Egyptian Journal of Bronchology

Vol. 5, No 2, December, 2011

ORIGINAL ARTICLE

PREVALENCE OF MULTI-DRUG RESISTANT TUBERCULOSIS IN ABBASSIA CHEST HOSPITAL FROM JULY 2006 TO DECEMBER 2009

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Background: ***Pulmonary tuberculosis (TB) is a major cause of morbidity and mortality world-wide, resulting in the greatest number of deaths due to any one single infectious agent. Drug resistance threatens global tuberculosis control efforts.***

Objectives: ***This study was designed to evaluate prevalence and trends of Multi Drug Resistance Tuberculosis (MDR-TB) in Abbassia Chest Hospital from July 2006 to December 2009.***

Patients and methods: ***This retrospective study included 180 patients admitted to Abbassia Chest Hospital. All patients were resistant to at least Rifampicin and INH. This study reviewed the period between July 2006 and December 2009. Patients' files were analyzed for epidemiological data, causes and types of drug resistance, co-morbidities, side effects of treatment, fate of MDR-TB patients, cases with surgical intervention.***

Results: ***Total reported MDR-TB cases from July 2006 to December 2009 were 130 males and 50 females. Prevalence ranged from 0.31% at 2006, to 0.38% at 2007, 0.64% at 2008 and 0.48% at 2009. Mean age was 36.8 years. Manual workers were 62.2%, while specialized workers were 21.7% and 16.1% were housewives. Retreatment cases represent 97.2% of cases. Primary resistance was found in 30.6% of patients and acquired resistance was found in 69.4%. Diabetes was the most common co-morbidity in 18.3% of MDR cases, followed by COPD in 8.9%. Extra-pulmonary MDR-TB was confirmed in 1.7% of cases. Resistance to INH and rifampicin was a must in 100% of patients, Resistance to streptomycin in 81.1% and to ethambutol in 75.6%. Gastritis was the most common side effect of anti-TB drugs in 88.3 % of cases, followed by peripheral neuritis in 76.7%. Fate of treatment was 65% cured, 21.1% still under treatment, 1.7% treatment failure, 9.4% died and 2.2% defaulters. One case has been undergone surgical removal of the affected lobe.***

Conclusion: ***There is a rising trend of MDR-TB from 2006 to 2008. As regard 2009, a high percent of patients were still under treatment by the time of this study. MDR-TB is more liable to occur among retreatment patients. Acquired resistance is more common due to lack of adherence to treatment or inappropriate treatment. Diabetes and COPD are the most common co-morbidity with MDR-TB. The most common complications of anti-TB drugs were gastritis and peripheral neuritis. Cure was high in all age categories while death was significantly higher in older patients.***

Keywords: ***Tuberculosis, multi-drug resistance, prevalence.***

INTRODUCTION

Tuberculosis (TB) is a medical, social and economic disaster of immense magnitude that is occurring over the world.(1) Strains of Mycobacterium tuberculosis that are

resistant to both isoniazid (INH) and rifampicin with or without resistance to other drugs have been termed multi-drug resistant strains. INH and rifampicin are keystone drugs in the management of TB.[2]

While resistance to either INH or rifampicin may be managed with other first-line drugs, Multidrug resistant TB (MDR-TB) demands treatment with second-line drugs that have limited sterilizing capacity and are less effective and more toxic.[3] Emergence of MDR-TB is complicating TB control efforts.[4]

The incidence of drug resistance has increased since the first drug treatment for TB was introduced in 1943. The emergence of MDR-TB followed the widespread use of rifampicin since the 1970s. The WHO Stop TB Department estimated the number of cases (including new and retreatment cases) occurring worldwide in 2003 alone to be 458000.[5]

According to WHO TB profile for Egypt 2004, the incidence of new cases of MDR-TB was 2.2%, while that of previously treated TB cases which was discovered to be MDR-TB was 38%.[6]

The spectrum of this form of TB now ranges from basic MDR-TB, with resistance only to rifampicin and INH, to XDR-TB where there is additional extensive drug resistance to at least three of the six main classes of second-line drugs.[7]

Early detection of MDR-TB allows starting of an appropriate treatment, which has an impact on the better control of the disease.[8] The treatment of MDR-TB is a challenge which should be undertaken by experienced clinicians at centers equipped with reliable laboratory service for Mycobacterium tuberculosis culture and in vitro sensitivity testing.[9]

The recommended duration of treatment is guided by smear and culture conversion. The minimal recommended duration should be at least 18 months after culture conversion. Extension to 24 months may be indicated in patients defined as chronic cases with extensive pulmonary damage.[10] One of the major concerns about second-line anti-TB drugs is their potential to cause adverse effects. The experience of MDR-TB treatment pilot projects has contributed to greater knowledge about these adverse reactions in various population.[11]

Aim of the work: This study aimed at evaluating the prevalence and trends of MDR-TB in Abbassia Chest Hospital in the period from July 2006 to December 2009.

