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Vol. 35, No. 1, January 2011

ORIGINAL ARTICLE

Etiology and Outcome of Respiratory Distress in Newborn

Lutfan Nessa[1], Soofia Khatoon[2], Nazneen Akhter Banu[3], Abdur Rouf[4], Md. Shahedur Rahman Khan[4], Naimul Hoque[4], Biswas Akhtar Hossain[4], Barkat Ullah[4], Nihar Ranjan Saha

Abstract:

The present study was conducted to find out the etiology and out come of respiratory distress(RD) in newborn.Fifty sick newborns having respiratory distress were studied between the period of 1st October 2000 to 20th March 2001 in neonatal care unit of SSMC,Mitford Hospital,Dhaka.Diagnosis was made by taking history(antenatal,obstetric,postnatal and presenting complaints),doing examination(taking weight,scoring dubowitz,cyanosis,respiratory distress,respiratory rate) and relevant investigations(chest x-ray,screening test for infection,blood biochemistry,cranial USG and echocardiography). The newborns were managed with appropriate therapy(suction of oropharynx,gastric lavage,maintenance of temperature,appropriate feeding,incubator faciality,antibiotics,anticonvulsant,sodibicarb).There were 32 male and 18 female patient.The etiology of respiratory distress in studied cases was perinatal asphyxia 26(52%),meconium aspiration syndrome 7(14%),transient tachypnoea of newborn 6(12%),septicemia 6(12%),pneumonia 4(8%),and hyaline membrane disease 1(2%).The survival was 34 and 16 expired.The case fatality ratio was high in perinatal asphyxia,meconium aspiration syndrome and septicemia.

Key words:*Newborn,Respiratory Distress,Etiology,Outcome.*

[Chest & Heart Journal 2011; 35(1) : 1-4]

Introduction:

Respiratory distress is a common cause of admission of newborn in a medical college hospital with considerable mortality[1-4].It accounts for half of all neonatal deaths[5-7].It is a heterogenous group of illness with varying etiology,clinical course and outcome..So it is important to find out exact etiology of respiratory distress in newborn and diagnosis will be made by taking history (antenatal, obstetric, postnatal and presenting complains),doing examination and relevant investigations. A neonate showing one or more of the following signs for more than two hours considered to have respiratory distress[1,3]- I) Respiratory rate>60/ m, II) Grunting, III) Intercostal or subcostal retraction, IV) Cyanosis. This study is designed to investigate the etiology and outcome of neonatl respiratory distress in neonatal care unit of a tertiary hospital and this will enable the obstetrician and paediatrician to take appropriate measure as early as possible.So by this study,it will be possible to develop co-ordination between the obstetric and neonatal services which will reduce the neonatal mortality and morbidity with respiratory distress.

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In the recent years, neonatal respiratory disorders have evoked much interest and enthusiasism.There have been tremendous advances in ventilator therapy,surfactant replacement,extra-corporeal membrane oxygenation and sophisticated monitoring gadgets.They have improved the outcome among the babies with respiratory disorders with increasing cost of neonatal care.Epidemiology of RD in developed countries has been investigated in several studies[5,8,9].The present study will be designed to investigate etiology and outcome of Neonatal RD in SSMC,Mitford Hospital in Bangladesh.

Materials and Methods:

Place of study:Neonatal care unit of SSMC,Mitford Hospital Dhaka.

Period of study:Oct 2000 to March 2001

Number of patients investigated:50

Type of study:Prospective

Criteria of inclusion:

Any newborn showing one or more of the following signs

For more than two hours:

- Respiratory rate>60/min
- Expiratory grunting
- Cyanosis
- Severe intercostals or subcostal retraction

Criteria of exclusion:

Patients of either sex with

Following criteria:

- Moribund patient
- Poor co-operation from patient,s attendant

During the study period,50 ill newborn were included in this study. Intrapartum details with special reference to the fetal well-being,duration of rupture of membranes,quality of liquor and drugs especially analgesics and sedatives given to the mother were recorded.Apgar score, resuscitation details,sex,,gestational age(based on last menstruation date and clinical examination), birth weightand findings suggestive of respiratory distress also noted.

All babies with respiratory distress were cared for in neonatal care unit.Chest x-ray,blood for routine examination,serum electrolytes and TCO_2 were performed in allcases.Babies with RD in selected cases were also subjected to sepsis screening tests including ESR,Band Cell count,Total Leukocyte counts.Blood culture was done whenever any of the sepsis sceening test was positive or the clinical index of suspicion was very high.Other investigations including CSF study,cranial ultrasound,echocardiography were done whenever indicated.All babies with RD receieved standard care with frequent monitoring.

Causes of RD were classified using a system based on that of Hjalmarson[8] ,as follows.(i)Hyaline membrane disease(HMD):onset of RD within six hours of birthwith increasing severity during first 24 hours of life,positive shake test and reduced aircontent with reticulogranular pattern in chest X-ray,or autopsy evidence of HMD;(ii)Transient tachypnoea of newborn(TTN):onset of respiratory distress immediately after birth with improvement during first 24 hours and chest X-ray showing hyperinflation,prominent perihiler markings, interlober fissure oedema;(iii)Meconium aspiration syndrome(MAS):meconium staining of amniotic fluid and throat and patchybilateral infiltrates with atelectasis and emphysematous changes on chest X-ray;(iv)infection:a positive culture and/or three of the sepsis screening tests positive(Total Leukocyte Count<5000/mm^3 or>30,000/mm^3 ,Band cells to total polymorph ratio>0.2,ESR>10mm/first hour,C-Reactive protein>6ug/ml.)

Statistical Analysis

The results were subjected to statistical analysis according to standard procedure.Odds ratio,Risk ratio,Chi square(X^2) test,Z test were used as the test of significance.P value of <0.05 was considered statistically significant.

Results:

This study included 50 newborns with RD who were admitted in neonatal Care Unit.Out of 50 newborns 32(64%) were male and 18(36%) were female.The relation between sex and outcome of the cases was not significant because P value was >0.05.

Table-I

Number and percentage of patient by etiology

Disease pattern	Frequency	Percent
Perinatal asphyxia	26	52%
Meconium aspiration syndrome	07	14%
Transient Tachypnoea of newborn	06	12%
Septicemia	06	12%
Pneumonia	04	8%
Hyaline membrane disease	01	2%

The major causes of RD are shown in table-1 in relation to frequency and percentage.Perinatal asphyxia was found to be the commonest cause of RD(52%) and it was found to be common among term and preterm babies.Meconium aspiration syndrome was the second commonest cause and seen mostly among term and post-term babies whereas HMD was seen mainly among preterm babies.Septicemia and TTN were other important cause of RD in newborn.Mortality outcome of newborn by maternal factors-Antenatal care(P:<0.001),Maternal illness(P:<0.05),Multiple pregnancy(P:<0.001),Duration of rupture of membrane(P:<0.001) were significant. Parity, Mode of delivery,Place of delivery were not significant.Mortality outcome of newborn by neonatal factors-Age at arrival in neonatal care unit(P:<0.001),Gestational age(P:<0.05) were significant but Sex distribution was not significant.

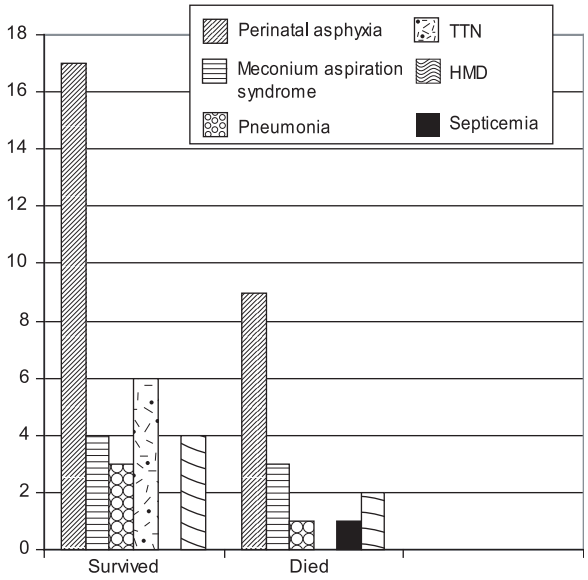

Fig.-1: *Mortality outcome by disease*

Table-II
Case fatality ratio(CFR) by cause of respiratory distress

Diagnosis	CFR
Perinatal asphyxia	34.61
Meconium aspiration syndrome	42.85
Pneumonia	25.00
Transient tachypnoea of newborn	0.00
Hyaline membrane disease	100.00
Septicemia	33.33
Overall	39.30

We found that perinatal asphyxia,meconium aspiration syndrome,hyaline membrane disease,pneumonia were in higher risk than other conditions so far mortality is concerned.The overall mortality in our study (CFR =39.3%)was higher than thosereported from developed countries which varies between 8.2% and 8.5%.[2,8]

Discussions:

In the recent years,there have been tremendous advances in ventilator therapy,surfactant Replacement,extracorporeal membrane oxygenation and sophisticated monitoring gadgets.They have improved the outcome among the babies with respiratory disorderswith increasing cost of neonatal care.Perinatal asphyxia continues to be a major cause of neonatal mortality in developing countries and developed countries alike,the incidence is much higher in developing countries.[13,14] In the present series 26(52%) of the total 50 newborns with RD had perinatal asphyxia.The inadequate training and resuscitation facilities and delayed arrival in neonatal care unit may contribute increased incidence and mortality among perinatal asphyxiated babies.[11]Misra et al[13] in 1994 found 66.6% mortality in babies with Apgar score of 0 to 3.A recent hospital study done by Andersonet al.[14] showed 15% mortality among severe perinatal asphyxia cases.Acute or chronic hypoxia may result in passage of meconium in utero.The incidence of MAS was 14%.Suresh & Sarkar[14] have found 8.5%,which is about half of our observation.In our serieshigh incidence may be due to inadequate resuscitation measures at birth and delayed referral into hospital with MAS.RDS is an important cause of fatal RD in the first week of life.[16] RDS constituted 2% ofthe neonates in the present study.Incidence was quite low,when compared with the study of Banu et al.[16] where they have found 5.8% cases of RDS.However RDS still remainsa contributing cause of high neonatal morbidity and mortality in western countries.[9]TTN constituted 12% of cases,in the present study.TTN has been found to be the commonest of RD in other studies from developed countries.[2,5,8] There was no mortality.TTN was related to caesarean section.Pneumonia was related to early rupture of membrane,with prolonged labour,recent febrile illness of mother.Neonatal septicemiaConstituted 12% of the cases,in the present study.There were

significant correlation between presence of septicemia and mortality outcome of the cases in present study,which is33.33%,similar results have been reported by Mishra,[13] where mortality was 38% with neonatal sepsis.Antenatal care would reduce the incidence of mortality and morbidity.[17] In the present study,there was significant correlation between absence of antenatal visit with mortality outcome,similar to observation of Tabib[17]et al.Early rupture of membrane and Gestational age influences mortality outcome of the newborn.In this study, the survival was best in transient tachypnoea of newborn (TTN).Hyaline membrane disease, septicemia and meconium aspiration had a poor outcome.The high mortality due to HMD and MAS as seen in our setup could be reduced by surfactantTherapy and better respiratory support.

Conclusion:

- Respiratory distress is a common cause of admission in neonatal care unit with very high mortality (40%).
- Perinatal asphyxia is the major cause of RD in newborn (52%).
- Lack of antenatal care, maternal illness, multiple pregnancy, premature rupture of membrane,delay in seeking care, home delivery and prematurity adversely affect the outcome.
- The incidence,morbidity and mortality from RD in the newborn can be prevented by proper antenatal care, intrapartum and postpartum management.

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ORIGINAL ARTICLE

Diagnostic Yield of Adenosine Deaminase Activity in Sputum in Pulmonary Tuberculosis

Rowshne Jahan[1], Md Shahedur Rahman Khan[1], Naimul Hoque[1], Md Abdur Rouf[1], Abdul Qayyum[1], Habib Uddin[2], Fatema Helali,[2] A.K.M.Mustafa Hussain[3] Mirza Mohammad Hiron[4], Md. Rashidul Hassan[4]

Abstract:

In many cases, physicians initiate anti tuberculosis (TB) treatment based only on symptoms or radiographic findings suggestive of PTB in patients with negative sputum smear for AFB as isolation of acid fast bacilli (AFB) by conventional culture method is not only time consuming (6-8 wks) but also cumbersome . High level of adenosine deaminase (ADA) in serum / pleural fluid is used for the diagnosis of pleural TB. ADA level is also high in lung cancer. The aim of the present study was to evaluate the adenosine deaminase (ADA) activity in sputum of patients suffering from pulmonary tuberculosis (PTB) compared with patients with Lung Cancer and elucidate the possible applicability of ADA activity in patients with smear negative pulmonary tuberculosis. This cross-sectional type of comparative study was carried out in the department of respiratory medicine of National Institute of Diseases of the Chest & Hospital Mohakhali from January 2010 to December 2010. Sputum samples were collected from 100 patients both male & female of 15-70 years of age & were enrolled in 2 groups, Pulmonary TB group as PTB(n=61) and lung cancer group as Non-tuberculosis pulmonary disease as NTB group(n=39). Patients were selected purposively and the sampling technique was randomized. The sputum samples were diluted 1:6 and homogenized with phosphate buffer (70mM; 0.5Mmol Nacl; PH=6) was kept on a bench rocker for 12 hours at 4°C. It was centrifuged at 16000 rpm for 30 mins. Thereafter, total ADA was determined in the supernatant by the Giusti method. Sputum samples were digested and decontaminated from other bacteria by the modified petroff method. The mean ADA value in the TB group was 21.02 U/L ± 6.21(range:7.8-30.3) and in the lung cancer group was 15.06 U/L ± 5.25(range:5.5-27.9). The difference was statistically significant (P=0.001). ADA activity in the AFB positive group was 19.85 U/L ± 5.25 & in the AFB negative group was 21.69 U/L ± 6.66. The difference was not statistically significant (P=0.269).The sensitivity, Specificity, PPV and NPV were 80.3%, 71.8%, 81.7% and 70.0% respectively. The accuracy of the test was 77.0%. Pretest probability was 61%, post test probability was 89%. Sensitivity & Specificity of this test as a diagnostic tool for smear negative pulmonary tuberculosis was high with a cut off value of 17.7 U/L. Patients suffering from pulmonary tuberculosis have higher sputum ADA activity than lung cancer. Sputum ADA activity may be a useful tool for the diagnosis of pulmonary tuberculosis when there is a diagnostic dilema especially in smear negative cases.

[Chest & Heart Journal 2011; 35(1) : 5-10]

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Introduction:

Tuberculosis is among the leading causes of death worldwide. It has been declared a global emergency by the World Health Organization. [1]

Bangladesh ranks 6th in the world of tuberculosis burden with an estimated 300,000 new cases & 70,000 deaths / year. Incidence & prevalence of tuberculosis in Bangladesh are 225/100,000 pop/ year & 391/100000pop/year respectively. [2].

The World Health Organization estimates that 32% of the world population is infected with *Mycobacterium tuberculosis*, the causative agent of TB . [3]. Approximately one third of the world population is infected and about three millions die each year from this disease [4] It remains the main l cause of death in the developing countries, probably due to poverty, lack of education, low detection rate, non-availability of experienced staff and insufficient coverage of the community by immunization programme [5].

Drug-resistant TB strains have emerged following the inappropriate use of anti TB drugs. The case-detection rate among new smear-positive cases has been showing an increase over the years, reaching 71% in 2006 compared to 61 % one year earlier.[6]The main reasons for emergence of drug resistance are omission of one or more prescribed agents, suboptimal doses and poor drug absorption.[7] Anti TB drugs are also freely available in the market, which leads to self treatment and improper regimen. Early diagnosis & appropriate treatment are essential for good outcomes. However this is not always possible. Sputum method is based on finding acid fast bacilli (AFB) in sputum or a positive sputum culture. microscopic examination can diagnose 50-60% of pulmonary tuberculosis in well equipped laboratory.[8] In developing countries, poor access to microscopic service contributes to even lower rate of AFB detection.[9]

As definitive diagnosis is based on the isolation and culture of Myco-bacterium tuberculosis in sputum samples, a 4-8 weeks period is required to prepare sputum culture results, a delay is unacceptable in emergency situation. [10]Thus, it is necessary to find faster methods with higher sensitivity.[11]

30% patients are smear negative of which 16% become culture positive and culture is again time consuming due to prolonged turn over time of AFB bacilli, it is cumbersome, needs heavy equipments & risky.[12] 5% cannot be diagnosed by culture.. For this reason there is a need to develop a scheme to determine the most cost effective approach for the diagnosis of pulmonary tuberculosis.[13] It may be mentioned here that smear negative PT is associated with high mortality in areas of high HIV sero positive prevalence.

Adenosine deaminase is an enzyme catalyzing the hydrolytic & irreversible demamination of adenosine to ionosine & deoxy adenosine to deoxy ionosine. [14]ADA is used for the diagnosis of pleural TB and there are studies showing high levels of ADA in sera & bronchoalveolar lavage fluids of TB patients . However, only a few studies have focused on ADA activity in materials obtained by non-invasive methods such as sputum. [15]

So the aim of the present study was to evaluate ADA activities in sputum among pulmonary tuberculosis patients compared with Lung cancer in order to assess its diagnostic value, which will subsequently help in early detection & treatment of smear negative pulmonary tuberculosis.

Methodology:

This cross-sectional type of comparative study was carried out in the National Institute of Diseases of The Chest and Hospital (NIDCH), Mohakhali, Dhaka from January 2010 to December 2010. Samples were collected from both OPD & IPD of NIDCH.All the laboratory works were performed in National Tuberculosis Research Laboratory (NTRL) in NIDCH .

A total of 100 consecutive patients of 15-70 years of age of both sexes with pulmonary tuberculosis & non-tuberculosis pulmonary disease (Lung cancer patients) were included with the following inclusion criteria ,patients presented with symptoms for PTB & lung cancer (like cough for .>3wks, fever for >2wks,&/ haemoptysis were enrolled along with other radiological findings (pre set) together with at least one of the following-

a) AFB positive/ in Ziehl-Neelsen stain.

b) Patients who were smear negative for AFB are confirmed for Lung cancer or PTB by one of the following 1) a positive culture for

AFB in Lowenstein-Jensen media 2) histopathology revealed caseating granuloma/ or /malignant lesion 3) FNAC from suspected lesion positive for AFB or MC 4)BAL positive for AFB/MC

Exclusion criteria

Previous History of treatment with anti-TB drugs, Systemic diseases like CLD/CRF/DM/CTD./

All data were recorded systematically in preformed data collection form (questionnaire) and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance.

