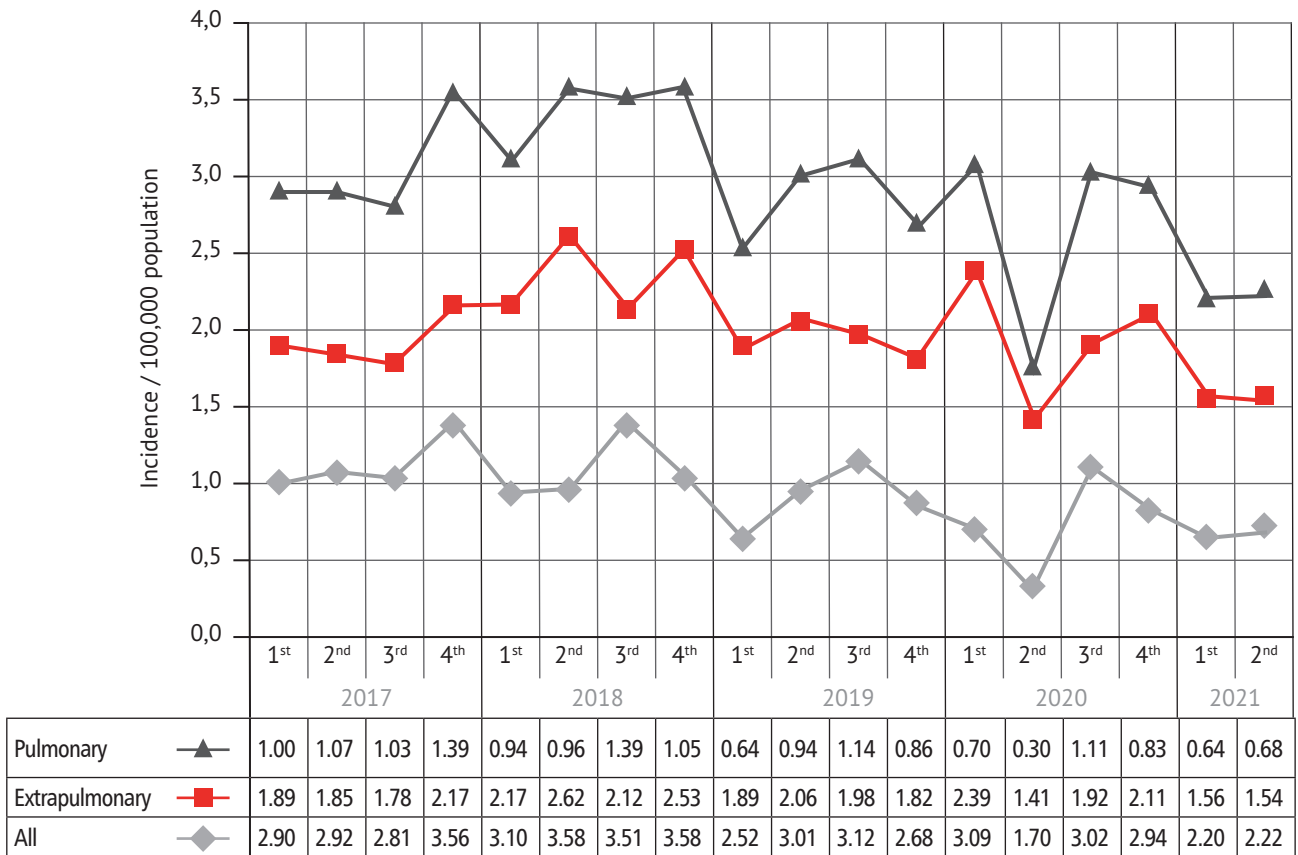
Years	Incidence rate difference (per 100,000)	P value*
2017 vs. 2018	-1.6	0.038 <sup>^</sup>
2017 vs. 2019	0.86	0.236
2017 vs. 2020	1.43	0.044 <sup>^</sup>
2018 vs. 2019	2.46	0.001 <sup>^</sup>
2018 vs. 2020	3.03	<0.001 <sup>^</sup>
2019 vs. 2020	0.57	0.410

Notes: \* chi-square test; ^ significant P value.