PATIENTS AND METHODS

The MDR-TB department in Abbassia Chest Hospital in Cairo is the referral department of MDR-TB cases for most of the Egyptian governorates. Almamora Chest Hospital in Alexandria is the second hospital with a MDR-TB department. This retrospective study included 180 MDR-TB patients admitted to Abbassia Chest Hospital from all governorates from July 2006 to December 2009. During the same period, 25 MDR-TB patients, not included in this study, were admitted to Almamora Chest Hospital.[12]

Patients were subjected to:

- Full history taking.
- Full clinical examination.
- Chest imaging.
- Full hematology and chemistry lab.

Samples, such as sputum or broncho-alveolar lavage, were subjected to Mycobacterium tuberculosis studies:

- Direct smear stained by Ziehl-Neelsen.
- Culture on Lowenstein-Jensen medium.
- Culture on BACTEC 460 TB system.
- Culture on mycobacteria growth indicator tube (MGIT).

The patients' files have been analyzed for the following data:

1. Epidemiological data of patients; Age, sex, occupation, residence, special habits, contacts.
2. Type of resistance; secondary or primary.
3. Causes of drug resistance; irregular drug intake due to side effects of drugs, irregular intake due to unavailability of certain drugs, poor adherence to treatment.
4. Pattern of drug resistance to INH, rifampicin, streptomycin, ethambutol.
5. Type of resistant patients; defaulters, treatment failure, relapse, new cases.
6. Co-morbidities; diabetes, COPD, hypertension, chronic liver disease.
7. Side effects of anti-tuberculosis drugs; gastritis, peripheral neuritis, irritable bowel disease, hypothyroidism, hypokalemia.
8. Fate of MDR-TB cases; cured cases, died cases, still under treatment cases, defaulters, treatment failure (suspected XDR-TB), surgical interference.
9. Radiological classification of disease extent:[13]

   Minimal lesion; lesions of slight to moderate density but do not contain demonstrable cavitations. They may involve a small part of one or both lungs, but the total extent regardless of distribution, should not exceed the volume of the area above the second

chondro-sternal junction and the spine of the fourth or the body of the fifth thoracic vertebra on one side.

Moderately advanced lesion; lesions may be present in one or both lungs, but the total extent should not exceed the following limits:

a) Disseminated lesions of slight to moderate density that may extend throughout the total volume of one lung or the equivalent in both lungs.

b) Dense and confluent lesions limited in extent to one third the volume of one lung.

c) Total diameter of cavitation(s), if present, must be less than 4 cm.

Far advanced lesion; more extensive than moderately advanced lesion.

10. Sputum specimens; collection of three morning sputum specimens,[14] preparation of ZN staining,[15] microscopic examination and reporting of smears results,[16] concentration and decontamination of sputum specimens and culture.[17]

11. Drug susceptibility testing; susceptibility was performed by conventional drug incorporation method using 4 anti-TB agents; INH, rifampicin, streptomycin, ethambutol.[18]

RESULTS

During the period of this study, the number of MDR-TB cases reported in Egypt was 205 cases (180 cases in Abbassia Chest Hospital and 25 cases in Almamora Chest Hospital). This number represents 0.5% of all TB patients reported in Egypt in the same period (40233 TB cases).[12] Unfortunately, we could not reach to the files of the 25 cases admitted to Almamora Chest Hospital.

All the following results considered the 180 cases admitted to Abbassia Chest Hospital only. According to residence of patients; 33 (18.3%) were from Cairo, 33 (18.3%) from Dakahlia, 15 (8.3%) from Qaliubia and 12 (6.7%) from Sharkia. There was less than 9 cases from each of Aswan, Domietta, Souhag, Beheira and Giza. There was less than 6 cases from each of Fayoum, Kafr ElSheikh, Menia, Port Said, Alexandria, Assiut, Gharbia, Menoufia, Qena and Benisweif. There was less than 3 cases from each of Ismailia, Suez, Albahr Alahmar and Luxor.