Results and Observations:

A total number of 100 patients of both sexes were enrolled in this study, of which, 61 patients were finally diagnosed as pulmonary tuberculosis (both smear positive & smear negative) & the rest 39 patients were diagnosed as lung cancer.

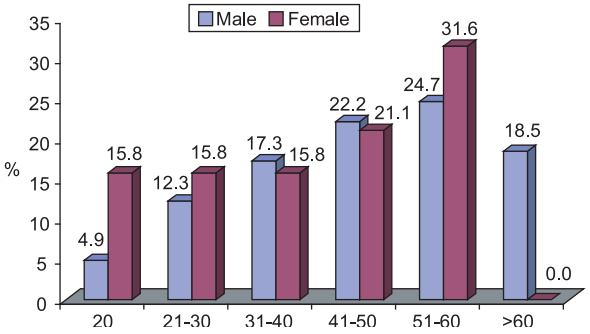

Fig.-1: *Bar diagram of the study population according to age and sex*

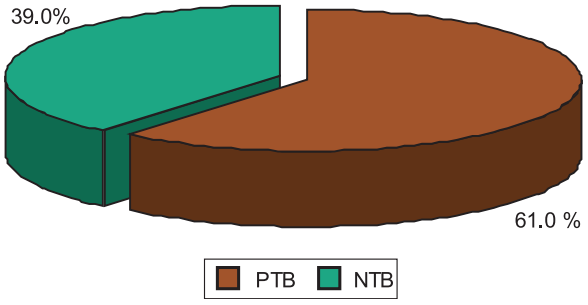

Fig.-2: *Pie chart of distribution of the final diagnosis of total cases (N=100)*

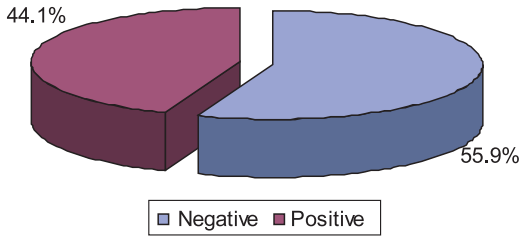

Fig.-3: *Pie chart of Distribution of the cases among PTB group (n=61)*

Table-I

Distribution of the PTB sputum smear negative cases (n=34)

PTB (n=34)	Frequency	Percentage
Granuloma positive	13	38.24
Culture positive	12	35.29
BAL (AFB) positive	9	26.47
Total	34	100.0

Table-II

Distribution of the NTB cases (n = 39).

Diagnosis (n=39)	Frequency	Percentage
Sq. cell carcinoma	12	30.77
Adenocarcinoma	27	69.23
Total	39	100.0

The optimum cut-off points of ADA were found to be 17.7 U/L.

Table-III

Distribution of ADA status in Pulmonary TB and lung cancer(N=100)patients.

ADA Level	ADA Result		Total
	Pulmonary TB	Lung cancer	
Positive (>17.7)	49 (TP)	11 (FP)	60
Negative	12 (FN)	28 (TN)	40
Total	61	39	100

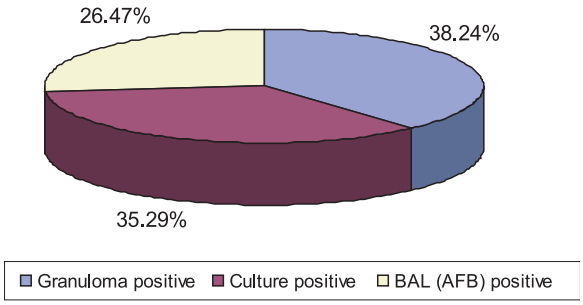

Fig.-4: *Pie chart of distribution of the PTB negative cases.*

TableIV

Validity tests of the ADA level determination in this study

	Value (%)
Sensitivity	80.3
Specificity	71.8
PPV	81.7
NPV	70.0
Accuracy	77.0
Positive Likelihood Ratio (LR+ve)	8.752
Negative Likelihood Ratio	0.079
Pre-test probability	61.0%
Post test Probability (LR+ve)	89.0%

PPV = Positive Predictive Value
NPV = Negative Predictive Value

Table-V

Sputum ADA level between AFB positive and negative in Pulmonary TB patients

AFB Status	ADA level		p value*
	Mean ± SD	Range	
positive	19.85 ± 5.25	9.6-30.3	0.269
negative	21.69 ± 6.66	7.8-29.9	

*t test was done to measure the level of significance.

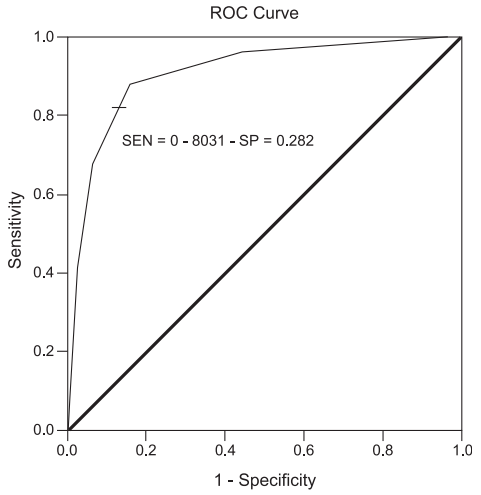

Fig.-5: *The ROC analysis for determining the optimum cut-off point of different ADA level in distinguishing PTB from non TB patients.*

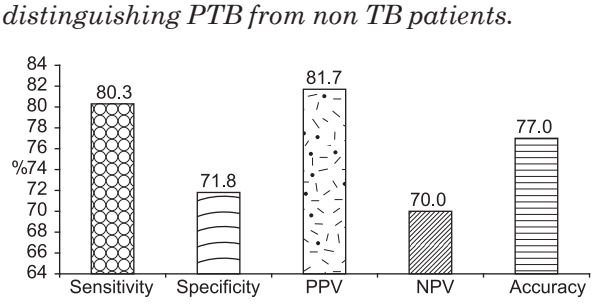

Fig.-6: *Bar diagram Shows the Validity tests of the ADA level detected in sputum of tuberculosis patients.*

Discussion:

A total number of 100 patients of both sexes were enrolled in this study of which 61 patients were diagnosed as pulmonary tuberculosis (PTB) in both smear positive & smear negative & the rest 39 patients were taken as lung cancer . The distribution of the study population according to age and sex was recorded in this study. . This study result has got consistency with that of Bennedsen where the ratio was was 2.4:1.[16] This difference is partly due to the fact that women have less access to diagnostic facilities in some settings, but the broader pattern also reflects real epidemiological differences between men and women, both in exposure to infection and in susceptibility to disease.[17] In regions where the transmission of *M. tuberculosis* has been stable or increasing for many years the most cases are caused by recent infection or re-infection.[18]

Among 81 male patients maximum were from the age group of 51-60 years which was 20 (24.7%) cases followed by 41-50 years, more than 60 years, 31-40 years and 21-30 years which were 18 (22.2%) cases, 15 (18.5%) cases, 14 (17.3%) cases and 10 (12.3%) cases respectively. Only 4 (4.9%) cases were present in the age group of less than or equal to 20 years . Among 19 female patients majority were from the age group of 51-60 years which was 6 (31.6%) cases followed by 41-50 years, 31 -40 years and 20-30 years which were 4 (21.1%) cases, 3 (15.8%) cases, 3 (15.8%) cases and 3 (15.8%) cases respectively. The mean age was 45.72 ± 14.89 with a range of 11-75 years. Dye C et al mentioned that the majority of the patients were in this age group. Ansari reported that the mostly affected age group was the older age group. The present study result is consistent with the above mentioned studies..[19]

The reason of high prevalence in this age group may be the reactivation of latent infection.

The distribution of presenting features by groups was recorded in this study. Fever was found in 61 (100.0%) cases in PTB and 39 (100.0%) cases in NTB group. Cough was present in all cases in both the groups (100%). Haemoptysis was present in 24 (39.3%) and 20 (51.3%) cases in PTB and NTB groups respectively . Chest pain was present in 48 (78.7%) cases and 33 (84.6%) cases in PTB and NTB patients respectively. Loss of appetite

was present in 45 (73.8%) cases and 32 (82.1%) cases in PTB and NTB groups respectively. Among other informations : Night sweats was present in 1 (1.6%) case and 2 (5.1%) cases in PTB and NTB respectively, weight loss was found in 56 (91.8%) case and 31 (79.5%) cases in PTB and NTB respectively.

Final diagnosis of the cases were recorded.Out of 100 patients (N=100), 61 were pulmonary TB, of which 27 were AFB positive (44.10%) and 34 were AFB negative (55.90%).In the AFB negative group (n=34) , granuloma (with caseation) was found in FNA from lung lesion in 13 cases(38.24%) , culture was positive in 12 cases (35.29%), AFB found in BAL (FOB) was 9 cases (26.47%). In Lung cancer group (n=39) Squamous cell carcinoma was 12 cases (30.77%) and Adenocarcinoma was 27 cases(69.23%

Adenosine deaminase (ADA) is essential for the differentiation of lymphoid cells, in particular T cells and is found also to play an important role in the maturation of monocytes to macrophages. ADA is considered to be an indicator of cell-mediated immunity.Monocyte/macrophage activation by intracellular infection and inflammatory diseases leads to the release of ADA and elevated levels in serum.[16] Increased serum ADA levels in pulmonary TB may result from stimulation of cell-mediated immunity .

The ADA level in sputum of the patients in PTB and NTB group was recorded. The ADA level was 21.02 ± 6.21,mean ± SD with a range of 7.8-30.3 in PTB group and 15.06 ± 5.25 with a range of 5.5-27.9 in NTB cases. The difference was statistically significant (p=0.001). The distribution of ADA positive in PTB and NTB was recorded. ADA level was positive in 60 cases of which 49 (TP) was in PTB groups and 11 (FP) was in NTB group. ADA level was negative in 40 cases of which 12 (FN) was in PTB groups and 28 (TN) was in NTB group. The sputum ADA level between AFB positive and AFB negative in PTB patients was recorded. The mean ADA level in AFB positive patients was 19.85 ± 5.25 with a range of 9.6-30.3 and in AFB negative cases it was 21.69 ± 6.66 with a range of 7.8-29.9. the difference was not statistically significant (p=0.269).

The validity tests of the ADA level determination in the present study was recorded. The sensitivity of the test was 80.3% & Specificity was 71.8%. The PPV and NPV was 81.7% and 70.0% respectively. The accuracy of the test was 77.0%. The cut off value of sputum ADA was 17.7 U/L.

Another study showed that ADA activity in sputum of 22 TB patients compared with 13 lung cancer patients, Sensitivity was 60% specificity was 92% with a cut-off level of 15 U/L & my study result is consistent with this.[18]

The present study has got some limitations like sample size was not large enough ,multi centre study was not possible, ADA test is not available in all the laboratorys either government or private.

Conclusion:

Rapid detection of Pulmonary tuberculosis is possible by using this test which will subsequently reduce the morbidity and mortality of the patients suffering from this disease. The simplicity of obtaining material such as sputum makes this measurement a useful diagnostic tool especially in AFB smear negative patients who are strongly suspected of having this disease.

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ORIGINAL ARTICLE

Influence of Bronchial Asthma on Menstrual Cycle in Adolescent Girls

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Abstract:

Ninety six adolescent girls, where forty eight asthmatic and similar number of healthy girls, responded to a questionnaire concerning the influence of bronchial asthma on menstrual cycle. All of the respondents were in between 9-17 years and already experienced the occurrence of menstruation cycle. The mean age of the study population was 12.56±1.32 yrs. The age of the menarche and menstruation cycle parameters were analyzed. The finding of the study revealed that asthmatic girls experienced the occurrence of their first menstruation (menarche) earlier than that of the healthy girls (p=.000) and suffered shorter duration of menstrual cycle (p=.001). They experienced significantly more of the irregular menstrual cycles (p=.038). Besides, the healthy adolescents had statistically more olegomenorrhoea than the asthmatic adolescents (p=.000). Thus, we conclude that bronchial asthma disturbs the regular course of menstrual cycle.

Key word: *bronchial asthma, menarche, menstrual cycle.*

[Chest & Heart Journal 2011; 35(1) : 11-15]

Introduction:

Bronchial asthma, a chronic respiratory disease, itself a serious public health problem all over the world. About 300 million people, including children and adolescent, suffer from bronchial asthma. In a population of children and adolescents, bronchial asthma occurs with frequency of 5-10%.[1]

As a chronic systemic disease, bronchial asthma may have a negative influence on general somatic development of the children[2-4]. Clinical trials confirmed growth disorders, delayed sexual maturation in children with bronchial asthma and the influence of the following factors: sex, severity level, duration, the level of clinical control and the kind of applied medication on parameters of physical development[2-4].

Regular course of menstrual cycle depends on genetic and environmental factors as well as on numerous hormonal reactions integrating the function of hypothalamous, pituitary gland and ovaries. In physiological terms, the first menstruation (menarche) should occur between 8-9 and 16 years of age[5-7].

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Endocrine glands function disorders as well as chronic systemic or metabolic diseases can lead to menstruation disturbances[5-7]. It is also thought that bronchial asthma might have influence in the regular course of menstrual cycle. Both chronic character of the disease and the kind of medication applied can lead to increased rate of menstruation disorders [8-9]

In view of above mentioned , the intend of the present study was to assess the effect of bronchial asthma on menstrual cycle.

Material and Methods:

This study was a cross sectional study that was carried out in Maternal and Child Health Training Institute (MCHTI), Azimpur and Mohammadpur Fertility and Services Training Centre (MF&STC), Mohammadpur during the period of July, 2010 to July 2011 among the 98 adolescent girls, who already experienced menstruation. There were 48 adolescent girls treated for bronchial asthma in the Outpatient Units of the two above Institutes (after diagnosed so by a pulmonologist) and a control group consisted of similar number of adolescent girls (48 in number).

Data were collected from the study groups according to the questionnaire that include i) social and demographic factors (age, place of livings), ii) somatic development of the girls (weight, height) iii) menstrual history (age of menarche, type, rhythm, duration of menstrual cycle, pain and blood loss in menstruation), iv) history of allergic disorders, v) exposure history of smoking and animal contact

The regular menstrual cycle (eumenorrhoea) was defined as menstruation appearing every 28±4 days and lasting or about 5 days, with physiological loss of approximately 30-70 ml of blood. Menstruation appearing less frequently, once every 35 days or more, were defined as oligomeorrhoea, and those shorter than 21 days as polymenorroea (5-7) days. Menstruation was classified as hypermenorrhoea when blood loss was 80 ml or more during single cycle and/or more pads or tampons were used (5-). Painful menstruation (algomenorrhoea) was assessed as based on occurrence of strong pain localized within the lower abdomen (A).

Statistical analysis of the studied variables were performed using SPSS with appropriate tests. A value of $p<0.05$ was considered as statistical significance for all performed analyses.

Results:

The mean age of the all girls was 12.56 ±1.32 yrs. But the mean ages of the asthmatic girls was 12.69 ± 1.35 yrs and that in the healthy girls was 12.44 ± 1.29 year. There was no statistical difference in the means of the two groups (table-I).

Similar non-significant results were observed in body weight (kg) and body height when statistical tests were done among the asthmatic and healthy groups (table I).

The mean duration of asthma, in the asthmatic group, was 3.92 ± 0.94 yrs with the range of suffering 2 to 6 years.(table-I).

Table-I

General profile of the respondents (study population)

Characteristics	Asthmatic girls (Mean ± SD)	Healthy girls (Mean ± SD)	p value
Age (years)	12.69 ± 1.35	12.44 ± 1.29	NS
Body weight (kg)	38.08 ± 2.55	34.73 ± 2.47	NS
Body height (cm)	97.02 ± 5.38	95.64 ± 4.78	NS
Duration of asthma	3.92 ± 0.94	-	-

Table-II revealed the followings:

Slum dwellers, among the adolescent girls, statistically suffered more from asthma than those who came from urban or semi urban regions (p=.020).

About sixty seven percent of the girls with diagnosed bronchial asthma had family history of asthma compared with thirty seven percent of the healthy and the difference of frequencies was statistically positive (p=.014).

Exposure to tobacco smoking at home had also played a statistically positive role in the prevalence of bronchial asthma (p=.001) among the groups.

Asthmatic girls had more prevalence of allergic disorders than the healthy girls (64.6% vs 37.5% respectively). Relationship of allergic disorders and bronchial asthma was statistically proved (p=008).

There was no significant influence of handling pet animals and occurrence of bronchial asthma.

Table-II

Socio-demographic characteristics of the respondents

Characteristics		Asthmatic girls	Healthy girls	p value
Pace of residence	Urban	10 (20.8%)	13 (27.1%)	p = .020
	Semi Urban	14 (29.2%)	24 (50.0%)	
	Slum	24 (50.0%)	11 (22.9%)	
Bronchial asthma in family		30 (62.5%)	18(37.5%)	p=.014
Exposure to tobacco smoking at home		32 (66.7%)	16 (33.3%)	p=.001
History of allergy	31 (64.6%)	18 (37.5%)	p=.008	
Contact with animals and pet		4 (6.3%)	1(2.1%)	NS

Table III presents characteristics of menstrual cycle parameter in the asthmatic girls compared with the control healthy girls.

The mean age of menarche in the asthmatic group was 10.21 ± 0.74 years and that in the healthy group was 10.81 ± 0.73 years. On average, the girls with bronchial asthma had their first menstruation (menarche) at least 6 months earlier compared with the healthy ones, which was a significance (p=.000).

Almost one day shorter menstrual duration was observed in asthmatic girls in comparison to the healthy girls (mean duration in asthmatic girls was 3.87 ± 1.02 day and 4.5 ± 0.77 day in healthy girls) and the difference was significant (p=.001).

Irregular menstrual cycles were found in 68.1% of the asthmatic girls and less frequently (47.9%) in the healthy and a significant difference was observed among the two groups (p=.038).