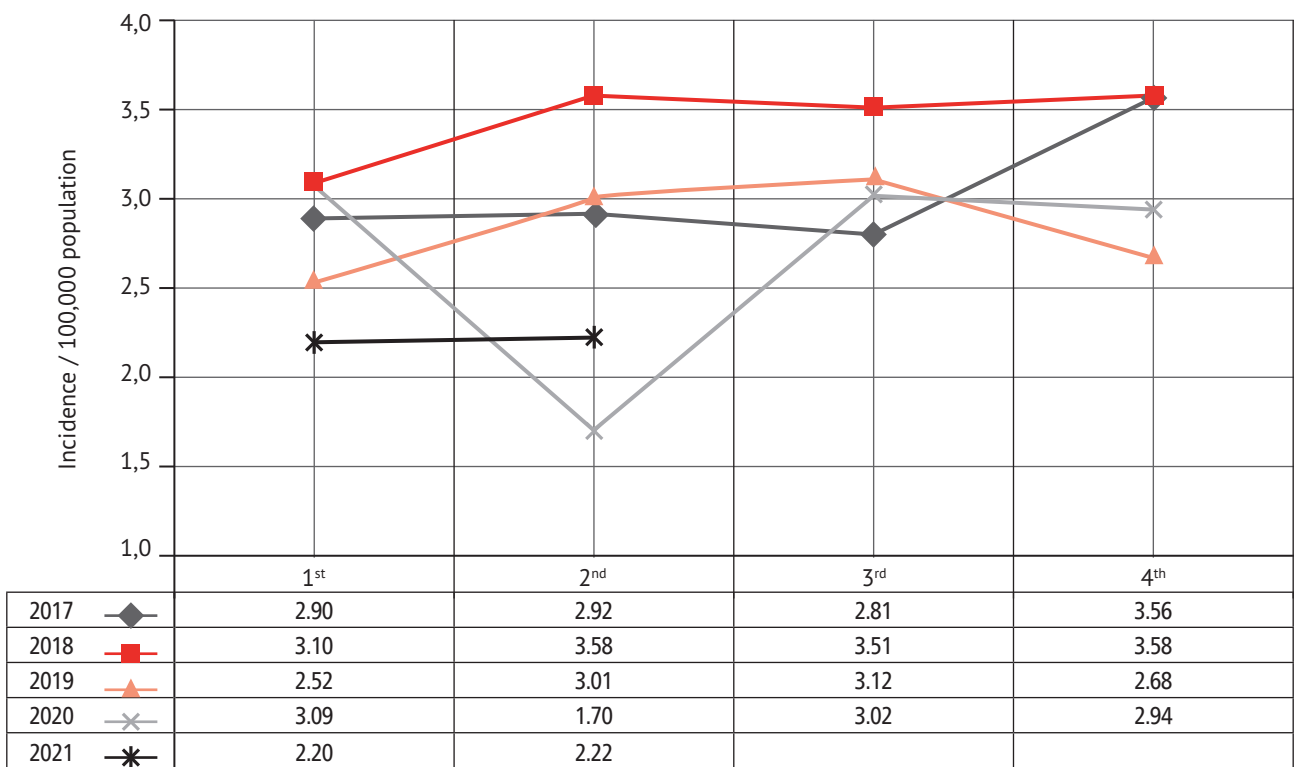


**Fig. 1.** Yearly TB incidence from 2017-2020 in Assiut Chest Hospital, Egypt

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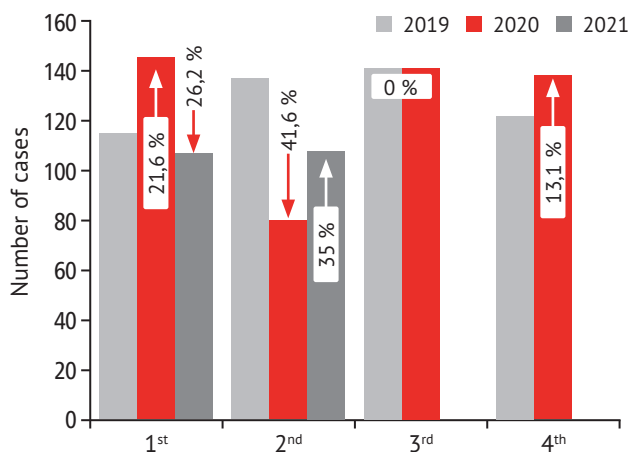


**Fig. 2.** TB incidence over quarters of years (2017-2021) in Assiut Chest Hospital, Egypt TB incidence over quarters of years (2017-2021) in Assiut Chest Hospital, Egypt



**Fig. 3.** TB incidence trends in different years (2017-2021) with comparison between quarters in Assiut Chest Hospital, Egypt(2017-2021) in Assiut Chest Hospital, Egypt

