Frequency and Risk factors responsible for Multidrug Resistant Tuberculosis in Khyber Pakhtunkhwa

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UF UU MAK conceived idea, SMN SH NA NU drafted the study, MAK SMN collected data, UF SH UU statistics analysis and interpretation, UU MAK critical review manuscript, All approved final version to be published.

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The authors declare that there is no conflict of interest.

Abstract

Background: Occurrence of Tuberculosis (TB) in the form Multidrug Resistant TB (MDR-TB) poses challenges to the health systems throughout the world. Familiarities with risk factors related to disease transmission and exact rate of disease can be used to decrease the infection rate and control of disease.

Objective: Present study was conducted with the aims to find out rate and factors responsible for the occurrence of MDR- TB in a tertiary care hospital Peshawar, Khyber Pakhtunkhwa.

Methodology: This is a cross sectional descriptive study conducted at PMDT Unit, Lady Reading hospital Peshawar, Pakistan with time duration of six months form February 2018 to August 2018. Data of interest through special designed proforma were collected from all suspected cases visited this unit for their checkup. Data was then entered into Microsoft excel sheet and transferred into SPSS software for analyses purposes.

Results: A total of 846 respondents were included in this study including 429 (50.7%) females and 417 (49.3%) males. Majority of the cases 455 (53.7%) were in most gainful age group of > 42 years. Urbanized population accounted for 411 (48.5%). Majority of the respondent lacked education and conjugal status indicated 592 (69.9%) of married participants. Our result found that association between uneducated participants were 69% more likely to contract MDR-TB than those who were illiterate (OR = 1.693, 95% CI [.976-2.938], P = .059). Participants residing in urban areas have 60% lower chances of MDR-TB than rural once. Close contact of patients with MDR-TB has also showed association within increase and occurrence of disease.

Conclusion: The patients of TB and MDR-TB are already suffered a lot by the myths and stigmas that surround the illness. It is highly recommended the community that only food and shelter is not enough, the patient required full support of family and colleagues need full guidance and counseling. Provide financial and practical support for the treatment of disease. All suspected cases with lower education level, residence of far flung areas and close contact of MDR-TB must nominated as special cases for disease occurrence and treated as special cases to stop and cut the chain of this disease.

Key Words: TB; MDR-TB; Khyber Pakhtunkhwa

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Introduction

TB or tubercle bacillus (TB) is the leading infectious disease in the world that has remained among the ten key roots of global mortality. This lethal microorganism killed almost 5,000 daily lives and 40,000 lives per week.[1] According to the expert's estimate, if the control measures are not significantly enriched, the infection rate will be one billion, of which more than 150 million will only develop the disease and 36 million will die in the year 2020.[2]

Symptoms of TB include prolonged productive cough for over 2 weeks, supplemented by shortness of breath, chest pain, hemoptysis, loss of appetite, weight reduction, fever, night sweats and weakness. The transmission of this contagious disease occurs by air when the infected patient expels droplets containing bacilli by coughing, sneezing and laughing. These tiny drops dry quickly but have the ability to suspend in the air for up to four hours, so some of the droplets (10 microns) enter the pulmonary alveoli of the healthy individual by inhalation that consequently contamination.[3]

TB appeared to be manageable in the early 1990s, and declared it a global emergency throughout in the world. Its resurgence in the form of MDR-TB is a new threat to the health system of all countries. MDR-TB is the type of resistance in which the organism becomes resistant to first-line anti–TB drugs Like Rifampicin (RIF) and isoniazid (INH) and is problematic and expensive to treat.[4] The eradication of drug-resistant TB is more urgent and serious on account of the high frequency rates that have positive effect on relapse and mortality rate.[5]

The duration of treatment causes problems in the consistency of the regimen that can be achieved by appropriate treatment with adequate TB prescription. Failure to comply with the regime causes the increase and spread of MDR-TB. Non-effective therapies in MDR-TB, HIV co-infection and noncompliance are three main clinical trials for the treatment of TB that was demonstrated by the MDR-TB high risk in previously treated cases.[6]