The menstrual rhythm was classified into three sub groups like i) Eumenorrhoea, ii) oligomenorrhoea and iii) polymenorrhoea. The prevalence of Eumenorrhoea, oligomenorrhoea and polymenorrhoea were 29.2%, 66.7% and 4.2% in the asthmatic girls and those were 52.1%, 43.8% and 4.2% in healthy girl. No significant differences were marked among the two study groups (p>.05).

Regarding menstrual blood loss, severe blood loss (43.8% vs 29.2%), moderate blood loss (37.5% vs 33.3% and slight blood loss (18.8% vs 37.5%) were observed among the asthmatic and healthy adolescents.

Pain in lower abdomen during menstruation (algomenorrhoea) was acknowledged by 58.3% of the girls with asthma and 93.8% of the healthy ones; p=.000.

Table-III

Characteristics of menstrual cycle among asthmatic and healthy girls

Characteristics		Asthmatic girls	Healthy girls	P value
Age of menarche	10.21 ± 0.74	10.81 ± 0.73	P=.000	
Length of menstruation (days)	3.87 ± 1.02	4.5 ± 0.77	P= .001	
Irregular menstrual cycle	33(68.1%)	23(47.9%)	P=.038	
Menstrual cycle rhythm	Eumenorrhoea	14(29.2%)	25(52.1%)	NS
	Oligomenorrhoea	32 (66.7%)	21 (43.8%)	
	Polymenorrhoea	2 (4.2%)	2 (4.2%)	
Menstrual blood loss	Severe blood loss	21(43.8%)	14 (29.2%)	NS
	Moderate blood loss	18 (37.5%)	16 (33.3%)	
	Slight blood loss	9 (18.8%)	18 (37.5%)	
Oligomenorrhoea	Absent	20 (4.7%)	3 (6.3%)	p=.000
	Pain at the beginning of menstruation	16 (33.3%)	27 (56.3%)	
	Pain during the whole menstruation	12 (25.0%)	18 (37.5%)	

Discussion:

Several factors might have influence over the menstrual cycle of the adolescent girls but this study reveals only the effect bronchial asthma on menstrual cycle.

Although the limitations included potential selection bias inherent in cross sectional studies, there was chance of recall bias in addition in this study.

Reviewing the available literature, we came across only few studies concerning the influence of bronchial asthma on the course of menstrual cycle of the women specially in adolescents.

While assessing the age at menarche and menstrual cycle, performed in this study, fining revealed the early onset of menarche and more frequency of irregular menstrual bleeding in the asthmatic adolescent girls.

In this study, the mean age at menarche of girls with bronchial asthma was 10.21 ± 0.74 years and approximately 6 months earlier than that in the healthy girls. Similar results were also found by other authors, like Dorodzol et al[10] (by 17 months), Sadowska et al[18-19] (by 5 months) and Doull (by 1-3 years)[2].

The mean duration of menstrual cycle of the asthmatic girls 3.87 ± 1.02 days and that of the healthy girls was 4.50 ± 0.77 days and a significant variation was observed. A literature review does not turn up another study performed in this topic in pubescent girls.

The confirmation of more frequent of irregular menstruation in girls with diagnosed bronchial asthma (68.1%) compared with control group (47.9%) in the present study have the correlate with finding of the study done by Dorodzol et al[10] but however cannot be directly related to the study of Svanes et al[13], as they studied a group of women at reproductive age.

Conclusion:

According to the findings of the present study, we therefore able to state that bronchial asthma disturbs the rhythm and regularity of the menstrual cycle as well as accelerates the age at menarche and decrease the occurrence of oligomenorrhoea.

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ORIGINAL ARTICLE

Comparison of the Single Versus Double Chest Tube Application After Pulmonary Lobectomies

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Abstract

Introduction: *Post operative drainage of the chest cavity is the most important part after lobectomy. Drainage of the chest cavity after lobar resection of the lung is generally performed by using two chest tubes; one is placed into the basal region to drain fluid, while the other is directed towards the apex for removing the air. It has been proposed that successful use of a single chest drain after lobectomy instead of two classical drains is equally effective.*

Aims & Objectives: *This study is aimed to compare the effectiveness & post operative outcome of double and single chest tube drainage after pulmonary lobectomies.*

Materials & Methods: *This observational study was conducted in the Departmental of Thoracic surgery, NIDCH between the periods of March 2009 to February 2010. Sample size was 60. It was divided into two groups. Among them 30 were in Group I (Single chest tube) and another 30 were in Group II (Double chest tube). All patients under going pulmonary lobectomy due to any cause during the study period were included in the study.*

Results: *There is no statistically significant difference in age or in sex distribution between the groups. The distribution of pre operative diagnosis shows that in both Groups highest number was bronchiectasis 12(40.0%) followed by Ca lung 10(33.3%) and then post TB fibrosis 5 (16.7%) and aspergiloma 3(10.0%). Minimum duration of chest tube drainage in Group I was 3 days and maximum was 6 days. In Group II minimum duration of chest tube drainage was 5 and maximum was 7 days. Statistically significant difference in duration of chest tube drainage was observed between the groups ($p<0.05$). The distribution of amount of drainage shows that there is no statistically significant difference in amount of drainage between the groups. Post operative pain was evaluated by Numeric Verbal Pain Score (NVPS) in both groups. The distribution of pain shows that in Group I most of the patients noted less pain and only one patient developed more pain during first and second and third follow up. In Group II 28 (93.3%) patients developed more pain during first and second and 27 (90.0%) patients developed*

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more pain in third follow up. Statistically significant difference was noted in pain development in the first, second and third follow up between the groups ($p<0.05$).

Conclusion: *Double chest tube application has no additional benefit than the single chest tube after pulmonary lobectomies.*

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Introduction:

Pulmonary resectional surgery is one of the most common surgical procedures in thoracic surgical practice. Lobectomy is the most commonly practiced operation for different pulmonary diseases in our institution. Post operative drainage of the chest cavity is an important part of the procedure. Successful drainage can provide the re-expansion of remaining lung tissue by removing air or any collection. Main aim of keeping the drains is evacuation of the space, re expansion of the lung & control of infection by keeping the pleural space dry and favourable[1].

Drainage of the chest cavity after lobar resection of the lung is generally performed by using two chest tubes one is placed into the posterior and basilar region to drain fluid, while the other is directed towards the apex for removing the air form the pleural cavity. It has been assumed that a complete control on fluid and air in the pleural space could only be maintained by inserting two chest tubes (Fell and Kirby, 2006; Khan and Vaughan, 1999)[1,2]. It has been found that successful use of a single chest drain after lobectomy instead of two classical drains is more effective (Gomez-Caro et al. 2006)[3]. The use of a single chest tube after lobar resections has been reported in a few studies (Alex et al. 2003; Pawelczyk et al. 2007)[4,5]. Theoretically using a single chest tube causes less pain and discomfort during the postoperative period and it is more economical. Less pain in the postoperative period may improve the patient's capability to perform respiratory exercise and thereby facilitate better lung expansion and decrease the rate of complication. It can also result in an earlier discharge from the hospital. Presently, superior technology is being used in lung resection operations, such as linear stapler for incomplete fissures, sealing materials for parenchymal air leaks or other advanced materials for haemostasis. As a result air leaks and bleeding are observed to a lesser extent after lung resections than they were two or three decades ago. This may also be another reason why only one chest tube is preferred nowadays after pulmonary lobectomy[7].

Aims & Objectives:

To compare the post operative outcome between double and single chest tube drainage after pulmonary lobectomies among the Bangladeshi population.

Materials & Methods:

This observational study was conducted in the Department of Thoracic surgery of National Institute of Disease of the Chest & Hospital (NIDCH) between the periods of March 2009 to February 2010. Patients admitted in the department of Thoracic surgery, NIDCH, for lobectomies were the study population. A total of 60 patients were included in the study that underwent lobectomy due to any cause during the study period. They were divided into two groups - Group I and Group II, each group containing the same number of patients; in Group I single tube and in Group II double tube was used after lobectomies.

Few parameters were considered during pre operative assessment, diagnosis and preparation of the patients. These are the age, sex and clinical features of the patients namely Cough, Sputum production, Haemoptysis, Fever, Chest pain, Dyspnoea. Duration of illness was also recorded. Among the investigations done were CBC, Fasting blood sugar, Serum creatinine, Serum urea, Chest X-ray postero-anterior and lateral view, Spirometry, Sputum for AFB/ CS, CT scan of the Chest with CT guided FNAC for lung cancer.

All patients were operated via posterolateral thoracotomy without transecting the serratus anterior muscle and by entering the chest through the fifth intercostal space. Adhesions were dissected where present with proper haemostasis. Lobectomy was performed following the standard procedure. Air leaks from the lung parenchyma and bronchial stump were checked by instilling normal saline to

the hemithorax and inflating the lung at 30 cm water positive pressure. After haemostasis, in the Group I (Single-tube group), chest tube of 32 FR size was inserted in the midaxillary line in all patients at the dependent site of the hemithorax and directed to the apex. An extra hole was made in the lowest part of the tube that stayed inside the chest. In Group II (Double-tube group) two chest tubes were inserted. One 28 FR chest tube in the midaxillary line in the most dependent site of the hemithorax, and another 28 FR chest tube was placed through the anterior axillary line towards the apex. No prophylactic space-reducing procedures such as pleural tenting or pneumoperitoneum were performed in any patients in either group. Then the chest was closed in layers.

During the post operative period all patients were treated with 3rd generation cephalosporin, aminoglycosides and metronidazole in injectable form up to 5th POD followed by oral form. Adequate analgesia was ensured.

Post operative pain was evaluated by the Numeric Verbal Pain Score (NVPS) (Alex et al. 2003)[4].

The Numeric Verbal Pain Score

0 : No pain at rest or on movement
1 : No pain at rest, mild pain on movement
2 : Mild pain at rest, moderate pain on movement
3 : Moderate pain at rest, severe pain on movement
4 : Severe continuous pain

The amount of drainage from the chest tubes recorded twice a day. In both groups the chest tube was removed when the amount of pleural drainage decreased to <50 ml/ day, colour is serous; remaining lung tissue is fully expanded both clinically and radiologically and there is no air leakage. After discharge patients were followed up for three months at one-month interval. In every follow up patients were evaluated clinically and radiologically for any evidence of complications. Patients presented with any complication during follow up were re admitted and treated accordingly.

All relevant data were collected from each participant using a pre-designed individual data collection sheet. A master data sheet was compiled and prepared from information gathered through individual data sheet for complete evaluation. All data were recorded systematically in preformed data collection form and quantitative data were expressed as mean and standard deviation and qualitative data as frequency distribution and percentage. Statistical analysis was performed by using SPSS for windows version 13.0. 95% confidence limit was taken. Probability value <0.05 was considered as level of significance.

Results:

The present prospective observational study was conducted in the Departmental of Thoracic surgery, National Institute of Diseases of the Chest & Hospital (NIDCH) between the periods of March 2009 to February 2010. Total 60 patients under going pulmonary lobectomies were included in the present study. Among them 30 were in the Group I (Single chest tube) and another 30 were in the Group II (Double chest tube). The results of the study as followed:

(i) Distribution of pre operative diagnosis:

The distribution of pre operative diagnosis shows that in both Groups highest number was bronchiectasis 12(40.0%) followed by Ca lung 10(33.3%) and other pre operative diagnosis were post TB fibrosis 5 (16.7%) and aspergiloma 3(10.0%) (Table 1)

Table-I

Distribution of pre operative diagnosis by groups

Pre operative diagnosis	Groups	
	Group I	Group II
Bronchiectasis	12(40.0)	12(40.0)
Ca lung	10(33.3)	10(33.3)
Post TB fibrosis	05(16.7)	05(16.7)
Aspergiloma	03(10.0)	03(10.0)
Total	30 (100.0)	30 (100.0)

Figure within parentheses indicates in percentage.

(ii) Resected lobe:

The distribution of resected lobe shows that in Group I right upper lobe resection was done in 5(16.7%) patients and right lower lobe resection was done in 6(20.0%) patients and left upper lobe resection was done in 04(13.3%) patients and left

lower lobe resection was done in 15 (50.0%) patients. In Group II right upper lobe resection was done in 09(30.0%) patients and right lower lobe resection was done in 03 (10.0%) patients and left upper lobe resection was done in 05 (16.7%) patients and left lower lobe resection was done in 13 (43.3%) patients. There is no statistically significant difference in resection of lobe between the groups (p>0.05). (Table 2)

Table-II

Distribution of resected lobe by groups

Resected lobe	Groups		p value
	Group I	Group II	
Right			
• Upper	05(16.7)	09(30.0)	0.147
• Lower	06(20.0)	03 (10.0)	
Left			
• Upper	04(13.3)	05 (16.7)	0.634
• Lower	15 (50.0)	13 (43.3)	
Total	30(100.0)	30(100.0)	

Chi-square test was done to measure the level of significance.

(iii) Duration of chest tube drainage:

The duration of chest tube drainage shows that in Group I and Group II the Mean ± SD was 4.40 ± 0.77 and 5.93 ± 0.58 days respectively. Minimum duration of chest tube drainage in Group I was and 3 days and maximum was 6 days. In Group II minimum duration of chest tube drainage was 5 and maximum was 7 days. Statistically significant difference in duration of chest tube drainage was observed between the groups (p<0.05) (Table 3).

Table-III

Distribution of duration of chest tube drainage by groups

Duration of chest tube drainage	Groups		p value
	Group I	Group II	
Mean ± SD (day)	4.40 ± 0.77	5.93 ± 0.58	0.001***
Minimum (day)	03	05	
Maximum (day)	06	07	

t test was done to measure the level of significance.
***Highly significant

(iv)) Distribution of amount of drainage:

The distribution of amount of drainage shows that in Group I and Group II the Mean ± SD was 715.33 ± 63.01 and 726.33 ± 92.27 ml respectively. Minimum amount of drainage in Group I was 550 ml and maximum was 850 ml. in Group II minimum was 500 ml and maximum was 890 ml. there is no statistically significant difference in amount of drainage was observed between the groups (p>0.05) (Table 4).

Table-IV

Distribution of amount of drainage by groups

Amount of drainage	Groups		p value
	Group I	Group II	
Mean ± SD (ml)	715.33 ± 63.01	726.33 ± 92.27	0.065
Minimum (ml)	550	500	
Maximum (ml)	850	890	

t test was done to measure the level of significance.

(v) Post operative pain:

Post operative pain in all patients was managed with appropriate analgesics. Injectable analgesics were used during immediate post operative period followed by oral and/or per rectal suppository. Post operative pain was evaluated by Numeric Verbal Pain Score (NVPS) in both groups. In Group I score was less than 2 in 8 (26.7%) and more than 2 was in 22 (73.3%) patients. In Group II score was less than 2 in 3 (10.0%) and more than 2 was in 27 (90.0%) patients. Statistically no significant difference in post operative pain was observed between the groups (p>0.05). (Table 5)

Table-V

Post operative pain

Post operative pain	Groups		p value
	Group I	Group II	
<2	08(26.7)	03 (10.0)	0.095
>2	22 (73.3)	27 (90.0)	
Total	30(100.0)	30(100.0)	

Fisher's Exact test was done to measure the level of significance.

Figure within parentheses indicates in percentage.

(vi). Post operative complications:

Post operative complication shows that in Group I only one patient developed wound infection and in Group II 2 (6.7%) developed space infection, 1 (3.3%) developed wound infection, 1 (3.3%) undergone reopening of bleeding and 1 (3.3%) developed stump leakage (Table 6).

Table-VI

Post operative complications

Post operative complications	Groups	
	Group I	Group II
Space infection	0(0.0)	2(6.7)
Wound infection	1(3.3)	1(3.3)
Reopening for bleeding	0(0.0)	1(3.3)
Stump leakage	0(0.0)	1(3.3)

Figure within parentheses indicates in percentage.

(vii) Duration of post operative hospital stay:

The duration of hospital stay shows that in Group I and Group II the Mean ± SD of hospital stay was 10 ± 0 and 10 ± 0 days respectively. Post operative hospital stay in both Groups minimum and maximum was 10 days (Table 7).

Table-VII

Duration of post operative hospital stay by groups

Post operative hospital stay	Groups	
	Group I	Group II
Mean ± SD (day)	10 ± 0	10 ± 0
Minimum	10	10
Maximum	10	10

(viii) Distribution of pain at follow-up:

Post operative pain was evaluated by Numeric Verbal Pain Score (NVPS) in both groups. The distribution of pain shows that in Group I most of the patients noted less pain and only one patient developed more pain during first and second and third follow up. In Group II 28 (93.3%) patients developed more pain during first and second and 27 (90.0%) patients developed more pain in third follow up. Statistically significant difference in pain development was noted in first, second and third follow up between the groups ($p<0.05$). Here only the result of the final follow up is shown (Table 8).

Table-VIII

Distribution of pain during 3rd follow up by groups

Pain	Groups		p value
	Group I	Group II	
3rd follow up			
• >2	01 (03.4)	27 (90.0)	0.001**
• <2	29 (96.6)	03 (10.0)	

Fisher's Exact test was done to measure the level of significance.
Figure within parentheses indicates in percentage.
***Highly significant

(ix) Distribution of lung expansion

Lung expansion was evaluated by chest X-ray postero-anterior view during follow up. The distribution of lung expansion shows that in Group I 27 (90.0%) patients were presented with fully lung expansion during 1st, 2nd and 3rd follow up. In Group II 28(93.3%) patients were presented with full lung expansion and 2 (6.7%) were presented with partially expanded during 1st and 2nd follow up and 3rd follow up. There is no statistical difference in lung expansion between the groups ($p>0.05$) (Table 9).

Table-IX

Lung expansion during 3rd follow up

Lung expansion	Groups		p value
	Group I	Group II	
3rd follow up			
Fully expanded	27 (90.0)	28(93.3)	0.640
Partially expanded	03 (10.0)	02(06.7)	

Fisher's Exact test was done to measure the level of significance.
Figure within parentheses indicates in percentage.