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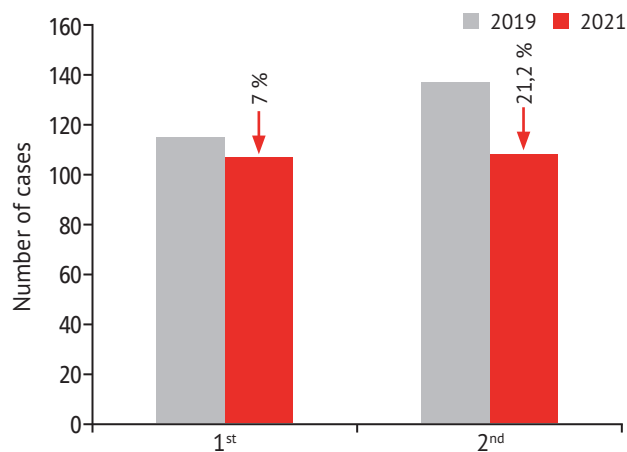
**Fig. 4.** Percent changes in number of TB cases in different quarters (2020 vs. 2019 and 2021 vs. 2020) in Assiut Chest Hospital, Egypt (↑ – increase, ↓ – decrease)

The percentage of changes in the numbers of reported cases has been demonstrated in figures 4 and 5. Comparing 2020 with 2019 showed an increase in the first quarter by 26 % and a decrease by 41.6 % in the second quarter (with 67.4 %, 29.8 % decline in the number of the diagnosed cases of pulmonary and extrapulmonary TB, respectively), was reported. The third quarter showed no changes. In the last quarter, the cases increased by 13 %. Comparing the first two quarters of 2021 with 2020 demonstrated a first-quarter decline of 26 % and a second-quarter increase of 35 %. Moreover, comparing the first two quarters of 2021 to the same period in 2019 demonstrated a decrease of 7 %, 21 %, respectively. Four cases were diagnosed as multidrug-resistant TB (MDR-TB) in 2020, and only one case in the first two quarters of 2021. Since 2015, 42 cases have been diagnosed as MDR-TB, with an average of 8 cases yearly (ranging from 7 to 11 cases per year in the pre-COVID-19 era). Moreover, in 2019, 8 cases of MDR-TB were diagnosed with 50 % drop in MDR-TB detection during the pandemic. However, this was not included in the statistical analysis due to the small number.

### Discussion

Since being declared a global pandemic, COVID-19 exhibits a great burden on healthcare services. To evaluate the impact of COVID-19 on TB case detection, this retrospective chart review study has been conducted. By the beginning of total lockdown in Egypt due to COVID-19 pandemic, a noticeable decline in the incidence of pulmonary TB during 2020 was recorded. The second quarter of 2020 showed the lowest TB incidence rate with a 41.6 % decline in the diagnosed cases. A 67.4 % and 29.8 % decline in pulmonary and extrapulmonary TB cases were reported, respectively.

TB is considered one of the most critical healthcare problems in Egypt. The incidence of TB in Egypt decreased gradually from 26 cases per 100,000 people in 2000 to 12 cases per 100,000 people in 2019 [3]. In the current study, TB decreased from 12.18 cases per 100,000 people in 2017 to 10.75 cases per 100,000 people in 2020. Nevertheless, extrapulmonary TB was higher than pulmonary TB throughout the 4 years reviewed in the study. These findings are inconsistent with



**Fig. 5.** Percent changes in number of TB cases in first two quarters (2021 vs. 2019) in Assiut Chest Hospital, Egypt (↓ – decrease)

data showing that extrapulmonary TB was more prevalent by 64.14 % in a previous study performed in the exact center [12], and 51 % in another center in North Africa [13]. Risk factors for extrapulmonary TB include higher age, female gender, geographical distribution, birth in high TB-prevalent countries, exposure at place of residence or work, homelessness, and presence of other comorbid conditions [14, 15]. Moreover, the COVID-19 pandemic witnessed a noticeable decline in TB incidence, especially in the second quarter of 2020 and the first and second quarters of 2021, correlating with many TB management settings reports [16-19].