Table 1. Prevalence of MDR-TB cases admitted in Abbasssia Chest Hospital in relation to total TB cases reported in Egypt.

Year	Total TB cases in Egypt	TMDR-TB cases in Abbassia	Prevalence of MDR-TB
2006	10400	32	0.31%
2007	10050	38	0.38%
2008	9746	62	0.64%
2009	10037	48	0.48%

Table 2. Demographic and socio-economic characteristics of MDR-TB cases.

Character		Total number	%
Gender	Male	130	72.2%
	Female	50	27.8%
Age category	< 25	42	23.3%
	26-35	40	22.2%
	36-45	51	28.3%
	>45	47	26.1%
Age	Mean + SD	36.8 + 12.5	
Occupation	Specialized work	39	21.7%
	Manual work	112	62.2%
	Housewife	29	16.1%

Seventy one cases denied history of contact to TB patients. The other 109 cases with history of contact included 8 medical staff (one male doctor, one male nurse and six female nurses) who were contacts to MDR-TB cases.

Among MDR-TB cases, 63 (35%) were smokers while 20 (11.1%) were drug addicts.

As regard co-morbidity; 33 (18.3%) were diabetics, 16 (8.9%) had COPD, 13 (7.2%) had HTN, 6 (3.3%) had chronic liver disease and 4 (2.2%) had Ischemic heart disease.

According to localization of TB, there was 177 (98.3%) pulmonary TB cases while only 3 (1.7%) had extra-pulmonary TB. As expected, all cases were resistant to both INH and rifampicin. Resistance to streptomycin was documented in 146 (81.1%) cases and resistance to ethambutol was found in 136 (75.6%) cases.

Primary resistance was reported in 55 (30.6%) cases while secondary (acquired) resistance was reported in 125 (69.4%) cases. Retreatment cases represent 97.3% of all MDR-TB cases. Retreatment cases include defaulters (54.5%), treatment failure (41.9%) and relapse cases (0.9%). New cases represent 2.7% of all cases.

Table 3. Adverse effects of anti-TB drugs among MDR-TB cases.

Adverse effect	Number affected	% of total MDR-TB
Peripheral neuritis	138	76.7%
Ototoxicity	24	13.3%
Gastritis	159	88.3%
Irritable Bowel disease	84	46.7%
Hepatic toxicity	15	8.3%
Hypothyroidism	80	44.4%
Hypokalemia	42	23.3%
CNS complications	29	16.1%
Gout arthritis	26	14.4%
Gynecomastia	9	5.0%

Table 4. Place of treatment and Fate of MDR-TB cases.

		Number	%
Place of treatment	Home	109	61.9%
	Hospital	67	38.1%
Fate	Cured	117	65%
	Death	17	9.4%
	Under treatment	38	21.1%
	Defaulter	4	2.2%
	Treatment failure	3	1.7%
	Surgery	1	0.6%
Respiratory Failure		2	1.1%

Among died cases, six were diabetics, two were COPD with respiratory failure and one case had chronic liver disease. The rest died from drug side effects especially hepatic toxicity; 3 of them developed XDR-TB. The 3 treatment failure cases were all suspected to have XDR-TB.

Table 5. Effect of socio-demographic characteristics on fate of MDR-TB.

Character		Death		Cured		X2	P
		number	%	Number	%		
Gender	Male	14	82.4%	84	71.8%	0.842	0.359
	Female	3	17.6%	33	28.2%		
Age category	< 25	2	11.8%	26	22.2%	8.253	0.033
	26-35	2	11.8%	28	23.9%		
	36-45	3	17.6%	37	31.6%		
	> 45	10	58.8%	26	22.2%		
Occupation	Specialized	4	23.5%	26	23.0%	0.489	0.783
	Manual	11	64.7%	66	58.4%		
	Housewife	2	11.8%	21	18.6%		

There was a significant association between death and older age as 58.8% of deaths occurred in the > 45 yr old age group, as shown in table 5. Smoking did not influence fate of MDR-TB while addiction significantly affected results; 29.4% of deaths where addicts and only 10.3% of cured were addicts (p=0.027). Diabetes showed a non-significant trend to influence fate as 35.3% of died cases were diabetics while only 16.2% of cured cases were diabetics (p=0.06).