Discussions:

The present observational study was conducted in the Departmental of Thoracic surgery of National Institute of Diseases of the Chest & Hospital (NIDCH). Total 60 patients under going pulmonary lobectomies were included in the study. Among them 30 were in the Group I (Single chest tube) and another 30 were in the Group II (Double chest tube). Draining of chest cavity with two chest tubes after lobectomy is a common practice, this study was aimed to investigate whether using two tubes after a pulmonary lobectomy is more effective than using a single tube or not.

In the present study patients age by groups shows that mean ± SD of Group I and Group II were 38.40 ± 14.45 years and 32.00 ± 10.73 years respectively while the distribution of sex by groups shows in Group I male and female ratio was 1:0.76. In Group II male and female ratio was 1:0.36.

The pre operative diagnosis in both Groups, highest number was bronchiectasis 12(40.0%) followed by Ca lung 10(33.3%) and other pre operative diagnosis were post TB fibrosis 5 (16.7%) and aspergiloma 3(10.0%).

The distribution of resected lobe shows that in Group I right upper lobe resection was done in

5(16.7%) patients and right lower lobe resection was done in 6(20.0%) patients and left upper lobe resection was done in 04(13.3%) patients and left lower lobe resection was done in 15 (50.0%) patients. In Group II right upper lobe resection was done in 09(30.0%) patients and right lower lobe resection was done in 03 (10.0%) patients and left upper lobe resection was done in 05 (16.7%) patients and left lower lobe resection was done in 13 (43.3%) patients. There is no statistically significant difference in resection of lobe between the groups ($p>0.05$). As the inflammatory diseases affect the left side more and in the present study large number were the cases of bronchiectasis, the lobectomies performed in our study more in left lung.

The distribution of duration of chest tube drainage shows that in Group I and Group II the Mean ± SD of duration of chest tube drainage was 4.40 ± 0.77 and 5.93 ± 0.58 days respectively. Minimum duration of chest tube drainage in Group I was 3 days and maximum was 6 days. In Group II minimum duration of chest tube drainage was 5 and maximum was 7 days. Statistically significant difference in duration of chest tube drainage was observed between the groups ($p<0.05$). Alex et al. in a study found no significant difference in the duration of drainage (mean, 4 days for group A vs 4.3 days for group B; p = NS). In a randomised study, Gomez-Caro et al.[3] found that the duration of the chest tube drainage were similar in both groups. The finding of the present study differs from their findings, because in the present study maximum number of patients diagnosed inflammatory lung disease. So, the pleural collection is more.

The distribution of amount of drainage shows there was no statistically significant difference in amount of drainage observed between the groups ($p>0.05$). Alex et al.[4] in a study found that there was no significant difference in the amount of drainage (mean, 667 mL for group A vs 804 mL for group B; p = NS). In a randomised study, Gomez-Caro et al. (2006)[3] found that the amount of drainage of the chest tube drainage were similar in both groups. The finding of the present study differs from their findings as the significant difference observed in amount of drainage between the groups.

In the present study post operative complication shows that in Group I only one (3.3%) patient developed wound infection and in Group II 2 (6.7%) developed space infection, 1 (3.3%) developed wound infection, 1 (3.3%) undergone reopening of bleeding and 1 (3.3%) developed stump leakage. Nadeem et al. in a study showed that the most patients (37/55, 67.3%) had uneventful postoperative recovery, while 18/55 (32.7%) developed some sort of complication. The most common postoperative complication was infection (wound infection and empyema) accounting for 8 patients (14.6%), followed by air leak (5/55, 9.1%). Complication was less in the present study than in the study done by Nadeem et al.[6].

The distribution of duration of hospital stay shows that in Group I and Group II the Mean ± SD of hospital stay was 10 ± 0 and 10 ± 0 days respectively. Post operative hospital stay in both Groups minimum and maximum was 10 days. The majority of patients in our institute are poor, uneducated and come from all across the country. So, our practice is to discharge patients from hospital after the stitches are removed. This is probably the reason for increased postoperative hospital stay in our study. Pawelczyk et al.[5] in their retrospective nonrandomised series found that placing a single chest tube after lobectomy reduces the hospitalisation time. Alex et al. (2003)[4] in a study found that there was no significant difference in the length of stay (mean, 7.7 days for group A vs 7.8 days for group B; p = NS). The present study differs from the study done by Alex et al.[4] in significance of post operative hospital stay between the groups. Wright et al. (1997)[7] in a study showed that the mean length of stay of 10.6 days. The result of their study was comparable to the present study.

In Group II 28 (93.3%) patients developed more pain during first and second follow up and 27 (90.0%) patients developed more pain in third follow up. Statistically significant difference in pain development in first, second and third follow up between the groups ($p<0.05$). In a nonrandomised study, Alex et al.[4] first used a single tube in a group of 60 lobectomy patients and compared the results with those observed in another group with two chest tubes. In their study they observed less pain was in the single-tube group. In a randomised study, Gomez-Caro et al.[3] found that a single-tube group required a lesser amount of analgesics than

the double-tube group. Okur et al.[8] in a prospective randomised study investigated whether using two tubes after a pulmonary lobectomy is more effective than using a single tube. In their study the mean values of postoperative pain assessed on the visual analogue scale (VAS) in the early (second day) period were 4.28 ± 0.21 in the single-tube group and 5.10 ± 0.23 in the double-tube group (p = 0.014). The VAS scores in the late (second week) period were 1.48 ± 0.13 in the single-tube group and 2.00 ± 0.17 in the double-tube group (p = 0.01). All other related parameters were similar in both groups. They concluded that using a single tube is in fact more effective than using two tubes in that it causes less postoperative pain.

In the present study lung expansion was evaluated clinically and radiologically during follow up. The distribution of lung expansion shows that in Group I 27 (90.0%) patients were presented with fully lung expansion during 1st, 2nd and 3rd follow up. In Group II 28(93.3%) patients were presented with full lung expansion and 2 (6.7%) were presented with partially expanded during 1st and 2nd follow up and 3rd follow up. There is no statistical difference in lung expansion between the groups (p>0.05).

Summary:

This study was aimed to investigate whether using two tubes after a pulmonary lobectomy is more effective than using a single tube. No such study had been done in our country previously. So it strongly demanded research work on this particular issue. Total 60 patients who underwent pulmonary lobectomies were included in the present study. Among them 30 were in the Group I (Single chest tube) and another 30 were in the Group II (Double chest tube). Between the groups there is no statistically difference in age, sex, side of diseased lung, amount of chest tube drainage, post operative hospital stay but significant difference were found in duration of chest tube drainage. During follow up period significant difference were observed in pain at the final follow up with satisfactory lung expansion.

Conclusion:

It can be concluded from this study that double chest tube application has no additional benifit to single chest tube after pulmonary lobectomies.

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ORIGINAL ARTICLE

Proportion of MDR-TB and Risk Factors in CAT-I Failure Patients at NIDCH

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Abstract:

Background and Objectives: *Tuberculosis is the world's most important communicable disease. Multi drug resistant tuberculosis (MDR-TB) and HIV epidemic are two important challenges to tuberculosis control worldwide. MDR-TB is mainly a man-made phenomenon due to ineffective use of effective first-line anti-TB drugs due to microbial, clinical and programmatic causes. Treatment of MDR-TB is started after failure of CAT-II, but the prevalence of MDR-TB among CAT-I failure is also very high. There are no much study on proportion of MDR-TB in CAT-I failure patients in Bangladesh. This study was designed to see the proportion of MDR-TB and risk factors in CAT-I failure patients attending at NIDCH.*

Methods : *This cross sectional type of observational study was carried out at NIDCH, Dhaka, Bangladesh, during the period from January 2010 to December 2010. A total of 100 Bangladeshi patients with H/O recent CAT-I failure, both male and female, were consecutively selected and admitted. After admission, sputum were collected from all patients for AFB culture and DST maintaining SOP and sent immediately to NTRL, NIDCH. The culture and DST reports were collected from NTRL for analysis. All relevant data were collected through preformed data collection sheet and data were analyzed using SPSS version 14.0.*

Results: *Analysis of socio demographic parameters in the study population like - age, gender, nutrition, education, economic conditions, etc. showed that TB is a disease of young age group (mean age 33.96 years, SD±14.1) with male predominance (M:F = 4:1) and malnourished (mean BMI 15.88 kg/m², SD±2.9), and TB is predominant in less educated (higher secondary or above 9%) and*

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mostly in the lower income groups (72%). 30% of the CAT-I failure patients were MDR-TB with S- and H-mono resistance being 10% and 12% respectively; whereas Pan sensitive and No growth were 19% and 20% respectively. 76% of the patients received anti-TB treatment from partner NGOs and 78% of the patients had questionable regularity of anti-TB intake. Only 11% of patients had any type of anti-TB drug reaction. Association between CAT-I failure and DM, Br. asthma, COPD, H/O STD/high risk behaviour, H/O travel abroad, etc. were insignificant, but 48% of the patients had H/O active smoking habit. 32% of the patients failing CAT-I had H/O contact with known case of TB or MDR-TB and all the patients (33%) undergoing HIV testing were negative.

Conclusion: *Significant proportion of CAT-I failure patients might be MDR-TB which might have developed from irregularity in anti-TB treatment or contact with known cases of TB or MDR-TB. No strong positive relationship could be established between CAT-I failure and DM, Br. asthma, COPD, H/O STD/high risk behaviour, H/O travel abroad or anti-TB drug reaction, but strong positive relationship was observed between CAT-I failure and active smoking habit. HIV status seems to be still unimportant in Bangladeshi CAT-I failure patients.*

[Chest & Heart Journal 2011; 35(1) : 23-33]

Introduction:

According to WHO estimate, Bangladesh ranks sixth on the list of 22 highest burden TB countries in the world - approximately 391 TB cases (all forms) per lac population, 225 new cases each year per lac population, approximately 101 per lac are infectious cases, i.e. able to transmit TB in the community and about 45 per lac people die of TB each year; so, there are approximately 1,44,397 new smear-positive cases and 64,335 people dying from TB each year[1-4].

To combat the TB problem, at present, it is the global strategy to diagnose as much of the infectious TB cases as possible and bring them under quality assured DOTS treatment with short course of multi drug first line anti-TB as early as possible. With the adoption of DOTS, worldwide, TB scenario changed. At present, Bangladesh attained 100% DOTS coverage with case detection rate of more than 72% and treatment success rate more than 92%, whereas the global targets are 70% and 85% respectively[4]. But the global success in TB control became upset by the resurgence of TB due to an increased frequency of Drug Resistant Mycobacterium tuberculosis (DR-TB). Inconsistent or partial treatment for a given individual remains the prominent cause of drug resistance. It has been found that HIV infection is the main risk factor of Primary MDR-TB which is a major threat to TB control[5]. The recrudescence of TB has been exacerbated by the emergence and spread of MDR-TB (which is defined as a case of TB that is resistant to both isoniazid and rifampicin, with or without resistance to other drugs) as well as the expanding HIV epidemic and according to WHO, at present, there are about 50 million people worldwide infected with the DR-strains of TB[6]. Despite the longer course of treatment, the cure rate decreases from over 90% for non resistant strains of TB to 50% or less in MDR-TB.

In the most recent phase of the global project (i.e. Phase 4, which covers the period 2002–2007), among the new cases the proportion of MDR-TB ranged from 0% in eight countries to 19.4% in the Republic of Moldova and 22.3% in Baku City, Azerbaijan[7].

Bangladesh ranks 9th among the 25 high burden MDR-TB countries. There is no nation wide drug resistance survey, but some small-scale surveys were carried out sporadically. Recently, WHO estimates that in Bangladesh –

a) Total MDR-TB cases – 14,583 (*total MDR-TB – 4.0%*)

b) MDR-TB among New TB cases – 12,562 (*Primary MDR-TB – 3.6%*)

c) MDR-TB among Previously treated TB cases – 2,021 (*Acquired MDR-TB – 19.3%*)[7].

MDR-TB is a catastrophic man-made phenomenon due to ineffective administration of effective drugs

which is virtually a death sentence to the patients especially in the resource-poor countries. The most common mistakes in TB treatment that result in the development of multi-drug resistance are:

- Administering an additional medication after a failed treatment regimen;
- Inappropriate primary regimen;
- Failure to make a timely diagnosis of drug resistance[8].

The most common indicator of MDR-TB is a history of erroneous TB treatment[9,10].

Ongoing transmission of infection from MDR-TB cases in a population lead to contribute to new primary drug-resistant cases[11].

MDR-TB is prevalent among CAT-II failure, irregularly treated TB patients, patients treated with multiple courses of anti-TB or patients getting unsupervised non standardized anti-TB treatments. But prevalence of MDR-TB among the CAT-I failure patients is also very high. In one study undertaken in Mumbai reveals a high proportion of MDR-TB among CAT-I failure cases (41%)[12]. In one study in Iran shows about 56% MDR-TB cases among patients failing CAT-I[13]. One study conducted at Vietnam found >23% MDR-TB among CAT-I failure patients[14] and another study conducted in Vietnam showed about 80% of CAT-I failure patients to be MDR-TB[16]. Another study conducted in Thailand shows 15% of MDR-TB cases among CAT-I failure patients[15]. One interesting study from Lima, Peru showed about 90% of the CAT-I treatment failures to be MDR-TB[17]. In one study from Tomsk region of Russia showed about 55% of MDR-TB cases among CAT-I failure cases[18].

In Bangladesh, there are few studies to see prevalence of MDR-TB among CAT-I treatment failure. One study conducted at NIDCH showed 13% MDR-TB cases among CAT-I failure patients[19]. The Damian Foundation Bangladesh, found 58% MDR-TB cases among CAT-I anti-TB failure patients[20]. So, in many of the developed countries it is the common practice to do a culture and DST at the beginning of treatment applying the rapid diagnostic methods and formulating anti-TB treatment regimen according to the initial anti-TB resistance pattern. This might be helpful in preventing the amplifier effect of anti-TB drugs and development of MDR-TB in unrecognised initial INH or Rifampicin resistance. This is not possible in case of resource-poor developing countries. But, if at least culture and DST could be done in those patients on CAT-I treatment showing persistent smear positivity and failing CAT-I anti-TB treatment regimen so that many of the MDR-TB could be diagnosed earlier to start second-line anti-TB treatment earlier to achieve better treatment outcomes in these patients and to prevent the spread of MDR-TB in the community from these patients.

Rationale

The patients who failed CAT-II and developed MDR-TB, were most probably MDR-TB when they failed CAT-I treatment. So, if these patients could be diagnosed as MDR-TB by Sputum AFB culture and DST when they were failing CAT-I, they could be started with second line anti-TB drugs well before, thus - 1) Transmission of MDR-TB in the community by the CAT-I failed MDR-TB cases could be stopped earlier, thus decreasing the number of contact MDR-TB or Primary MDR-TB cases, 2) resources spent to treat the pt. with CAT-II regimen would be saved and possibly the patient could be cured from MDR-TB much before, 3) The toxic effects of Inj. Streptomycin could be avoided, thus avoiding the double dose effect of aminoglycosides. The study aims at rationality of introducing Sputum for AFB culture and DST routinely in all patients who are failing CAT-I anti-TB treatment to diagnose the MDR-TB cases earlier, so that second line anti-TB drugs can also be introduced earlier, thus saving time and resources for treating MDR-TB patients and decreasing the transmission of MDR-TB in the community.

Aims And Objectives

General Objective:

The present study is aimed at assessing the proportion of MDR-TB cases among CAT-I failure patients.

Specific Objectives:

- o To estimate the AFB Culture positivity of sputum and Drug-resistance pattern in CAT-I failure patients.
- o To assess the risk factors associated with CAT-I failure of patients.
- o To see HIV positiity in patients with CAT-I failure.

Materials and Methods:

t was a Cross-sectional type of Observational Study done in National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka, Bangladesh during the period. The study was carried out from January 2010 to December 2010.

Data was collected through pre-designed Data collection Sheet.

Data Collection technique: The Patients with CAT-I failure attending out patient department (OPD) of NIDCH were consecutively selected and were admitted into NIDCH for data collection and further evaluation for the study. After taking patient's consent, each patient was thoroughly interviewed following a pre-formed Data Collection Sheet. Treatment history of patients was taken through and through by meticulous questioning about their taking anti-TB therapy under quality assured DOTS and also by examining the Treatment & Follow-up documents. After finishing the interview and physical examination, all the relevant data were recorded, rational treatment initiated, appropriate investigations ordered and ensured including collection of sputum samples following the SOP. During the stay of the patients indoor, all the patients were requested for HIV screening at the VCT centre at NIDCH; associated underlying risk factors were sought in appropriate conditions. Besides the OPD patients at NIDCH, some already admitted patients fulfilling the inclusion criteria set for the study were also included in the study. If any patient fulfilling the inclusion criteria refused admission, they were not included for the study.

Study Population:

A total of 100 Bangladeshi patients of 16-70 years of age and both sexes with history of recent CAT-I anti-TB treatment failure who attended the OPD of NIDCH from March, 2010 to August, 2010 and also those patients who were already been admitted at NIDCH during the study period having the history of recent CAT-I anti-TB treatment failure, were included in the present study following inclusion and exclusion criteria.

Sampling was consecutive and purposive as it was not possible to allocate the patients randomly within the time limit of study.

Inclusion Criteria: Recent CAT-I failure patients who were under supervised and quality assured DOTS therapy.

Exclusion Criteria:

1. The patients who never got anti-TB treatment before.
2. The patients who are still under CAT-I anti-TB treatment but have not yet fulfilled the criteria of failure.
3. The patients who are on CAT-II anti-TB treatment or failed CAT-II treatment.
4. The patients who are under MDR-TB treatment.
5. Patients who refused to be part of the study.

Results:

Table–I

Distribution of study population according to drug susceptibility pattern (N=100)

Drug susceptibility result	Number of cases (%)
MDR	30 (30%)
S-mono resistance	10 (10%)
H-mono resistance	12 (12%)
E-mono resistance	4 (4%)
H&S-poly resistance	2 (2%)
H&E-poly resistance	1 (1%)
R-mono resistance	2 (2%)
Pan sensitive	19 (19%)
No growth	20 (20%)
Total	100 (100%)

In order to observe the drug susceptibility among the study population, it was seen that 30 (30%) of the patients failing CAT-I anti-TB treatment regimen were MDR-TB cases followed by No growth and Pan sensitive groups, the numbers being 20(20%) and 19(19%) respectively. S- & H-mono resistance being 10(10%) & 12(12%) respectively, and other groups not significant.