The COVID-19 pandemic overwhelmed the healthcare system worldwide, including TB screening and management facilities. Three months after the pandemic, an investigation was carried in 165 countries, with 42 % reporting partial interruptions in TB case detection and treatment [20]. After finalizing data for 2020, a 21 % fall in TB notifications was recorded globally from 2019 to 2020. A substantially more significant reduction was demonstrated in nations with high burdens of TB, such as Indonesia, India, South Africa, and the Philippines. Substantial interruptions will continue in several countries, as indicated by the Primary information for 2021. Countries with a high prevalence of TB, such as Indonesia, Angola, Myanmar, and Lesotho, witnessed a decline of more than 25 % compared to the average for 2019 [21]. In the current study, there was a marked decline in TB incidence during the second quarter of 2020 by a 41.6 % decline in the total number of diagnosed cases; 67.4 % and 29.8 % decline in cases of pulmonary and extrapulmonary TB, respectively. However, the following quarters of 2020 showed restoration of the incidence rate toward that of the same period in the previous year. It may be assumed that the drop in the second quarter was related to the lockdown by the end of March 2020, thus resulting in limited healthcare resources following the national TB program and a reduction in public transportation hours that made the access to public health services more difficult.

Moreover, the growing fear of getting COVID-19 infection during the pandemic's peak resulted in missed or delayed diagnosis of TB cases. These assumptions were supported by reports of COVID-19 prevention assessments requiring the use

of facemasks and social distancing, reduced public attendance at healthcare facilities due to fear of infection with COVID-19, reduced healthcare worker capacity due to the closure of numerous TB outpatient clinics, a lack of personal protective equipment in some health facilities forcing them to cease conducting TB tests temporarily [16, 22].

The rise in the third quarter incidence might be due to the cumulative cases seeking medical services after the lockdown period has been ended. Another hypothesized cause for that rise was the increased indoor/household infections. Again, the first two quarters of 2021 showed a steady drop in both pulmonary and extrapulmonary TB incidence despite the end of lockdown and restoration of most daily activities with the protective measures being applied. The possible explanations for this phenomenon were: the fear of the TB patients from getting COVID-19 infections during transportation to the healthcare facility or from healthcare workers themselves, especially after using Assiut Chest Hospital main building as a COVID-19 isolation hospital. The similarities in symptoms between TB and COVID-19 masked some TB cases who were treated empirically as COVID-19 or refused to seek medical advice. The exhaustion of human resources and equipment in health care facilities affected the competency and efficacy of TB screening programs and the direction of media and social awareness activities, and programs towards COVID-19 prevention are all assumed causes for this continues decline.

The continued decline in TB case detection during 2021 clarify that the burden of COVID-19 on TB is not a temporary problem. With COVID-19 continue to grow and spread, there is an urgent need to restore TB case detection and treatment efficacy to pre-COVID-19 levels. Numerous suggestions to improve TB services in the face of the pandemic have been studied, with being a financial issue and a state of knowledge and awareness. First, improved integration of COVID-19 diagnosis and TB screening at the community and health facilities is required. Second, laboratories must share testing methodologies and multiplexing equipment like GeneXpert platforms. Third, assuring effective infection, control activities, and prevention within health facilities. Fourth, mobilizing TB

networks supporting communities and survivors. Fifth, providing extended 3-month follow-up consultations for drug collection and patient check-ups. Sixth, increasing digital platforms used for drug adherence, case finding, and management. Seventh, spreading awareness in communities and health facilities. It was also advised that recently developed geospatial tracking systems be repurposed to identify contacts of TB and that virtual systems be used to verify compliance with treatment. Additionally, the extraordinary resources and cash gathered to tackle the pandemic should be used to also tackle TB, with a priority to the poor [17, 23–27]. In Egypt, application of the World Health Organization control strategy for TB, including Bacillus Calmette-Guerin (BCG) vaccine at birth, case detection, and treatment of cases with directly observed therapy short-course, is mandatory even during the pandemic. More attention is needed to improve case detection by increasing the awareness and diagnostic facilities in the primary healthcare centers making them closer and more accessible to the patients.

Limited information about TB cases and their demographic and social characteristics resulted in difficulty to track the nature of care for TB cases during COVID-19. Thus, the efficacy of the diagnosis system concerning local circumference was not evaluated in depth in this study. Moreover, the commitment to treatment and visits rates and regularity to outpatient clinics, by patients diagnosed to have TB either before or during the pandemic, was not evaluated. Thus, the infection sequelae and treatment outcome could not be known accurately. Finally, the impact of the COVID-19 pandemic on MDR-TB is needed to be studied nationally, considering a greater sample size.

### Conclusion

There was a noticeable drop in TB case detection and follow-up during the COVID-19 pandemic. The lockdown led to a remarkable decline in the second quarter of 2020. However, a steady partial decline was continued during the first and second quarters of 2021, demonstrating a growing problem. Concerns must be raised against the burden of the pandemic on TB diagnosis and management programs to avoid affecting TB patients' prognosis and survival.

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