Familiarity with risk factors related to disease transmission can be used to decrease the infection rate. TB and MDR-TB generally marks the lowest socioeconomic class that commonly faces problems such as malnutrition, unsafe cooking practices, illiteracy and overcrowding.[1] It is discovered that smoking increases the incidence of the disease. The morbidity of diseases such as diabetes, HIV and hepatitis worsens TB / MDR-TB. A threefold higher recurrence of TB was found in diabetic patients.[3] Migrants and refugees from countries with high incidence are also responsible for the disease. To a certain extent, these groups can disseminate diseases in the general population.[1]

Pakistan is one of the smallest countries in Asia where the burden of TB is high. It is among the high burden countries that reported 60% of TB cases with fourth highest prevalence of MDR-TB. TB Report assessed that 510,000 people suffered from the disease in the nation with 270 out of every 100,000 people affected. In Pakistan, 70,000 deaths are attributed annually to the disease with a reporting rate of 331,809 cases, respectively. However, by the year 2025, Pakistan will occupy fourth place in the list with 14.5 million people who experience this infection if the condition remains the same.[2]

This study is a hospital based study conducted at Programmatic Management of Drug Resistant TB

Table 1. Profile of patients in term of demographic characteristics

Characteristics	Frequency	Percent
Gender		
Female	429	50.7
Male	417	49.3
Age		
> than 42 years	455	53.7
< than 42 years	391	56.3
Marital Status		
Single	253	29.9
Married	593	70.1
Education		
No	759	89.7
Yes	87	10.3
Residence		
Rural	404	47.7
Urban	442	52.3

Unit, Lady Reading hospital, Peshawar, Pakistan, to document rate of MDR-TB in district Peshawar. This also aims to increase the information on the risk factors responsible for MDR-TB in these populations.

Aims and Objectives

Our study has the following objectives:

1. To assess the frequency of TB including MDR- TB in a tertiary care hospital at Peshawar KPK, Pakistan.

2. To investigate different risk factors and the association between different risk factors of this disease

Methodology

Cross sectional descriptive study design was used to recruit the study, based on hospital admissions that have been recorded. We have chosen this study because this is very practical, quick and low cost design that provides us more information in limited time. This study was done in PMDT, Lady Reading hospital (LRH), Peshawar that offers the full scope of inpatient and outpatients services. Location wise this hospital has great importance because it lies in the center of the city. This study consists of all suspected cases for TB/MDR-TB visited this unit due to their illness. Our time period was six months from February 2018 to August 2018. We have followed strict inclusion and exclusions criteria in the selection of the study population for our study.

Data collection tool

Simple random sampling of primary data was obtained through direct communication with the participants. We had opted to a questionnaire method because of its validity, unbiased and low cost. By existing literatures we have developed a structured questionnaire, written in English language and

Table 2. Profile of patients in term of socio-economic characteristics

Characteristics	Frequency	Percent
Facility		
No	474	56.0
Yes	372	44.0
House occupants		
>than 10	313	36.9
<than 10	533	63.1
Rooms		
0 – 5	751	88.7
6 – 10	82	9.6
11 – 15	6	0.7
Above 16	7	0.8
Overcrowding		
No	526	62.1
Yes	320	37.9
Dependent status		
No	621	73.4
Yes	225	26.6
Occupation		
Labor	726	85.8
Office work	120	14.5
Income		
0 – 20000	723	85.4
> than 20000	123	14.6

Note: Overcrowding represented by greater than 5 individual sharing same rooms

translated verbally to the Urdu and Pashto language to remove ambiguity in the translation. Questionnaires were filled up for each patient. Paper based data were entered into computer record system Microsoft Excel program then transferred it Statistical Package for the Social Sciences (SPSS) program for analysis.