In order to observe the age distribution in the study population, it was found that the mean age in the entire CAT-I failure patients was 33.96 years (SD ± 14.097) with an age limit from 16 to 70 years. The age limit of MDR-TB group was from 16 to 70 years with mean age 31.03 years (SD ± 12.952).

Table–II

Cross tabulation showing relationship between drug susceptibility report and age of the study population (N=100)

Age	Drug resistance pattern	N	Mean (Yr)	Std. Devi-ation (Yr)	Minimum (Yr)	Maximum (Yr)
	MDR	30	31.03	12.952	16	70
	S-mono resistance	10	28.30	9.334	18	42
	H-mono resistance	12	45.92	19.902	18	68
	E-mono resistance	4	38.00	4.690	35	45
	H&S-poly resistance	2	30.50	3.536	28	33
	H&E-poly resistance	1	27.00	-	27	27
	R-mono resistance	2	62.00	4.243	59	65
	Pan sensitive	19	35.42	13.301	18	65
	No growth	20	29.70	10.209	16	50
	Total	100	33.96	14.097	16	70

Table–III

Cross tabulation showing relationship between drug susceptibility report and Educational status in the study population (N=100)

Drug resistance pattern		Educational status				Total
		Primary	Secondary	H. Secondary & above	No profile	
MDR	Count	4	16	3	7	30
	% within education	22.2%	32.7%	33.3%	29.2%	30.0%
S-mono resistance	Count	*4*	*4*	*0*	*2*	*10*
	% within education	22.2%	8.2%	0.0%	8.3%	10.0%
H-mono resistance	Count	*2*	*4*	*2*	*4*	*12*
	% within education	11.1%	8.2%	22.2%	16.7%	12.0%
E-mono resistance	Count	*1*	*3*	*0*	*0*	*4*
	% within education	5.6%	6.1%	0.0%	0.0%	4.0%
H&S-poly resistance	Count	*2*	*0*	*0*	*0*	*2*
	% within education	11.1%	0.0%	0.0%	0.0%	2.0%
H&E-poly resistance	Count	*0*	*1*	*0*	*0*	*1*
	% within education	0.0%	2.0%	0.0%	0.0%	1.0%
R-mono resistance	Count	*0*	*0*	*0*	*2*	*2*
	% within education	0.0%	0.0%	0.0%	8.3%	2.0%
Pan sensitive	Count	*0*	*10*	*3*	*6*	*19*
	% within education	0.0%	20.4%	33.3%	25.0%	19.0%
No growth	Count	*5*	*11*	*1*	*3*	*20*
	% within education	27.8%	22.4%	11.1%	12.5%	20.0%
Total	Count	*18*	*49*	*9*	*24*	*100*
	% within education	100%	100%	100%	100%	100%

In order to assess the educational status of the respondents, it was found that 18(18%) and 49(49%) of the respondents reported their educational qualifications up to Primary and Secondary levels respectively; whereas 9(9%) respondents had educational qualifications of Higher secondary level or above and 24(24%) had no profile about educational qualifications.

In order to measure the BMI value as a nutritional status in the study population, it was found that the mean BMI value was 15.88 Kg/m² (SD ± 2.90) with a range from 9.91 to 26.50 Kg/m². In MDR-TB group, mean BMI value was 15.91 Kg/m² (SD ± 2.84) with a range from 9.91 to 20.69 Kg/m².

Table–IV

Cross tabulation showing relationship between drug susceptibility report and Body Mass Index (BMI) level in the study population (N=100)

BMI	Drug resistance pattern	N	Mean (Kg/m²)	Std. Deviation (Kg/m²)	Minimum (Kg/m²)	Maximum (Kg/m²)
	MDR	30	15.9137	2.84594	9.91	20.69
	S-mono resistance	10	16.4460	2.72548	11.97	19.53
	H-mono resistance	12	16.2125	1.29298	14.11	17.96
	E-mono resistance	4	14.4550	1.29121	13.68	16.37
	H&S-poly resistance	2	14.0300	1.23037	13.16	14.90
	H&E-poly resistance	1	15.1500	-	15.15	15.15
	R-mono resistance	2	14.2000	1.97990	12.80	15.60
	Pan sensitive	19	14.9458	3.38470	10.08	23.70
	No growth	20	16.8995	3.50857	12.66	26.50
	Total	100	15.8781	2.90201	9.91	26.50

Table–V

Cross tabulation showing distribution of drug resistance pattern among different Socio-economic status in study population (N=100)

Drug resistance pattern		Socio-economic status		Total
		Middle	Lower	
MDR	Count	*8*	*22*	*30*
	% within socio-economic group	28.6%	30.5%	30.0%
S-mono resistance	Count	*3*	*7*	*10*
	% within socio-economic group	10.7%	9.7%	10.0%
H-mono resistance	Count	*3*	*9*	*12*
	% within socio-economic group	10.7%	12.5%	12.0%
E-mono resistance	Count	*0*	*4*	*4*
	% within socio-economic group	0.0%	5.6%	4.0%
H&S-poly resistance	Count	*1*	*1*	*2*
	% within socio-economic group	3.6%	1.4%	2.0%
H&E-poly resistance	Count	*0*	*1*	*1*
	% within socio-economic group	0.0%	1.4%	1.0%
R-mono resistance	Count	*0*	*2*	*2*
	% within socio-economic group	0.0%	2.8%	2.0%
Pan sensitive	Count	*9*	*10*	*19*
	% within socio-economic group	32.1%	13.8%	19.0%
No growth	Count	*4*	*16*	*20*
	% within socio-economic group	14.3%	22.3%	20.0%
Total	Count	28	72	100
	% within socio-economic group	100%	100%	100%

In order to analyze the socio-economic condition of the respondents, only two categories were found – 1) Lower (monthly family income < Tk. 4,000/=) and 2) Middle (monthly family income Tk. 4,000/= to Tk. 7,000/=). Among all the respondents, only 28(28%) belonged to middle and the rest 72(72%) belonged to the lower socio-economic groups.

In order to assess the relationship between CAT-I failure and drug resistance pattern with history of source of CAT-I initiation, it was found that 76(76%) of the patients received their CAT-I treatment from partner NGOs and only 8(8%) and 6(6%) patients received CAT-I treatment from TB clinics and NIDCH respectively.

Table–VI

Cross tabulation showing relationship between drug susceptibility report and sources of CAT-I initiation in study population (N=100)

Drug resistance pattern		History related to source of CAT-I initiation							Total
		TB clinic	UHC	NGO	GP	Specialist	NIDCH	Sadar Hospital	
MDR	Count	*4*	*0*	*24*	*0*	*0*	*1*	*1*	*30*
	% within H/O CAT-I source	50.0%	0.0%	31.6%	0.0%	0.0%	16.7%	50.0%	30%
S-mono resistance	Count	*1*	*0*	*5*	*1*	*0*	*3*	*0*	*10*
	% within H/O CAT-I source	12.5%	0.0%	6.6%	33.3%	0.0%	50.0%	0.0%	10%
H-mono resistance	Count	*0*	*2*	*7*	*0*	*2*	*1*	*0*	*12*
	% within H/O CAT-I source	0.0%	100%	9.2%	0.0%	66.7%	16.7%	0.0%	12%
E-mono resistance	Count	*0*	*0*	*2*	*2*	*0*	*0*	*0*	*4*
	% within H/O CAT-I source	0.0%	0.0%	2.6%	66.7%	0.0%	0.0%	0.0%	4%
H&S-poly resistance	Count	*0*	*0*	*2*	*0*	*0*	*0*	*0*	*2*
	% within H/O CAT-I source	0.0%	0.0%	2.6%	0.0%	0.0%	0.0%	0.0%	2%
H&E-poly resistance	Count	*0*	*0*	*1*	*0*	*0*	*0*	*0*	*1*
	% within H/O CAT-I source	0.0%	0.0%	1.3%	0.0%	0.0%	0.0%	0.0%	1%
R-mono resistance	Count	*0*	*0*	*2*	*0*	*0*	*0*	*0*	*2*
	% within H/O CAT-I source	0.0%	0.0%	2.6%	0.0%	0.0%	0.0%	0.0%	2%
Pan sensitive	Count	*1*	*0*	*16*	*0*	*1*	*1*	*0*	*19*
	% within H/O CAT-I source	12.5%	0.0%	21.1%	0.0%	33.3%	16.7%	0.0%	19%
No growth	Count	*2*	*0*	*17*	*0*	*0*	*0*	*1*	*20*
	% within H/O CAT-I source	25.0%	0.0%	22.4%	0.0%	0.0%	0.0%	50.0%	20%
Total	Count	8	2	76	3	3	6	2	100
	% within H/O CAT-I source	100%	100%	100%	100%	100%	100%	100%	100%

Table–VII

Cross tabulation showing relationship between drug susceptibility report and history of regularity of CAT-I treatment in study population (N=100)

		H/O Regularity of CAT-I treatment		
	Drug resistance pattern	Regular	Questionable	Total
MDR	Count	*3*	*27*	*30*
	% within H/O regularity	13.6%	34.6%	30.0%
S-mono resistance	Count	*4*	*6*	*10*
	% within H/O regularity	18.2%	7.7%	10.0%
H-mono resistance	Count	*7*	*5*	*12*
	% within H/O regularity	31.8%	6.4%	12.0%
E-mono resistance	Count	*0*	*4*	*4*
	% within H/O regularity	0.0%	5.1%	4.0%
H&S-poly resistance	Count	*0*	*2*	*2*
	% within H/O regularity	0.0%	2.6%	2.0%
H&E-poly resistance	Count	*0*	*1*	*1*
	% within H/O regularity	0.0%	1.3%	1.0%
R-mono resistance	Count	*0*	*2*	*2*
	% within H/O regularity	0.0%	2.6%	2.0%
Pan sensitive	Count	*5*	*14*	*19*
	% within H/O regularity	22.7%	17.9%	19.0%
No growth	Count	*3*	*17*	*20*
	% within H/O regularity	13.6%	21.8%	20.0%
Total	Count	*22*	*78*	*100*
	% within H/O regularity	100%	100%	100%

In order to asses the H/O regularity of CAT-I treatment in the study population, it was observed that, only 22(22.0%) of the respondents were confident about taking CAT-I treatment regularly, whereas in 78(78.0%) of respondents the regularity was questionable.

In order to identify smoking habit among the study population, it was found that, 48(48.0%) of the respondents gave H/O active smoking habit, while 52(52.0%) were non smokers.

Table–VIII

Cross tabulation showing relationship between drug susceptibility report and H/O smoking in the study population (N=100)

			Drug resistance (DR) pattern									Total
			MDR	S-mono resistance	H-mono resistance	E-mono resistance	H&S-poly resistance	H&E-poly resistance	R-mono resistance	Pan sensitive	No growth	
H/O Smoking	Present	Count	10	2	11	3	2	1	2	8	9	48
		% within DR pattern	33.3 %	20.0 %	91.7%	75.0%	100%	100%	100%	42.1%	45.0%	48.0%
	Absent	Count	20	8	1	1	0	0	0	11	11	52
		% within DR pattern	66.7%	80.0%	8.3%	25.0%	0.0%	0.0%	0.0%	57.9%	55.0%	52.0%
	Total	Count	30	10	12	4	2	1	2	19	20	100
		% within DR pattern	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

Table–IX

Cross tabulation showing relationship between drug susceptibility report and H/O contact with known case of TB/MDR in the study population (n=32)

			Drug resistance (DR) pattern									Total
			MDR	S-mono resistance	H-mono resistance	E-mono resistance	H&S-poly resistance	H&E-poly resistance	R-mono resistance	Pan sensitive	No growth	
		Count	*8*	*3*	*2*	*0*	*0*	*1*	*0*	*4*	*5*	*23*
	TB	% within DR pattern	80.0%	60.0%	100%	0.0%	0.0%	100%	0.0%	50.0%	83.3%	71.9%
H/O Contact with known case of		Count	*2*	*2*	*0*	*0*	*0*	*0*	*0*	*4*	*1*	*9*
	MDR-TB	% within DR pattern	20.0%	40.0%	0.0%	0.0%	0.0%	0.0%	0.0%	50.0%	16.7%	28.1%
	Total	Count	*10*	*5*	*2*	*0*	*0*	*1*	*0*	*8*	*6*	*32*
		% within DR pattern	100%	100%	100%	0.0%	0.0%	100%	0.0%	100%	100%	100%

Table–X

Table showing HIV screening test results in the study population (N=100)

HIV screening status N		HIV screening test		Total
		Positive	Negative	
Screened	*33*	*0*(0.0%)	*33*(100%)	*33*(33.0%)
Not screened	*77*	-	-	*77*(77.0%)
Total	100	0	33	100(100%)

To find out the association between H/O contact with known cases of TB/MDR-TB and CAT-I failure in the study population, it was observed that 32(32.0%) patients had H/O contact with known cases of TB/MDR-TB within few months.

In order to observe the HIV infection status among the study population, all the patients were requested for HIV screening test at VCT centre at NIDCH, but only 33(33.0%) patients could be motivated for doing the test. The HIV screening test done in all the 33(100%) patients was negative.

Discussion:

In order to assess the casual relationship between different variables and its frequency, it was found that, out of 100 CAT-I failure respondents, 30% of the respondents had MDR-TB. The age limit of the respondents, who had MDR-TB, was in between 16 to 70 years and their average age was 31.03 years (SD±12.95). 19% respondents were reported pan sensitive whose average age was 35.42 years (SD±13.3) with an age range from 18 to 65 years. Apart from this 20% respondents had no growth whose average age was 29.70 years (SD±10.2) with an age range from 16 to 50 years. The overall mean age was 33.96 years (SD±14.1). In the above discussion, there are two variables – one is the resistant pattern among the CAT-I anti-TB treatment failure patients on culture and DST which shows a moderately high rate of MDR-TB patients (30%). This finding of resistant patterns among CAT-I anti-TB treatment failure coincides with findings from other studies worldwide[12,13,14,16,17,18]; in these studies MDR-TB in CAT-I failure ranged from >23% to as high as 90%. The Damian Foundation Bangladesh, found 58% MDR-TB cases among CAT-I anti-TB failure patients in their study area[20]. The second variable in the above discussion is age the mean of which is 33.96 years in our study which coincides with the fact that TB is mainly a disease of the productive age group ranging mostly in between 15 to 54 years[22].

In order to assess the educational status of the respondents, it was found that, out of 100 respondents, 18% respondents had their educational qualification up to primary level and 49% respondents were educated up to Secondary level. 9% respondents had higher secondary and above education and in case of the rest 24%, no profiles were reported. So it is evident from the study that prevalence of TB is more in those having less education. This finding is supported by other studies[23,24]

With a view to measure the nutritional status in the study population BMI values were evaluated, and mean BMI level of respondents with MDR-TB was 15.91 kg/m² (SD±2.85), whereas the range of BMI was in between 9.91 to 20.69. The study shows that almost all the patients from all the groups of CAT-I failure had low nutritional status as reflected by the below average BMI level which is an established fact that TB is a disease of the poor, malnourished and illiterate.

In order to analyze the socio economic condition of the respondents it was found that only 2 category of the socio economic condition prevailed among the groups of study population. The socio economic strata for the respondents were the middle socio economic group (Monthly family income Tk 4,000 – 7,000/=) and lower socio economic group (Monthly family income less than Tk 4,000/=). It was found that out of 100 respondents from all groups, only 28 respondents belonged to middle socio economic group and rest 72 from lower socio economic group. Our finding is also supported by findings in a study by Pant, et al., 2009, which found 87% of the MDR-TB patients belonging to lower socio economic group.

While analyzing the History related to source of initiation of CAT-I treatment, it was found from the list that most of the respondents (76%) received the anti TB treatment from the NGO partners, whereas the ratio of receiving anti TB treatment from other sources-like TB clinics, Sadar hospitals, NIDCH, UHCs, GPs, Specialists etc. were negligible. NGOs are the implementation partners of NTP and through DOTS they provide anti-TB treatment throughout whole of the country. So, it is rational that the TB patients will get anti-TB treatment through the NGOs of their corresponding area rather than other Govt. facilities.

Regularity of anti-TB treatment under quality assured DOTS is a pre requisite for good treatment outcome and to prevent development of anti-TB drug resistance[25]. In order to assess the regularity of taking anti-TB drugs during CAT-I treatment, only 22 (22%) respondents confidently expressed their regular intake of anti-TB during CAT-I treatment. However, in case of rest of the respondents (78%), regularity was questionable; they might be irregular in taking the anti-TB drugs during CAT-I treatment, which might have resulted in drug resistance.

In order to identify association between active smoking habit and CAT-I failure, it was found that 48.0% of the respondents had H/O active smoking. This high prevalence of active smokers among CAT-I failure patients correlates with a study done at Nepal showing 74% of the TB patients to be smokers which proves the linkage between poor lung health and smoking beyond doubt, though the linkage between smoking and anti-TB drug resistance is yet to be established[24,25].

When a person with active tuberculosis coughs, sneezes or spits, people nearby may breathe in the tuberculosis bacteria and become infected. Left untreated, each person with active tuberculosis will infect on an average between 10 and 15 people every year[26]. In case of assessing the association of contact with known cases of TB or MDR-TB and CAT-I failure, it was found that 32(32.0%) patients gave H/O contact with known cases of TB (23 cases) or MDR-TB cases (9 cases).

HIV infection gradually destroys the acquired immunity of the body and makes a person more susceptible to many bacterial infections including tuberculosis. So, HIV infection is a boost for TB flare up as well as treatment failure due to anti-TB drug resistance[27]. Earlier surveys conducted in Bangladesh to evaluate the prevalence of HIV infection in TB patients have shown insignificant levels. So, in case of treatment failure cases HIV testing should be done to diagnose any underlying HIV infection which might have affected the anti-TB treatment. In our study we could motivate only 33(33.0%) patients to undergo HIV testing both for HIV-1 and HIV-2 antibody at the VCT centre at NIDCH. The HIV testing of all the 33 patients were negative which correlates with the low prevalence of HIV infection in Bangladesh.