Fifteen cases of those treated in hospital died, representing 93.8% of all deaths, while only 2 (6.2%) of those treated at home died. On the other hand, only 25.6% of cured cases were hospitalized and 74.4% of cured cases were treated at home (p=0.0001).

DISCUSSION

MDR-TB is a rapidly increasing health problem with major socio-economic and individual consequences.[19] The spread of MDR-TB can only be prevented by rapid identification of these cases and treatment with a combination of effective drugs. The first important step in achieving this goal is that microbiological laboratories become able to perform reliable and rapid drug susceptibility tests to both first and second line anti-TB drugs.[20]

In this study mean age was 36.8 yrs, representing the period of physical, mental and occupational stress. Similar finding was reported in other Egyptian studies.[18,21-23]

The majority of MDR-TB cases in the present study were males (72.2%) while females represented 27.8% of cases. Similar results was reported by other Egyptian studies.[21,24] This reflects the total TB distribution in Egypt as reported by two other Egyptian studies; 76% males and 24% females.[22,25]

Manual (skilled) workers were 62% in this study population, while specialized workers were 21.7% and housewives were 16%. This might be due to exposure of manual workers to infection more than other categories. Besides, they suffer more from lower income, worse housing and work environment, ignorance and illiteracy.[21,23,26,27]

The most frequent special habits were smoking (35% of cases) and drug addiction (11.1% of cases). However, as mentioned in other studies,[18,21] we did not find a significant effect of smoking on fate of MDR-TB while drug addiction was a significant cofactor in outcome of MDR-TB.

In the present study, retreatment cases (defaulters, treatment failure and relapse) represent 97.3% while new cases represent 2.7% of MDR-TB cases. This conflicts with other studies that found 0% new cases,[28] or 46% new cases.[18] This conflict may be explained by the relatively small number of patients in both studies; 21 cases and 26 cases respectively.

Acquired resistance predominates in the present study (69.4% of MDR-TB cases) while primary resistance was found in 30.6% of cases. This data confirms the previous studies in the Egyptian society.[21,23,29]

Surprisingly, we did not find reported cases of MDR-TB with HIV +ve or AIDS. The most common co-morbid disease was diabetes (18.3%) followed by COPD (8.9%). Diabetes showed trend of influence on fate of MDR-TB although this did not reach to significant level (p=0.06). Similar results were reported by others.[23,30]

We noticed, high prevalence of resistance to streptomycin (81.1%) and ethambutol (75.6%). This was found in other studies.[18,21]

We found in this study that gastritis and peripheral neuritis were so common among MDR-TB cases (88.3% and 76.7% respectively). This is in agreement with results of Dhingra et al 2004.[31] Hepatic toxicity was much less (8.3%) than that reported in other studies.[32,33] This difference could be due to difference in regular follow-up and frequency of laboratory monitoring. However, hepatic toxicity in this study was the most significant cause of death among drug adverse effects (p=0.0001).

Good news was that present results indicate good fate of MDR-TB cases. Cured patients were 117 (65%) while died patients were 17 (9.4%). Very near results were reported in Iran and Uzbekistan.[34,35]

Another good news was the significantly better fate in patients treated at home in comparison to those treated in hospital (p=0.0001). This indicates that most of MDR-TB cases can be treated at home under close observation and regular follow-up without over abuse of hospital resources.

We must admit that this study reported a prevalence of MDR-TB in Egypt of around 0.5%, a result much less than that reported by WHO report 2004.[6] This difference means that we need better collection and analysis of data, transparency of information, more departments for MDR-TB isolation in other governorates and better notification policy from private sector of health service.

CONCLUSION

MDR-TB is slowly rising in Egypt from 2006 to 2009. As regard 2009, a high percent of patients were still under treatment by the time of this study. MDR-TB is more liable to occur among retreatment patients reflecting the danger of poor adherence and observation of TB cases. Acquired resistance is more common than primary resistance due to lack of adherence to treatment, inappropriate treatment or lack of follow-up. Diabetes and COPD are the most common co-morbidities with MDR-TB. The most common complications of anti-TB drugs used in treatment of MDR-TB were gastritis and peripheral neuritis. Cure was high in all age categories while death was significantly higher in older patients. No accurate or enough data is available as regard the size of XDR-TB in Egypt. We need more units for management of MDR-TB to serve other governorates.

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