Risk factor variables were grouped into demographic variables that included name, (ID number), sex (female/ male), address (districts names), education (illiterate/ secondary), marital status (married/ single) and resident (urban/ rural).Socioeconomic variables were employment (Yes/ No), occupation (labor/ others), total house hold income per month (20000/ < 20000 rupees. Overcrowding characteristics described household size 4 persons per room cooking fuel, (gas/ biomass, coal, cow dung and kerosene). Personal behavior related variables included smoking (active/ passive/ ex-smoker (6 months ago). Symptoms and awareness variables like Productive cough, hemoptysis and weight loss (Yes/ No)). Comorbidity includes arthritis, hepatitis and diabetes. Productive cough referred to prolong cough for more than two weeks while in weight loss term the person will loss 20 kg in month. Additional data on patient clinical category was abstracted from the patient record cards. Clinical history included (New/ Follow up), Treatment category (cat i/ cat ii) and Treatment outcome (cured/ completed/ default/ failure), (Appendix 2 for the definition of variables). Microscopy results (scanty, Up to 1^{+} and > than 1^{+}), Gene Xpert (high/ low/ medium) and RRD (Detected/ Not detected).

Data analysis

Data analysis plan was to examine the association between different risk factors and MDR-TB. Here univariate and bivariate logistic regression used for prediction purposes. We have generated descriptive statistics to support the examination of how the scores of the variables under study were distributed, and the underlying characteristics of the raw data, to provide a platform for inferential statistics.

The Chi-Square test was used to evaluate the statistically significant association between the factors and the prevalence of tuberculosis and MDR-TB. A p-value of 0.05 and the confidence interval (CI) were used to evaluate the statistical significance of the association between independent and dependent variables. All the variables that were analyzed at the bivariate level were entered into the multivariate analysis.

Results

A total of 846 respondents were included in this study including 429 (50.7%) females and 417 (49.3%) males. Majority of the cases 455 (53.7%) were in most gainful age group of > 42 years. Urbanized population accounted for 411 (48.5%). Majority of the respondent lacked education and conjugal status indicated 592 (69.9%) of married participants. (Table 1).

Approximately 474 (56.0%) of the people did not have gas facilities, using biomass and other fuel for cooking. In 532 (62.8%) of the cases, the members of the family were <10 individuals. In most cases, 751 (88.7%) families lived in houses with 1-5 rooms. The cases of congestion represented 319 (37.7%). Around 621 (73.4%) of the participants were dependent. Large proportion of the cases 726 (85.8%) were labors with monthly income around 20,000/month (Table 2).

Table 3. Behavioral of study cases

Characteristics	Frequency	Percent
Active Smoker		
No	419	49.5
Yes	427	50.5
Ex-Smoker		
No	765	90.4
Yes	81	9.6
Passive Smoker		
No	668	78.9
Yes	178	21.1
TB Contacts		
No	531	62.7
Yes	315	37.3

Table 4. Clinical manifestations of the disease

Characteristics	Frequency	Percent
Gene Xpert Result		
MTB detected	507	59.9
Not detected	339	40.1
RRD Detection		
Not detected	777	91.8
Detected	69	8.2
Severity Level		
Not detected	338	39.9
Very low	123	14.5
Low	173	20.4
Medium	192	22.6
High	20	2.6

The smoking status revealed 419 (49.5%) active smokers, 80 (9.4%) ex-smokers and 177 (20.9%) passive smokers. Only about 207 (24.4%) of the participants had knowledge about TB and recognized germs / bacteria as a cause of TB, while only 219 (28.8%) had knowledge about MDR-TB. The question about the contagious nature of TB was answered by 219 (28.8%). Regarding family history, 314 (37.1%) cases belong to families that encountered TB previously and in 30 (3.5%) of the families had family members tainted with MDR-TB (Table 3).

As for the symptoms of TB, the most obvious symptom was productive cough for more than 2 weeks 777 (91.8%). Weight loss was experienced by 528 (62.4%) cases while hemoptysis was reported by 491 (58.0%) (Table 4).