Conclusion:

From this study it, seems to be that a significant proportion of patients failing the CAT-I anti-TB treatment regimen under supervised DOTS develop multi drug resistant tuberculosis (MDR-TB) (30%). From this study it is also seen that a significant percentage of patients who fail CAT-I regimen, have INH and Streptomycin mono-resistance (12% and 10% respectively). One important finding of the study is, a fairly good number of the MDR-TB patients have H/O contact with known case of TB or MDR-TB patients (33%) which might have resulted in transmission of Primary drug resistance. Another important finding of the study is that 78% of the CAT-I failure patients had H/O questionable regularity in taking anti-TB. The study shows positive relationship between CAT-I failure and smoking (48%), but it failed to establish positive relationship between CAT-I failure and DM (16%) or Br. asthma (14%) or COPD (9%) or H/O STD/High risk behaviour (5%) or H/O travel abroad (10%). We may conclude that if sputum for AFB culture and DST is done routinely in CAT-I anti-TB treatment failure patients and also in contact of sputum smear positive known cases of TB or MDR-TB, it may help to diagnose a significant number of MDR-TB patients earlier.

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ORIGINAL ARTICLE

Usefulness of Serum Adenosine Deaminase (ADA) Level In Pulmonary Tuberculosis

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Abstract:

Tuberculosis continues to be a major cause of morbidity and mortality worldwide. The diagnosis is usually based on clinical presentation, radiologic findings and positive tuberculin and/or BCG tests. However, clinicoradiological features are variable and the latter tests may be falsely negative. Under such circumstances, anti-tuberculous therapy is started empirically. It therefore becomes imperative to find some rapid and useful tests for the diagnosis of tuberculosis. Adenosine deaminase is involved in the propagation and differentiation of various lymphocytes, particularly T-lymphocytes, so that estimation of its level of activity in various body fluids has been used in the diagnosis of tuberculous effusions especially pleural forms. Conversely its decrease has been noticed in treated cases. In diagnosis of tuberculosis, microbiologic, genetic, immunologic and biochemical methods are used. It is a significant indicator of active cellular immunity. The level of serum ADA increases in various diseases in which cell immunization is stimulated. Some previous studies have confirmed the diagnostic value of ADA activity in effusions due to pleural, pericardial, meningeal, and peritoneal tuberculosis especially in countries with high tuberculosis prevalence .The measurement of ADA activity in body fluids has been helpful for the diagnosis of tuberculous effusions, especially tuberculous pleuritis, and a decrease in pleural fluid ADA has been demonstrated following treatment.

The mean serum ADA level is compared with healthy controls, higher in patients of pulmonary tuberculosis as well as non-tubercular respiratory disease. ADA level between pulmonary tuberculosis and non-tubercular lung disease are statistically significant. Sensitivity and specificity of this test, as a diagnostic tool for pulmonary tuberculosis is high with a cut of value of 30 u/l.Though ADA level may increase both in tuberculosis and non- tuberculous disease (e.g. typhoid, rheumatologic disease and lymphoproliferative disease) but ADA activity is higher in tuberculosis is (30 u/1) and p value <0.001. In the developing countries where TB is endemic, an ideal test for tuberculosis should be economic, minimally invasive, of high accuracy and quick to perform. Determination of ADA is not costly and time consuming. In many countries several studies were conducted to establish the ADA activity as a sensitive and specific marker of tuberculous pleural effusion. It is, therefore, recommended that ADA estimation should be done routinely, particularly if diagnosis of tuberculosis is in doubt. So, this non invasive procedure may help to establish a relatively cheap but effective marker for diagnosis of pulmonary tuberculosis.

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Introduction:

Tuberculosis is one of the oldest and commonest infectious diseases also known as master of death or captain of death .Tuberculosis continues to be a major cause of morbidity and mortality worldwide. [1] The diagnosis is usually based on clinical presentation, radiologic findings and positive tuberculin and/or BCG tests. However, clinicoradiological features are variable and the latter tests may be falsely negative. Under such circumstances, anti-tuberculous therapy is started empirically. It therefore becomes imperative to find some rapid and useful tests for the diagnosis of tuberculosis. Adenosine deaminase is involved in the propagation and differentiation of various lymphocytes, particularly T-lymphocytes, so that estimation of its level of activity in various body fluids has been used in the diagnosis of tuberculous effusions especially pleural forms. Conversely its decrease has been noticed in treated cases. The raised activity of adenosine deaminase is observed in the new born sera, six weeks after B.C.G. vaccination, raised serum adenosine deaminase activity was also observed in tuberculous cases compared to healthy individuals . [2]

Epidemiological studies have shown that tuberculosis is a disease that endangers health of community with increasing incidence rate. In diagnosis of tuberculosis, microbiologic, genetic, immunologic and biochemical methods are used. The measurement of adenosine deaminase (ADA) activity is one of the biochemical methods.ADA is an enzyme that converts adenosine to inosine, and deoxiadenosine to deoxiinosine in the pathway of purine catabolism, and by this way catalyses irreversible deamination. ADA acts in proliferation and differentiation of lymphocyte and especially T lymphocyte. It acts in maturation of monocytes and transforming them to macrophage. It is a significant indicator of active cellular immunity. The level of serum ADA increases in various diseases in which cell immunization is stimulated. The significance of ADA level in diagnosis of tuberculosis is known. Some previous studies have confirmed the diagnostic value of ADA activity in effusions due to pleural, pericardial, meningeal, and peritoneal tuberculosis especially in countries with high tuberculosis prevalence. [3]

The measurement of ADA activity in body fluids has been helpful for the diagnosis of tuberculous effusions, especially tuberculous pleuritis, and a decrease in pleural fluid ADA has been demonstrated following treatment. Although serum ADA (s-ADA) measurement should not be used in tuberculosis for diagnostic purposes, increased s-ADA levels have been found in some anecdotal reports composed, in most cases, of small groups of patients with tuberculosis. In two of these reports, a decrease in s-ADA levels was found 3 months after the initiation of therapy. [4]

Adenosine deaminase exists in all tissues. The presence of ADA activity is much more in lymphocytes than erythrocytes and in T lymphocytes than B lymphocytes. ADA has been accepted as a determinant of cellular immunity since it is an enzyme related to the lymphocyte differentiation and proliferation. ADA activity measurements were carried out in pleura, ascites, pericardial and cerebrospinal fluid and its diagnostic value were stated previously. Nowadays, there are still difficulties in diagnosis and follow-up of pulmonary tuberculosis despite the developed laboratory techniques. Especially in patients with symptoms and radiological findings which correlate with tuberculosis, but with negative acid fast basilli in sputum, a period of time is required to reach a conclusion about activation of disease, despite the applications of methods like radiological follow-up and sputum culture.[5] Diagnostic efficiency of serum ADA activity determination has been evaluated in cases of sputum negative patients of pulmonary tuberculosis who pose a problem of diagnosis in routine practice, when sputum smear results are negative. The mean serum ADA level, compared with healthy controls, higher in patients of pulmonary tuberculosis as well as non-tubercular respiratory disease. ADA level between pulmonary tuberculosis and non-tubercular lung disease are statistically significant. Sensitivity and specificity of this test, as a diagnostic tool for pulmonary tuberculosis is high with a cut of value of 30 u/l. [6] Though ADA level may increase both in tuberculosis and non- tuberculous disease (e.g. typhoid, rheumatologic disease and lymphoproliferative disease) but ADA activity is higher in tuberculosis is >30 u/1.

Methodology:

This study was conducted in the Department of Respiratory Medicine, National Institute of

Diseases of the Chest and Hospital, Dhaka from 1st July, 2008 to 30th June 2009. It was a cross-sectional study.

General objective: To establish the usefulness of serum ADA in the diagnosis of pulmonary tuberculosis.

Special Objectives: To compare serum ADA value in pulmonary tuberculosis with other respiratory disease and with healthy control.

To find out sensitivity, specificity, PPV and NPV of serum ADA for diagnosis of pulmonary tuberculosis.

To find out a cut off value of serum ADA in the diagnosis of PTB

Total 100 cases of which 35 were patients of pulmonary tuberculosis and 35 were patients of non tubercular pulmonary conditions enrolled. 30 normal healthy individuals were included in this study as control. Group 1: Thirty five cases of active pulmonary tuberculosis confirmed by positive sputum smears for acid fast bacilli and were negative for other kinds of infectious, malignant and autoimmune disorders. Group 2: Total 35 patients of Non-Tubercular pulmonary condition (Bronchial carcinoma, pneumonia, bronchiectesis etc) of which majority (26) are bronchial carcinoma. So, these patients are included in this group. Group 3: Total 30 healthy individuals lacking any infectious, malignant or autoimmune disorders.

Selection criteria

Inclusion criteria:

- Patients of any age group
- Patients of either sex
- Clinically and radio logically suspected pulmonary tuberculosis patients with sputum for AFB positive.
- Pulmonary diseases other than tuberculosis.

Exclusion criteria:

- Previous history of pulmonary tuberculosis
- Systemic diseases like CLD, CRF, DM, Rheumatological diseases
- Pregnancy.

Results and observations

The present study aimed at determining the value of serum ADA in the diagnosis of pulmonary tuberculosis and to compare serum ADA level in between PTB, Non- tubercular respiratory disease and in healthy people. All smear positive patients were taken as PTB. Total 100 cases were taken out of them 30 are healthy control who had no physical complaints. They were not investigated thoroughly. Only blood for ADA was done for them to compare the result with PTB and not-tubercular respiratory disease. Other 70 cases were analyzed finally. The findings obtained from data analysis are documented below. Mean age of the patients of group 1, group 2, and group 3 was 41.37, 54.09, and 42.67 years respectively. Significantly higher age group was observed in group 2. Multiple comparison of Bonferroni test revealed age difference of group 2 from group 1 and group 3 was statistically significant.

Out of all patients of group 1 85.7% were male and 14.3% were female, in group 2 80.76% were male and 19.23% were female, and in group 3 80.0% were male and 20.0% were female.

Table I

Clinical features of the patients

Clinical variables	Group		p value
	Group 1 (n=35)	Group 2 (n=26)	
Cough			
· Dry	31 (88.6)#	20 (76.9)	0.300**
· Productive	4(11.4)	6 (23.1)	
Fever	34 (97.1)	19 (73.1)	0.006**
Pattern of fever			
• Occasional	1 (2.9)	10 (52.6)	0.001*
• Continuous	4 (11.8)	1 (9.4)	
• Intermittent	29 (85.3)	8 (42.1)	
Grade of fever			
• Low grade	34 (100.0)	13 (68.4)	0.001
• High grade	0 (.0)	6 (31.6)	
Fever associated with sweating	7 (20.0)	2 (9.1)	0.272**
Evening rise of temperature	8 (22.9)	0 (.0)	0.016**
Loss of appetite	34 (97.1)	23 (88.5)	0.303**
Haemoptysis	9 (25.7)	6 (23.1)	0.813
History of contact with tuberculosis patient	2 (5.7)	1 (3.8)	0.999**
Vaccination	9 (25.7)	1 (3.8)	0.034**

* Chi square test was done to measure the level of significance
**Fisher's Exact test was done to measure the level of significance
Figure within parenthesis denoted corresponding column percentage
Group 1= PTB
Group 2 = Carcinoma

Out of all patients of group 188.6% had dry and 11.4% had productive cough and in group 2 74.3% had dry and 25.7% had productive cough.

In group 1 total 34 (97.1%) and in group 2 28 (80.0%) patients had fever. In group 1 among 34 cases 1 (2.9%) had occasional, 4 (11.8%) had continuous and 29 (85.3%) had intermittent fever and in group 2 among 28 patients 13 had occasional, 4 (14.3%) had continuous and 11 (39.3%) had intermittent fever. In group 1 all patients had low grade and in group 2 60.7% had low grade and 39.3%

had high grade fever. 20.0% patients of group 1 and 8 (26.7%) of group 2 had fever associated with sweating, evening rise of temperature observed in 22.9% patients of group 1 and 3.3% of group 2. Loss of appetite was a prominent finding

of both groups. Similar number of patients (25.7%) of both group had haemoptysis. Only 2 patients of group 1 and one patients of group 2 had history of contact with tuberculosis patients. 25.7% patients of group 1 and 8.6% of group 2 had history of previous vaccination

Table-I1

Smoking status of the patients

Smoking status	Group		p value*
	Group 1 (PTB)	Group 2 (Carcinoma)	
Smoker	9 (25.7)#	25 (96.2)	<0.001
Non-smoker	26 (74.3)	1 (3.8)	
Total	35 (100.0)	26 (100.0)	

* Chi square test was done to measure the level of significance
# Figure within parenthesis denoted corresponding column percentage

Maximum 80.0% patients of group 2 (NTRD) and only 25.7% of group 1 (PTB) were smoker. Statistically significant difference was observed between groups in term of smoking status (p<0.001).

Table-III

X-ray findings of the patients of both groups

CXR findings	Group		P value*
	Group 1 (PTB)	Group 2 (NTRD)	
Consolidation	1 (2.9)	14 (53.8)	
Cavitary lesion	4 (11.4)	0 (.0)	
Patchy opacity	29 (82.9)	0 (.0)	<0.001
Mass lesion	1 (2.9)	12 (46.2)	
Total	35 (100.0)	26 (100.0)	

* Chi square test was done to measure the level of significance
# Figure within parenthesis denoted corresponding column percentage

Table shows the chest X-ray findings of both groups. Out of all patients of group 1 82.9% had patchy opacity in their lung field, 11.4% had cavitary lesion, 2.9% had consolidation, and 2.9% had mass lesion. In group 2 maximum 51.4% patients had consolidation, 37.1% had mass lesion, 5.7% had cavitary lesion, 2.9% had raticulo nodular lesion and 2.9% had patchy opacity.

Table-IV

Distribution of the patients of group 1 and 2 by their site of lesion

Side of lesion	Group		p value
	Group 1 (PTB)	Group 2 (NTRD)	
Right	12 (34.3)	16 (61.5)	
Left	12 (34.3)	10 (38.5)	0.005
Both	11 (31.4)	0 (.0)	
Total	35 (100.0)	26 (100.0)	

* Chi square test was done to measure the level of significance
# Figure within parenthesis denoted corresponding column percentage

Table shows the sites of lesion in X-ray chest image of both groups. Out of all patients of group 1 (PTB) 34.3%, 34.3% and 31.4% had lesion on right, left and both sides respectively. In group 2 (NTRD) 60.0% had lesion in right side and 40.0% on left side. Statistical significant difference was observed in both groups in term of side of lesions (p>0.05).

Table-V

Distribution of the patients of group 1 and 2 by their zone wise chest findings

Sites of lesion	Group		p value
	Group 1 (PTB)	Group 2 (NTRD)	
Upper Zone	22 (62.9)	13 (50.0)	
Middle zone	11 (31.4)	8 (30.8)	0.246
Lower zone	2 (5.7)	5 (19.2)	
Total	46 (100.0)	26 (100.0)	

* Chi square test was done to measure the level of significance
# Figure within parenthesis denoted corresponding column percentage

In group 1 (PTB) lesions were identified in total 46 zones, of them 60.9% had lesion in upper zone, 32.6% had middle zone, 6.5% had in lower zone. In group 2 (NTRD) 57.1% had lesion in upper zone, 22.9% had in middle zone and 20.0% had in lower zone. No statistical significant difference was

observed in both groups in term of site of lesions (p>0.05).

Table-VI

ADA level in different types of respondents of study groups

Diagnosis	Mean ± SD	Range
Healthy person (n= 30)	12.23 ± 2.92	9.0-20.5
Carcinoma (n= 26)	29.82 ± 4.29	18.0-36.0
PTB (n= 35)	46.86 ± 12.69	30.2-86.8

Mean (±SD) ADA level of healthy person, patients of carcinoma and PTB was 12.23±2.92, 29.82±4.29, and 46.86±12.69 U/L respectively.

Table VII

Distribution of serum adenosine deaminase level among groups

	Group			Total
	Group 1 (PTB)	Group 2 (Carcinoma)	Group 3 (Healthy people)	
<10	0 (.0)	0 (.0)	7 (23.3)	7 (7.7)
11-20	0 (.0)	1 (3.8)	22 (73.3)	23 (25.3)
21-30	0 (.0)	12 (46.2)	1 (3.3)	13 (14.3)
31-40	12 (34.3)	13 (50.0)	0 (.0)	25 (27.5)
41-50	14 (40.0)	0 (.0)	0 (.0)	14 (15.4)
51-60	6 (17.1)	0 (.0)	0 (.0)	6 (6.6)
>60	3 (8.6)	0 (.0)	0 (.0)	3 (3.3)
Total	35 (100.0)	26 (100.0)	30 (100.0)	91 (100.0)

Group	Mean±SD
Group 1 (n=35)	46.86±12.69
Group 2 (n=26)	29.82 ± 4.29
Group 3 (n=30)	12.23±2.92

Statistical analysis

Groups	p value
Group 2 vs. Group 1	<0.001[sn]
Group 2 vs. Group 3	<0.001 [sn]
Group 3 vs. Group 1	<0.001 [sn]

Data is expressed as mean ±SD for statistical analysis

One way ANOVA (Post Hoc-Bonferroni) test was performed to compare ADA among groups.

Group 1= PTB
Group 2 = Carcinoma
Group 3 = Healthy people
sn= significant
n=number

Table-VIII

Association of ADA (Cutoff value 30U/L) with pulmonary tuberculosis and other lung conditions

ADA level	ZN staining		Total
	Positive (PTB)	Negative (Carcinoma)	
>30 U/L	35 (TP)	13 (FP)	48
d"30 U/L	0 (FN)	13 (TN)	13
Total	35	26	61

Table shows the frequency of diagnosis of pulmonary tuberculosis by adenosine deaminase by considering cut off value 30 U/L. Out of all patients of group 1 and 2, 53 were diagnosed as having tuberculosis when their ADA level was more than 30 U/L and of them 35 were ZN staining positive cases and 18 were negative. They were true positive and false negative respectively. No ZN staining positive cases and 17 negative cases had ADA level d"30 U/L. They were false negative and true negative cases respectively

Table IX

Sensitivity, specificity, accuracy, positive and negative predictive values of ADA in the diagnosis of pulmonary tuberculosis (30U/L cutoff level)

Test	Value	95% CI
Sensitivity	100.0	92.6-100.0
Specificity	50.0	40.1-50.0
PPV	72.9	67.6-72.9
NPV	100.0	80.2-100.0
Accuracy	78.7	70.2-78.7

PPV = Positive predictive value
NPV = Negative predictive value

Sensitivity of ADA (cut off level 30 U/L) to diagnose pulmonary tuberculosis was 100.0%, specificity 50.0%, PPV 72.9%, negative predictive value 100.0% and accuracy 78.7%

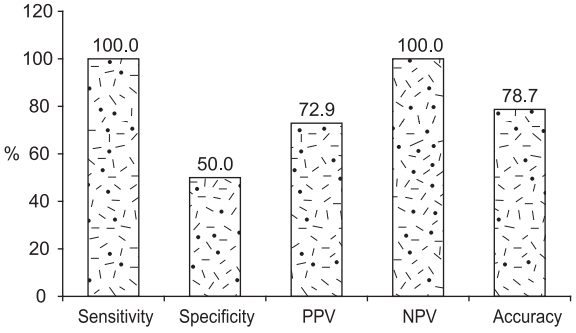

Fig.-1: *Validity tests at cutoff level 30 U/L*

Table-X

Association of ADA (Cutoff value 34U/L) with pulmonary tuberculaosis and other lung conditions

ADA level	ZN staining		Total
	Positive (PTB)	Negative (Carcinoma)	
>34 U/L	33 (TP)	4 (FP)	37
d”34 U/L	2 (FN)	22 (TN)	24
Total	35	26	61

Table shows the frequency of diagnosis of pulmonary tuberculosis by adenosine deaminase by considering cut off value 34 U/L. Out of all patients of group 1 and 2, 37 were diagnosed as having tuberculosis when their ADA level was more than 34 U/L and of them 33 were ZN staining positive cases and 4 were negative. They were true positive and false negative respectively. Two ZN staining positive cases and 22 negative cases had ADA level d”34 U/L. They were false negative and true negative cases respectively.

Table-XI

Sensitivity, specificity, accuracy, positive and negative predictive values of ADA in the diagnosis of pulmonary tuberculosis (34 U/L cutoff level)

Test	Value	95% CI
Sensitivity	94.3	85.7-98.2
Specificity	84.6	73.1-89.9
PPV	89.2	81.1-92.9
NPV	91.7	79.2-97.4
Accuracy	90.2	80.4-94.7

PPV = Positive predictive value
NPV = Negative predictive value

Sensitivity of ADA (cut off level 34 U/L) to diagnose pulmonary tuberculosis was 94.3%, specificity 84.6%, PPV 89.2%, negative predictive value 91.7% and accuracy 90.2%

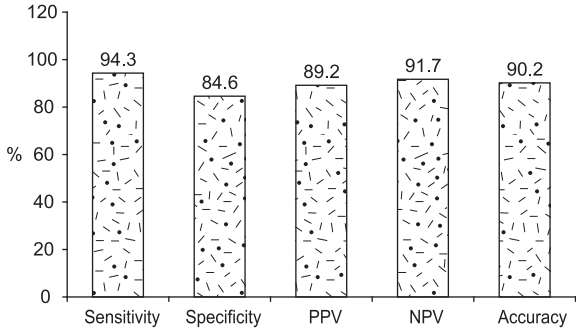

Fig.-2: *showing Sensitivity, Specificity, PPV, NPV & Accuracy*

Table-XII

Association of ADA (Cut-off value 37 U/L) with pulmonary tuberculaosis and other lung conditions

ADA level	ZN staining		Total
	Positive (PTB)	Positive (PTB)	
>37 U/L	29 (TP)	0 (FP)	29
d”37 U/L	6 (FN)	26 (TN)	32
Total	35	26	61

Table shows the frequency of diagnosis of pulmonary tuberculosis by adenosine deaminase by considering cut off value 37 U/L. Out of all patients of group 1 and 2, 29 were diagnosed as having tuberculosis when their ADA level was more than 37 U/L and of them 29 were ZN staining positive cases. They were true positive and false negative respectively. Six ZN staining positive cases and 26 negative cases had ADA level d”37 U/L. They were false negative and true negative cases respectively.

Table XIII

Sensitivity, specificity, accuracy, positive and negative predictive values of ADA in the diagnosis of pulmonary tuberculosis (37 U/L cutoff level)

Test	Value	95% CI
Sensitivity	82.9	75.6-82.9
Specificity	100.0	90.2-100.0
PPV	100.0	91.2-100.0
NPV	81.3	73.3-81.3
Accuracy	90.2	81.8-90.2

PPV = Positive predictive value
NPV = Negative predictive value

Sensitivity of ADA (cut off level 37 U/L) to diagnose pulmonary tuberculosis was 82.9%, specificity 100.0%, PPV 100.0%, negative predictive value 81.3% and accuracy 90.2%

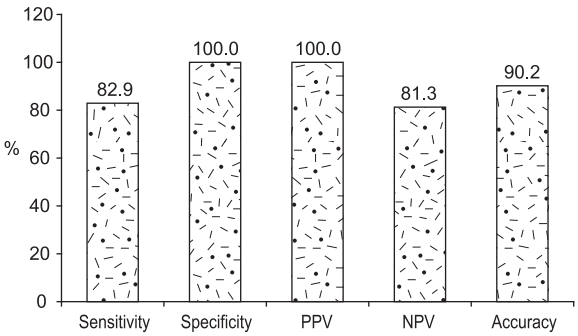

Fig.-3: *Validity tests at cutoff level 37 U/L*

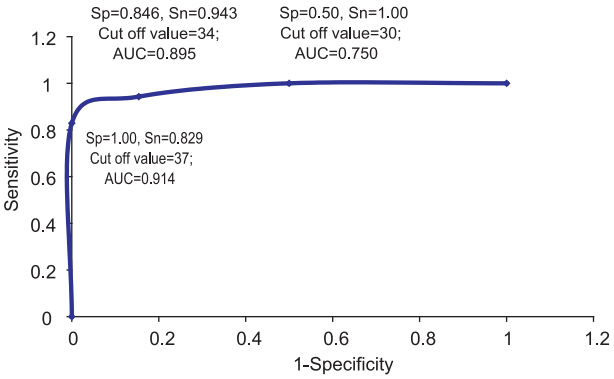

Fig.-4: *ROC curve in different cut of value*

Diagnostic accuracy was determined as receiver operating characteristic (ROC) curve, suggesting that the area under the curve (AUC) of ADA at cut off levels 30 U/L, 34 U/L and 37 U/L were 0.750, 0.895 and 0.914, respectively. So, we can conclude that cut off level 37 U/L is more appropriate for the diagnosis of pulmonary tuberculosis.

Discussion:

In the present study, mean serum ADA level in pulmonary tuberculosis (46.86±12.69U/L) and bronchial carcinoma (29.82±4.29U/L) was significantly more than controls (12.23±2.92U/L), ($p<0.001$ and $p<0.001$ respectively), ADA level was significantly more even in pulmonary tuberculosis group than NTRD ($p<0.001$). Similar observation was also made in Aminiafshar study. [7] Mean serum adenosine deaminase level in their study in pulmonary tuberculosis (42.4±21.5 IU/ml) and other infectious diseases (38.3±23.4 IU/ml) was significantly more than controls (26.6± 8.2 IU/ml), ($P<0.0001$ and $p<0.03$ respectively), but the difference between the pulmonary tuberculosis and other infectious diseases was not statistically significant.

In another study finding conducted by Agarwal is comparable to us. [8] serum adenosine deaminase (ADA) level of 38 healthy control, 36 cases of smear negative, culture positive patients of pulmonary tuberculosis, 37 cases of non-tubercular respiratory disease (malignancy lung 5, bronchial asthma 19, chronic bronchitis 2, pneumonitis/lung abscess 7 and bronchiectasis 4) were determined. The mean serum level of ADA in healthy controls was 15.30 ±0.22 U/Lit. in sputum negative, culture positive patients of pulmonary tuberculosis 38.48 ±1.56 U/Lit and in non-tubercular respiratory diseases 19.01 ± 0.68 U/Lit. The mean serum ADA levels, compared with health controls, were higher in smear negative, culture positive patients of pulmonary tuberculosis as well as non – tuberculosis respiratory disease. The different in ADA levels between pulmonary tuberculosis and non-tubercular lung diseases were statistically significant.

Various workers have found different values for normal human serum ADA level at 37°C: 17.05 ± 3.75 U/Lit and 19.09 ± 2.99 U/Lit High serum ADA levels have been reported by other workers in patients of pulmonary tuberculosis. [9] Though mycobacterial culture is sensitive and standard for diagnosing tuberculosis, the time for diagnosis requires a minimum of 2-3 weeks. Acid fast bacilli smear, the rapid screening method for the diagnosis of pulmonary tuberculosis is insensitive for detecting mycobacteria among tuberculosis patient. The assay of ADA activity in pleural and other infections is very useful in differential diagnosis, especially in the case of tuberculosis, which is characterized by an increase in activity.[10] However, the increased serum level of ADA has been reported for viral and bacterial pneumonia, HIV infection, and extra pulmonary tuberculosis.[10] In fact diseases caused by intracellular micro-organisms are characterized by an elevated level of ADA in serum.[11] Ungerer et al. (1994) studied serum levels of ADA isoenzymes in 51 cases of confirmed tuberculosis (41 pleural effusions, and 10 ascitic fluids), and 6 cases of bacterial pleural effusions (empyema), and noticed increased level of ADA2 in tuberculosis effusion (ADA2 / ADA total=88%), and ADA1 in non tuberculosis effusion (ADA1 / ADA total=70%), concluding that isoenzyme study is a helpful measure in differentiating these two kinds of effusions. [12]

Thora et al. (1995) studied ADA levels of 100 newborn sera who were vaccinated with BCG showing a significant increase, indicating human cell-mediated immune response against mycobacterium antigens. [13] Mishra et al. (2000) evaluated serum ADA levels of 51 children with confirmed tuberculosis (pulmonary, peritoneal, meningeal, and bone), and 20 healthy controls showing significant increase in the first group with a p-value of <0.001.[14] In our study we use three different cut-off values (30 U/L, 34 U/L, and 37 U/

L) of serum ADA to determine the best level for the diagnosis of pulmonary tuberculosis.[15] Sensitivity and specificity of these cut-off levels of the present series were 100.0% and 50.0%, 94.3% and 84.6%, and 82.9% and 100.0% respectively. [16] Receiver operating characteristic (ROC) curve suggesting that the area under the curve (AUC) of ADA at cut off levels 30 U/L, 34 U/L and 37 U/L were 0.750, 0.895 and 0.914, respectively. So, we can conclude that cut off level 37 U/L is more appropriate for the diagnosis of pulmonary tuberculosis. [17] Jhamaria et al (1988) using 33 U/Lit as the cut off limit had found 100% specificity and 98% sensitivity of serum ADA level test for diagnosis of pulmonary tuberculosis. In Agarwal et al (1991) series sensitivity and specificity of ADA, as a diagnostic tool for smear negative, culture positive pulmonary tuberculosis is high with a cut off value of 30 U/L. Our finding was not comparable with their result. [18] The determination of a cut-off value require a compromise between sensitivity and specificity and the considerations involved in this may vary from investigator to investigator depending upon the purpose for which the test is required. If ADA estimation is planned to be the definitive test for the diagnosis of tuberculosis, then a hundred percent specificity would be required. In our study he highest available sensitivity for a specificity of 100.0% was 50.0% and it occurred at a cut-off level of 30 U/L. In Sharma et al (2001) series it was 40.0% at a cut off level of 100 U/L and not comparable with our result. [19] On the other hand, if ADA estimation is planned as an initial phase screening test, then a high sensitivity with a reasonable specificity would be required. In our study we obtained a sensitivity of 94.3 % with a specificity of 84.6% at a cut-off level of 34 U/L and a sensitivity of 82.9% with a specificity of 100.0% at a cut-off of 37 U/L. Highest AUC (0.90) was observed at 37 U/L cut-off level. So we opted for 37 U/L as the appropriate cut off. In Sharma et al (2001) series sensitivity of 83.3% with a specificity of 66.7% at a cut-off of 35 IU/L was observed. [20] Above or below this cut-off value there were significant losses in sensitivity or specificity respectively, without a significant corresponding gain in specificity or sensitivity. So they decided 35 IU/L as the appropriate cut-off. [21]

Summary:

This cross-sectional study was conducted at the Department of Respiratory Medicine, National Institute of Diseases of Chest and Hospital, Dhaka from 1st July, 2008 to 30th June 2009. Total 61 patients of which 35 were patients of pulmonary tuberculosis and 26 were patients of bronchial carcinoma enrolled. 30 normal healthy individuals were also included in this study. In group 1 (PTB) all patient's sputum was ZN staining positive and in group 2 bronchial carcinoma all were negative. Mean (±SD) ADA level of healthy person, patients of carcinoma and PTB were 12.23±2.92, 29.82±4.29 and 46.86±12.69 U/L respectively. Sensitivity and specificity of three different cut-off values (30 U/L, 34 U/L, and 37 U/L) of serum ADA were 100.0% and 50.0%, 94.3% and 84.6%, and 82.9% and 100.0% respectively. The area under the curve (AUC) of ADA at cut off levels 30 U/L, 34 U/L and 37 U/L were 0.750, 0.895and 0.914, respectively.

Conclusions:

From this study it is concluded that using 37 U/L as the cut-off, it is possible to avoid other diagnostic procedures in as much as 50.0% (61 of 35) of the patients to ascertain the diagnosis of tuberculosis. Thus, serum ADA estimation seems to have the potential for being a single test for the diagnosis of tuberculosis which is adequately sensitive and specific and at the same time, inexpensive and easy to perform in the field setting.

Limitations:

1. Small sample size
2. Single center study
3. Only serum ADA level, not other body fluid ADA, was evaluated
4. ADA level of other body fluid should be evaluated.

Recommendations

1. Countries with a high prevalence of tuberculosis like Bangladesh with high degree of specificity and sensitivity for the ADA test at cut off level 37 U/L, should make it an integral part of a diagnostic workup
2. High negative predictive value of the ADA test should be provided an excellent means to rule out tuberculous etiology.
3. It should be added to the armamentarium of the diagnostic workup of body fluids in patients who are suspected of having tuberculosis
4. Multi centred study should be done.

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REVIEW ARTICLE

Lung Volume Reduction Surgery – An Update

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Abstract:

Lung volume reduction surgery (LVRS) is an innovative surgical treatment for selected patients with severe emphysema; one of several respiratory disorders labeled as chronic obstructive pulmonary disease (COPD) that improves dyspnoea, exercise tolerance and provides a good survival benefit. The goal of LVRS is to remove the worst areas of damaged lung tissue so that the remaining tissue can function better. During the procedure, surgeons remove 20-30% of the most diseased lung tissue. This allows the diaphragm to return to a more normal position so it can work effectively again. It also may improve lung elasticity.

LVRS is a procedure used for some patients with severe emphysema, a common pe o c ronic obstructive pulmonary disease (COPD), disabling dyspnoea and evidence of severe air trapping. LVRS may be an appropriate treatment for selected patients who meet established criteria. The results of the National Emphysema Treatment Trial (NETT) study, first published in 2003, identified four sub-groups of patients who had different risks and benefits from LVRS, specifically.

Group 1: Mostly upper lobe emphysema & low exercise capacity: These patient group may receive the most benefit from LVRS, as compared with the other patients group.

Group 2: Mostly upper-lobe emphysema and high exercise capacity: These patients are more likely to function better after LVRS than after medical treatment.

Group 3: Diffuse emphysema and low exercise capacity: These patients have similar survival and function after LVRS as after medical treatment.

Group 4: Diffuse emphysema and high exercise capacity. These patients have worse survival after medical treatment and do not appear to benefit from surgery.

Chest x-ray, Pulmonary function tests, Arterial blood gas analysis, o chest, Oxygen titration, Six-minute walk, Cardiopulmonary exercise test, Right heart catheterization, Cardiac stress test and Pulmonologist's consultation.

Sternotomy (Bilateral), Thoracotomy (Unilateral or One-Sided), Thoracoscopy:

LVRS is beneficial for patients with predominant upper lobe disease and low exercise capacity, as compared with medical treatment. While effective for some patients, there are risks involved with lung reduction surgery, including:, Air leakage (50%), Pneumonia or infection (19%), Stroke (<1%), Bleeding (2-5%), Heart attack (1%), Death (6-10%).

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Patients will stay in the **Cardiothoracie** *Intensive* **Care** *Unit (CTICU) post-operatively. While in the CTICU, patients will not require any items from home. One should expect to stay 5 to 10 days in the hospital following lung reduction surgery.*

Early ambulation, Deep Breathing, Coughing, Incentive Spriometer.

Patients *will be discharge 7 to post operative ay an patien wt e advised for joining his daily activities as soon as possible.*

After LVRS, patients are followed for five years through visits, phone calls and letters. One of the goals is to help patients make lifestyle changes, which include rehabilitation at least three days a week for the rest of their lives.

[Chest & Heart Journal 2011; 35(1) : 43-47]

Lung volume reduction surgery (LVRS) is an innovative surgical treatment for selected patients with severe emphysema; one of several respiratory disorders labeled as chronic obstructive pulmonary disease (COPD) that improves dyspnoea, exercise tolerance and provides a good survival benefit.

The goal of LVRS is to remove the worst areas of damaged lung tissue so that the remaining tissue can function better. Scientists believe that by surgically removing functionally useless tissue, air will move in and out of the remaining lung more readily, thereby easing symptoms associated with advanced emphysema and improving overall lung function.

During the procedure, surgeons remove 20-30% of the most diseased lung tissue. This allows the diaphragm to return to a more normal position so it can work effectively again. It also may improve lung elasticity. After surgery, patients spend several months regaining strength as their lungs heal.

While LVRS may lessen the effects of emphysema, it is not a cure. Because it is a new procedure, it is not yet clear how long the benefits will last. Potential benefits may include improvement in breathing, exercise tolerance and quality of life, decreased dependence on oxygen, as well as prolonged life.[1, 2]

Candidates for LVRS:

Lung volume reduction surgery is a procedure used for some patients with severe emphysema, a common type of chronic obstructive pulmonary disease (COPD), disabling dyspnoea (shortness of breath, difficulty in breathing) and evidence of severe air trapping.