Pulmonary TB was accounted for 746 (88.1%) and 99 (11.7%) were extra pulmonary TB. Under observation with LED microscope, 65% of the cases were reported as acid fast positive bacilli. Positive bacilli "Up to 1+" represent 303 (35.8%) of the cases, while "Greater than 1+" were 249 (29.4%).

The Gene Xpert MTB/RIF assay detected 507 (59.9%) of the positive cases, of which 192 (22.6%) of the cases were at a medium level. Among the 60% interpretable Gene Xpert MTB/RIF assay result; the mutant/resistant strains were identified in 68 (8.0%) cases.

Our result found that association between gender and MDR-MDR-TB was not statistically significant in light of the fact that there was no significant distinction between the female and male category (OR = 1.014, 95% CI [.707-1.453], p = .941. A statistically significant difference was found between the age group. Age group > 42 years have 56% less chances of MDR-MDR-TB (OR = .822, 95% CI [.441-.934], p = .020). There was a significant association between disease and education. Educated participants were 69% more likely to contract MDR-TB than those who were illiterate (OR = 1.693, 95% CI [.976-2.938], p = .059). Participants residing in urban areas have 60% lower chances of MDR-TB than rural once. This result was statistically significant (OR = .650, 95% CI [.448-.943], p = .023). Close contact of patients with MDR-MDR-TB has a negative relationship with the disease prevalence. There is 80% increase in the risk of disease when a person has close contact [Exp (B) = 0.208] (Table 5).

Discussion

The province of Khyber Pakhtunkhwa is harshly affected by TB, where the disease frequency is still high. In 2013, 32% of cases were documented in KPK but has increased to 59% in 2016.[7] MDR-TB is a major public health problem in developing countries. Pakistan ranks fourth among the 27 high MDR-TB burden countries but ranked 5th globally.[1] The estimated MDR-TB in Pakistan is 20% but the exact prevalence of MDR-TB in Pakistan is not known.[8]

The results of our investigation revealed the rate of MDR-TB among the suspected cases attending Lady Reading Hospital Peshawar. Other similar results were found by khan et al., and Ullah et al. and few other studies already conducted here in different years.[1-9] Drug resistance detection required special laboratory tests and technical staff. But in some rural and flank areas of KPK lack these requirements so cases are not properly diagnosed, cultured, and tested for sensitivity to drugs.

Table 5. Prevalence of MDR-TB and demographic factors

MDR-TB				95% Confidence Interval	
Factors	Negative	Positive	p-values	Odds ratios	[Lower-Upper]
Gender					
Female	229	35			
Male	210	33			
Total	439	68	.941	1.014	[.707-1.453]
Age					
> 42	238	44			
< 42	540	24			
Total	778	68	.020	.642	[.441-.934]
Education					
No	119	59			
Yes	659	9			
Total	778	68	.059	1.693	[.976-2.938]
Marital status					
Single	264	42			
Married	514	26			
Total	778	68	.254	1.241	[.856-1.798]
Residence					
Rural	223	43			
Urban	555	25			
Total	778	68	.023	.650	[.448-.943]

MDR-TB treatment is free of cost in Pakistan. Another important general impression among the public about the free drugs supplied by government facilities that these drugs are of low quality and potency, so they are not properly used by patients.

Similarly self-medication is another problem resulting in the increase of MDR-TB. Medicines have an easy access to medicines because these are available at small general stores in every corner of our country. Unfortunately educated people are more involved in self-medication practice.

In the areas where literacy rate is very low, people are unaware of their health condition even they do not realize the serious nature of disease. When they become ill instead of medical treatment they contact quacks, hakims, even soothsayers as illiterate people consider their disease the result of black magic but will not start proper treatment so result in MDR-TB emergence.

In our community there is very easy access to the antibiotics at drugs counters because of lack of implementation of drugs rules and regulations by the competent authorities, improper prescriptions, lack of guidance about the dose, duration of antibiotics, and use of single antibiotic to treat TB, prescription of antibiotic by quacks, all lead to resistance as well as spread of disease.

Gender has a marked impact on MDR-TB epidemiology. The result of our investigation found majority of female patients were associated with the disease 52%. This result is in line with the results found by Khan et al. and Ullah et al. in Peshawar KPK.[1,7] Another research in Punjab found similar result.[51]

Females are more prone to MDR-TB in KPK. Drug susceptible TB is although easy to treat but due to illiteracy, unawareness and attached stigma females hide their illness that result the emergence of MDR-TB. Women are care givers that make them prone to developing MDR-TB as they have longer contact at home with sick MDR-TB patients than men.

Age and the prevalence of MDR- TB have significant association. MDR-TB has affected economically productive stage of both female and male. Age category of up to 42 years has majority of the cases

(65%).Similar results were found by other studies also in Pakistan.[10,11] On the other hand, the study in Spain found that the disease is more frequent in age group < than 42.[12]

Younger people are more likely to have MDR-TB since they are more mobile and active compared to the older group. This economic and productive age group is mainly involved in domestic activities while females busy look after their children. An inconsistent work time makes them unable to take regularly monitored medications, which results in poor treatment compliance. Another possible reason could be that Rifampicin is familiarized in recent decades so younger age groups are in risk and many older people may not have been exposed to it.

A significant association was found between MDR-TB and the education of individual. In our study only 13% of the study participants were educated (18%). A person having basic education up to matric reduces the disease. Javed et al. in his cross sectional study found congruent result in Lahore Pakistan.[13]

Education provides knowledge and awareness about disease its transmission and treatment regimen. Due to lack of knowledge, patients generally leave treatment before completing the regimen that makes the condition adverse. Inadequate knowledge about the cause, spread and treatment of the disease leads to fear of stigmatization that augments the disease. So patients become averse to acquiring proper treatment.

A participants residing in rural area of KPK has higher chances of MDR-TB that is consistent with the research done by Khan et al.[1,14] Conflicting results were found in Punjab, Pakistan and some developing countries.[15] The majority of patients from rural areas of KPK are not properly diagnosed due to malfunction laboratories and technical staff. Specifically in these areas people are not aware of their health condition even they do not realize the serious nature of disease.

Close contacts of MDR-TB are prone to develop other active case of disease. In our investigation we have found an individual with MDR-TB has 5 times more risk to become MDR-TB (5.18, 95% CI 2.83-9.50). About 15% of the total cases have family members that are already under the influence of disease but contact cases or primary assumed MDR-TB was only 3%. Our study was in line with other.[16]

Close contacts are defined as people from the same household sharing common rooms and individuals with prolonged and frequent exposure for example, the workplace, school, prison, hospital ward, or social settings. In KPK again awareness comes into account because illiterate and unaware mothers transmit their disease to their children. Improper public transport and mismanage hospitals specially the waiting areas in hospitals of KPK give rise a proper setup for transmission.[15,17]

Xpert MTB/RIF assay can detect 98% of rifampicin resistance, which act as surrogate marker of MDR-TB. So we have considered all the detected cases of MDR-TB as RIF-resistant TB.[18,19]

In our case we have 137 positive cases RIF-resistant TB that accounts for 14% of the total cases. Our concern result has similarities with other studies. A cross sectional study by Khan et al., Javaid et al. and Ullah et al. found 11.5 and 11.3% resistance in Pakistan.[1,7,5] China accounted for 11% of the MDR-TB.[20]

This difference may be due to geographical location, sample size, and methodology for selection of presumptive patients for study. Another reason for this is difference is the variance in the health care delivery systems in our country indicates poor compliance, lack of treatment supervision ineffective control programs that give rise to the new cases of disease.[17]

High load of bacilli is an independent risk factor that correlates with the disease severity (.98, 95% CI .952-1.016). The present study found significant association between smear-positive MDR cases in comparison to smear-negative. We have identified that a positive bacilli 10 times increases the disease risk.

Conclusion

1. Our study concluded a high prevalence of drug susceptible and rising drug resistant TB in some of the districts of KPK that challenges the disease control.

2. The increasing proportion of MDR-TB patients among previous exposure to anti-TB drugs is a problem of great concern. There is possibility that MDR strains could spread rapidly to become the dominant form of TB unless quick interventions are introduced in the treatment.

3. Drug susceptible and resistant TB shares common risk factors that include gender, age, education and poverty. Females and productive age group of the individual are under the influence of this disease.

4. The problem of MDR and TB are more pronounced in rural residents of KPK.

5. Gaps were found in awareness of respondents interviewed regarding epidemiology, risk factors, signs and symptoms and appropriate prevention methods.

6. Individual who have a visit to another high burden

country for more than six months are at greater risk of contracting and transmitting the disease

7. Smokingand exposure to biomass add to the complications of disease.

8. Gene Xpert MTB/RIF is the best option in high settings due to short turn out time.

Recommendation:

The patients of TB and MDR-TB are already suffered a lot by the myths and stigmas that surround the illness. It is highly recommended the community that only food and shelter is not enough, the patient required full support of family and colleagues need full guidance and counseling. Provide financial and practical support for the treatment of disease.

The disease has infected lower socio economic class in which the proxy measures are poverty, illiteracy and overcrowding. We recommend the community to educate the community specially females that found to be indirectly influence the disease.

Cleanliness and proper ventilation helps to reduce the infection so we can recommend the community to make living environment clean and ventilation proper.It should be kept in mind that one who maintains cleanliness keeps away the diseases so they have to address this issue and advised not to spit everywhere and to cover their mouth while coughing.

We recommend researchers and institutions including universities, to emphasize more on health related studies and investigate the disease in-depth that can be used by health policy makers.

Campaign about awareness of TB among the general population can be augmentedby care workers, media, public leaders, councilors and local NGOs. We highly suggest them to take part and dispersed these facts to all of the community. Even we will recommend the religious leaders of our areas to support the community by mentioning the danger of TB and its spread in their sermons.

References

1. Khan, M.A., Mehreen, S., Basit, A., Khan, R.A., Jan, F., Ullah, I., Ihtesham, M., Khan, A., Ullah, U. and Javaid, A., 2015. Characteristics and treatment outcomes of patients with multi-drug resistant tuberculosis at a tertiary care hospital in Peshawar, Pakistan. Saudi medical journal, 36(12), p.1463.
2. World Health Organization, 2018. Global tuberculosis control: epidemiology, strategy, financing: WHO report 2018.
3. Khan, M. A., Mehreen, S., Basit, A., Khan, R. A., & Javaid, A. (2015). Predictors of poor outcomes among patients treated for multidrug-resistant tuberculosis at Tertiary Care Hospital in Pakistan. American-Eurasian J Toxicol Sci, 7(3), 162-172.
4. Khan, S., Khan, M. A., Ayaz, F., Nasir, M., Ashiq, N., Bahadar, Z., & Khan, M. Y. (2019). Clinical Profile and outcome of Tuberculosis Patients from 2013-2017 at Medical Teaching Institute in Peshawar. Pakistan Journal of Chest Medicine, 24(4), 212-218.
5. Javaid, A., Khan, M. A., Jan, F., Rauf, M., Khan, M. A., Basit, A., & Mehreen, S. (2018). Occurrence of adverse events in patient receiving community-based therapy for multidrug-resistant tuberculosis in Pakistan. Tuberkuloz ve toraks, 66(1), 16-25.
6. Ade, S., Affolabi, D., Adjobimey, M., Ade, G., Anagonou, S., Kumar, A.M. and Harries, A.D., 2017. Operational research within the national tuberculosis control programme in Benin. BMC research notes 10(1): 651.
7. Ullah, I., Javaid, A., Tahir, Z., Ullah, O., Shah, A.A., Hasan, F. and Ayub, N., 2016. Pattern of drug resistance and risk factors associated with development of drug resistant Mycobacterium tuberculosis in Pakistan. PloS one, 11(1): 147529.
8. Basit, A., Mehreen, S., Khan, M. A., Khan, A., Ghafoor, A., Naveed, A., ... & Khan, M. Y. (2018). Management of Drug Resistant Tuberculosis in a teaching hospital before and after implementation of Programmatic Management of Drug Resistant Tuberculosis. Pakistan Journal of Chest Medicine, 24(1), 10-06.
9. Iqbal, R., Munir, M. K., Saeed, S., Salam, A. A., Rehman, S., Qadeer, E., & Khan, S U. (2015). drug resistant tuberculosis among patients in chest unit of Mayo hospital Lahore. Pakistan Journal of Chest Medicine,19(4).
10. Mehreen, S., Khan, M. A., Basit, A., Khan, A., Ashiq, N., & Javaid, A. (2016). Frequency of depression in multidrug-resistant tuberculosis patients: an experience from a Tertiary care Hospital. Pakistan Journal of Chest Medicine, 21(4), 149-54.
11. Ahmad, A.M., Akhtar, S., Hasan, R., Khan, J.A., Hussain, S.F. and Rizvi, N., 2012. Risk factors for multidrug-resistant tuberculosis in urban Pakistan: A multicenter case–control study. International journal of mycobacteriology, 1(3): 137-142.
12. Glaziou, P., Falzon, D., Floyd, K. and Raviglione, M., 2013.Global epidemiology of tuberculosis. Semin Respir Crit Care Med, 34(1): 3-16
13. Javed, H., Tahir, Z., Hashmi, H.J. and Jamil, N.,

2016. A cross-sectional study about knowledge and attitudes toward multidrug-resistant and extensively drug-resistant tuberculosis in a high-burden drug-resistant country. International journal of mycobacteriology, 5(2):.128-134.

14. Erdem, H., Senbayrak, S., Gencer, S., Hasbun, R., Karahocagil, M.K., Sengoz, G., Karsen, H., Kaya, S., Inal, A.S., Pekok, A.U. and Celen, M.K., 2015. Tuberculous and brucellosis meningitis differential diagnosis. Travel medicine and infectious disease, 13(2): 185-191.
15. Hameed, H.M., Islam, M.M., Chhotaray, C., Wang, C., Liu, Y., Tan, Y., Li, X., Tan, S., Delorme, V., Yew, W.W. and Liu, J., 2018.Molecular Targets Related Drug Resistance Mechanisms in MDR-, XDR-, and TDR-Mycobacterium tuberculosis Strains. Frontiers in cellular and infection microbiology, 8:114.
16. Javaid, A., Khan, M. A., Khan, M. A., Mehreen, S., Basit, A., Khan, R. A., ... & Ullah, U. (2016). Screening outcomes of household contacts of multidrug-resistant tuberculosis patients in Peshawar, Pakistan. Asian Pacific journal of tropical medicine, 9(9), 909-912.
17. Larbi-Debrah, P. A. T. R. I. C. K. (2017). Tuberculosis Investigation Among Household Contacts Of Index TB Case In Ga West Municipal Of Greater Accra Region (Doctoral dissertation, University of Ghana).
18. Rie, A. V., Page-Shipp, L., Scott, L., Sanne, I., & Stevens, W. (2010). Xpert® MTB/RIF for point-of-care diagnosis of TB in high-HIV burden, resource-limited countries: hype or hope?. Expert review of molecular diagnostics, 10(7), 937-946.
19. Denkinger, C. M., Pai, M., & Dowdy, D. W. (2014). Do we need to detect isoniazid resistance in addition to rifampicin resistance in diagnostic tests for tuberculosis?. PLoS One, 9(1), e84197.
20. Chen, Y., Liang, W., Yang, S., Wu, N., Gao, H., Sheng, J., Yao, H., Wo, J., Fang, Q., Cui, D. and Li, Y., 2013. Human infections with the emerging avian influenza A H7N9 virus from wet market poultry: clinical analysis and characterisation of viral genome. The Lancet, 381(9881): .1916-1925.