Emphysema is an ongoing and progressive disease caused largely by cigarette smoking. The disease damages the lungs and makes breathing difficult.

The effectiveness of lung volume reduction surgery depends on the location or extent of the diseased tissue, as well as the patient's exercise tolerance and ability to tolerate surgery.[3]

Lung volume reduction surgery may be an appropriate treatment for selected patients who meet established criteria. The results of the National Emphysema Treatment Trial (NETT) study, first published in 2003, identified four sub-groups of patients who had different risks and benefits from LVRS, specifically:[4]

Group 1: Mostly upper-lobe emphysema and low exercise capacity. These patients are more likely to live longer and are more likely to function better after LVRS than after medical treatment. This patient group may receive the most benefit from LVRS, as compared with the other patient groups.

Group 2 : Mostly upper-lobe emphysema and high exercise capacity. These patients are more likely to function better after LVRS than after medical treatment.

Group 3 : Diffuse emphysema and low exercise capacity. These patients have similar survival and function after LVRS as after medical treatment.

Group 4 : Diffuse emphysema and high exercise capacity. These patients have worse survival after LVRS than after medical treatment and do not appear to benefit from surgery.

Patients who fall into Group 1 are the best candidates for LVRS. A high-risk patient has been defined by NETT criteria as a patient who would not benefit from LVRS but is more likely to be harmed, as outlined in Group 4. Specifically, the high-risk patient is one who has a forced expiratory volume in the first second (FEV1) that is 20% or less of their predicted value and either homogenous distribution of emphysema on CT Scan or low carbon monoxide diffusing capacity (DlCO) that is 20% or less of their predicted value. These specific criteria can be determined after the testing process has been completed. Finally, a patient with a certain underlying medical disease, condition or multiple surgical risk factors may also not be a surgical candidate for LVRS.

Tests to determine if LVRS is needed or not: [1, 5]

- Chest x-ray
- Pulmonary function tests
- Arterial blood gas (to measure levels of carbon dioxide and oxygen in the blood)
- Electrocardiogram (ECG)
- High resolution, computed tomography scan
- Oxygen titration
- Six-minute walk
- Cardiopulmonary exercise test
- Right heart catheterization (only if additional tests are required)
- Cardiac stress test
- Pulmonologist consultation

Procedure of LVRS

The goal of LVRS is to remove up to 20 to 30 percent of each lung, making the lungs smaller and allowing them to function better. It is done by the following ways: [2, 6]

Sternotomy (Bilateral)

An incision is made through the breastbone to expose both lungs. Both lungs are reduced at the same sitting in this procedure, one after the other. The chest bone is wired together and the skin is closed. This is the most invasive technique, used when thoracoscopy is not appropriate. This approach is usually used for upper lobe disease only.

Thoracotomy (Unilateral or One-Sided)

For the thoracotomy technique, an incision is made between ribs. The incision is approximately 5 to 12 inches long. The ribs are separated, not broken, and lungs are seen. Only one lung is reduced with this procedure. Muscle and skin are closed by sutures. Thoracotomy is often used when the surgeon is unable to see the lung clearly through the thoracoscope or when dense adhesions (scar tissue) are found.

Thoracoscopy:

A minimally-invasive technique, the thoracoscopy requires 3 to 5 small incisions made on both sides of the chest, between the ribs. A video scope is inserted through one of the incisions to allow the surgeon to see the lungs. A stapler and grasper are inserted in the other incisions and are used to remove the most damaged areas of the lung. The stapler is used to reseal the remaining lung.Thoracoscopy can be used to operate on either one (unilateral) or both lungs (bilateral) and allows surgeon to assess and resects any part of the lungs.

Benefits and risks of lung volume reduction surgery: [2, 7]

The National Emphysema Treatment Trial (NETT)'s results confirm that LVRS is beneficial for patients with predominant upper lobe disease and low exercise capacity, as compared with medical treatment.

While effective for some patients, there are risks involved with lung reduction surgery, including:

- Air leakage (50%,occurring when air leaks from the lung tissue, coming from the suture line into the chest cavity)
- Pneumonia or infection (19%)
- Stroke (<1%)
- Bleeding (2-5%)
- Heart attack (1%)
- Death (6-10%)(due to worsening of one of the above complications)

Hospital stays following lung reduction surgery:

Patients will stay in the *Cardiothoracic Intensive Care Unit (CTICU)* post-operatively. While in the CTICU, patients will not require any items from home. One should expect to stay 5 to 10 days in the hospital following lung reduction surgery.

Alarming symptoms and signs after surgery:

- Fever
- Warmth, redness, or swelling around the incision

- Difficulty breathing
- Drainage from the incision

Alternatives to surgery for lung volume reduction:

Approaches that use endobronchial valves to achieve lung volume reduction without the need for incisions are currently being investigated. These valves are placed into the inside of the lung via a bronchoscopy. During a bronchoscopy, a long, thin tube called a bronchoscope is passed through the nose or mouth and down the airway as far as necessary. A small camera conveys the images to a television monitor.[8]

Risk Factors of surgery:

There are numerous risks involved with lung reduction surgery. Lung reduction surgery has a higher risk than heart surgery, because the candidates have poor lung function and are generally older in age. The death rate for this surgery is approximately 6 to 10 percent nationwide. This is one of the highest risk elective procedures performed[9,10].

Pulmonary Rehabilitation:

During the pre-operative process, the patient has undergone extensive pulmonary rehabilitation. This process will need to be continued up until the time of surgery, as well as during the post-operative period, which includes the initial days after surgery[11].

It is very important to cough and breathe deeply after surgery. The lungs need to be fully expanded to prevent infection and collapse. Deep breathing, coughing and incentive spirometry are the most effective means of achieving this goal. One should practice coughing and deep breathing before one comes in for surgery[12].

Deep Breathing: One should fill one's lungs up slowly over a count of five (5), hold for a count of five (5) and then exhale slowly over a count of five (5).

This should be repeated 10 TIMES per hour when one is awake.

Coughing: Take three (3) slow breaths, filling your lungs up as much as possible. Initiate your cough on the second breath's exhale cycle. Make sure you hold your incision (splint) during your cough.

This should be repeated 10 TIMES per hour when one is awake[13].

Incentive Spriometer: This device will be given to the patient on the day of surgery.It should be held securely by two hands. Place one's mouth on the mouthpiece and should exhale around the mouthpiece, making a tight seal on the mouthpiece and inhale slowly to the count of five (5) –so that the disc move upward. It should be held for a count of five (5) and one should loosen the seal around the mouthpiece and exhale[14].

This should be repeated 10 TIMES per hour when one is awake.

When patient can expect to return to work and/or normal activities:

Patient's recovery and return to normal activities will depend on his/her lung function following surgery. Patients will be advised for the physical activities in order to regain their strength and return to a normal lifestyle. Additionally, he/she will return to work based on lung function and depending occupation[13,14].

Follow-Up

After LVRS, patients are followed for five years through visits, phone calls and letters. One of the goals is to help patients make lifestyle changes, which include rehabilitation at least three days a week for the rest of their lives[15].

Conclusion:

LVRS has definite improved benefit as compared with maximum medical management. Minimum improved is seen within the first year following operation usually at 3 to 6 months. In addition to the demonstrable objective benefit, subjective benefits in terms of reduced dyspnoea and overall improved quality of life have similarly been encouraging. However the overall surgical outcome depends upon appropriate selection of patients, the choice of operative technique and the optimal timing of intervention.

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REVIEW ARTICLE

Tuberculosis and Pregnancy

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Abstract

Tuberculosis is an important cause of significant maternal morbidity and mortality, especially in the context of HIV co-infection. Pregnancy has no adverse impact provided the disease is diagnosed early and treated effectively. Untreated or inadequate treatment has been associated with poor maternal and foetal outcome. Uncontrolled TB can result in congenital TB, foetal death, intrauterine growth retardation and low birth weight babies. Inadequate treatment increases the risk of treatment failure and development of drug resistance. Screening is recommended only in certain cases. Active TB should be treated without delay and safety of first line of drugs for the management has been established except streptomycin. Latent tuberculosis infection should be treated with INH prophylaxis in selected cases. Sufficient information regarding the safety of second line of drugs is lacking, but short trials have shown good pregnancy outcomes. Therapeutic abortion is not recommended even in MDR-TB cases. Breast feeding is encouraged in most cases. INH prophylaxis and BCG vaccination are to be considered in some cases, but the vaccine is contraindicated in pregnancy. Controversy exists in many areas of management of HIV-TB co-infection.

[Chest & Heart Journal 2011; 35(1) : 48-54]

Introduction:

Tuberculosis (TB) is a specific communicable disease that had for centuries struck millions of people all over the world. In spite of the availability of highly efficacious treatment for decades, TB remains a major global health problem. It is the second leading cause of death from an infectious disease worldwide after HIV[1] and it is also one of the leading non obstetric causes of maternal mortality, with an estimated one-third of deaths due to TB occurring in women of child-bearing age, the majority in resource limited countries.[2] The World Health Organization (WHO) estimates that there were 3.2 million incident cases of TB and 0.32 million deaths among women in 2010.[1] About 13% of TB cases occur among people living with HIV.[1] In resource limited settings, women of child bearing age, especially in the 15-24 year age group, are disproportionately affected by TB because of the high HIV prevalence rates in this group.[4] Pregnancy on its own has not been found to be associated with an increased risk of TB, but a general increase in incidence of TB will lead to an increase in TB infection rates in pregnant women.[5]

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Timely diagnosis and treatment of TB in pregnancy are important; TB is still a cause of significant maternal morbidity and mortality especially in the context of HIV co-infection. [6,7] The diagnosis and treatment of TB in pregnancy, co-infection with HIV, perinatal transmission, breast feeding, congenital TB and INH prophylaxis need special mention.

The influence of pregnancy on TB

Over the last two centuries, views regarding the effect of pregnancy on TB have varied. At one extreme – Hippocrates and Galen believed that pregnancy had a beneficial effect on TB and the view was generally held until the 19th century.[8] In the mid 19th century a dramatically opposite view emerged when Grissole concluded that pregnancy had a deleterious effect on TB and therapeutic abortion was recommended.[9,10] Immediately before the chemotherapeutic era, Hedvall [11] found no apparent relationship except a higher risk of activation of the disease during the first postpartum year; and the findings were supported by Crombie.[12] But a number of studies have failed to show either beneficial or detrimental effect of pregnancy on TB.[13,14] The advent of chemotherapy dramatically improved the prognosis of pulmonary TB and now most researchers believe that the impact of pregnancy on TB appears minimal and the recommendation for therapeutic abortion has long been abandoned.[8]

Effect of TB on maternal and neonatal outcomes

Most studies have suggested that with timely and appropriate treatment TB infection does not increase adverse outcome. There are some studies which have shown that outcome depends on site of the tuberculosis (pulmonary/extra pulmonary) and timing of diagnosis in relation to delivery. Pulmonary TB has been found to be associated with most problems.[15] Extra pulmonary TB is also fairly common and has been found in 20% of the cases. [16] With lymph node disease no effect was found in a study in India.[17] Other forms such as – intestinal, spinal, endometrial and meningeal TB are associated with higher admission rates because of disability.[17] With late diagnosis obstetric morbidity and preterm labour rates were higher.[18]

Reports regarding the perinatal outcome are different. But most studies reported higher rate of perinatal mortality, prematurity, small for dates and low birth weight babies.[14] These effects were even more pronounced in cases with late diagnosis, incomplete or irregular drug treatment and with those with advanced pulmonary lesions.[15]

In last few years, HIV co-infection and emergence of MDR TB is becoming major factors influencing overall outcome.[3] In HIV infected pregnant women, the effect of TB appears to be related more to HIV diseases rather than to pregnancy itself.[20]

Congenital TB is a rare complication of in-utero TB infection as a result of maternal haematogenous spread via the umbilical vein.[7,8,15] Alternatively, the foetus may be infected by aspiration or ingestion of infected amniotic fluid.[7,8]

Diagnosis

The infection in pregnancy may present with diagnostic challenges[20.] Diagnosis may be delayed by the non specific nature of early symptoms[21] and the frequency of malaise and fatigue in pregnancy.[22] Otherwise, the presentation of TB in pregnancy is similar to that in non pregnant women[23]. Pulmonary TB is the most common manifestation of the disease.[24] Good and co-workers reported that cough (74%), weight loss (41%), fever (30%) and malaise and fatigue (30%) were the most common clinical menifestations.[23] Extra pulmonary TB appears no more common among pregnant women than among other TB patients.[22] TB mastitis appears to be very rare entity.[25] The clinicians should have a high index of suspicion particularly in individuals with atypical symptoms.[26,27,28] Another important step of diagnosis is to identify the risk factors for TB infection.[4,24]

Routine screening for TB in pregnancy is not standard practice in many settings.[5] TB screening is recommended in settings of high HIV prevalence, as the rates of TB infection in pregnant women are high in these settings.[29-31] Women with symptoms compatible with TB, recent contacts of infectious cases and medical conditions which predispose to TB should be evaluated.[8] Immigrants from countries of high prevalence should also be screened.[32] Tuberculin testing using 0.5 ml (5 tuberculin units) purified protein derivative (PPD) is regarded as safe in pregnancy.[8,22,33] If the tuberculin skin test (TST) is greater than 10mm

of induration, a chest radiograph should be obtained in a symptomatic patient with proper abdominal shielding. In an asymptomatic patient chest radiograph should be delayed until the 12th week of gestation.[7] In case of women infected with HIV, an area of 5mm or greater induration is considered positive.[34]

Confirmation of *M.Tuberculosis* infection remains a difficult issue, especially in low resource settings. Interferon-8 (gamma) release assays IGRAs and Quanti-FERON-TB Gold In tube assay are new developments and have been used for the diagnosis of latent TB infection (LTBI). They have increased the specificity and diagnostic accuracy and are not affected by previous BCG vaccination or infection with non tuberculous mycobacteria.[35]

The usual diagnostic modalities – sputum microscopy for acid fast bacilli, culture of the sputum, and other specimens and chest radiography remain the main stay of diagnosis.[20]

Treatment of active TB during pregnancy

Pregnant women with TB should be treated without delay when discovered. Untreated TB represents a far greater hazard to a pregnant woman and her foetus then does treatment of the disease. [22] As with other medications particularly in the first trimester, the main concern is the risk of teratogenciy.[15] WHO recommends that the treatment of TB in pregnant women should be the same as that in non pregnant women; the only exception being that streptomycin should be avoided in pregnancy as it is ototoxic to the foetus.[36] The standard treatment is ethambutol, isoniazid, rifampicin, and pyrazinamide for two months in the intensive phase, followed by four months of isoniazid and rifampicin in the continuation phase. If pyrazinamide is not used in the first two months of therapy, isoniazid and rifampicin are given for seven months. Directly observed therapy is recommended especially if compliance to treatment is a concern. Pyridoxine supplementation is recommended for all pregnant women taking isoniazid as deficiency is more likely in pregnant women than in the general population. [32] If rifampicin is used in the last few weeks of pregnancy, vit K should be given to both mother and the infant postpartum (as it may cause hypoprothrombinaemia). Isoniazid may be associated with an increased risk of hepatotoxicity in pregnant women, liver function tests are recommended by some – fortnightly during first two months and monthly thereafter.[37] Pyrazinamide falls in category n/a (not available) but is probably safe as no reports of significant adverse events have been found.[38] WHO recommends its use in pregnancy. There is extensive clinical trial that it is safe.

Treatment of gestational multi drug resistant tuberculosis (MDT-TB) is controversial as large scale clinical experience with the use of second line agents during pregnancy is absent. The substantial risk of non treatment must be weighed against the possible toxicities of second line agents. On the basis of available evidence, it is recommended that the patients should have the option to continue with MDR-TB treatment during pregnancy rather than terminating or discontinuing treatment with close follow up provided by the clinical team.[39]

Although comprehensive reviews of second line drugs shows the risk of cartilage defects, ototoxicity, nephrotoxicity and neurotoxicity[38,40,41] but in some studies, good maternal and neonatal outcomes have been reported.[39,40,42,43] Drobac *et al.* found that there was no evidence of significant late presentation toxicity among 6 children exposed to second line Anti TB agents in utero except mild ototoxicity in one due to exposure to capreomycin during the first trimester.[43] But a review of ethionamide exposure during first trimester noted 4 out of 5 cases had central nervous system defects.[44] MDR-TB should only be treated after close consultation with clinicians experienced in the management of TB.[38]

Treatment of TB in pregnant women co-infected with HIV presents several challenges. Current recommendation is to start combination Antiretroviral therapy (ART) after starting TB treatment preferably within 8 weeks.[36] With ART, TB may be aggravated and there is risk of immune reconstitution inflammatory syndrome especially in the first two months of treatment and in patient with significant immune suppression.[24] Rifampicin reduces the plasma concentration of NNRTIs (non-nucloside reverse transcriptase inhibitors) and protease inhibitors.[45,46] Rifabutin may be used instead of rifampicin to avoid the risk of drug

interactions.[47] In individuals on rifampicin based TB treatment, efavirenz is the preferred NNRTIs[45,46] but efavirenz should not be used in first trimester as there is risk of teraogenecity.

Latent TB infection (LTBI)

Latent TB is diagnosed using tuberculin skin test (TST) which has always been debated especially since the introduction of more sensitive interferon gamma assays.[48] The recommended treatment is 9 months of isoniazid monotherapy.[49] Controversies exist regarding the management of LTBI in pregnancy. Considering the risk of hepatotoxicity with isoniazid in pregnancy and post partum, it is recommended that treatment should be delayed until after delivery unless there is high risk of progression to active disease.[50,57] The risk patients are – recent tuberculin converters, and/ or a recent exposure to close contact with active tuberculosis and immunocompromised women (e.g. HIV seropositivity)[7]. Usual dose of INH is 5 mg/kg body weight with a maximum of 300 mg/ day.[7] Pyridoxine should be given to decrease the risk of INH induced neuropathy.[36,52]

Congenital tuberculosis

This is very rare and the foetus can be infected in utero via the umbilical cord when placentitis results from dissemination in the mother.[15] Aspiration of infected amniotic fluid in utero at the time of birth is also a potential but rare mode of transmission.[8,22]

The revised criteria (suggested by Cantwell *et al.*[53]) include tuberculous lesions in the infant and one of the following:

- Lesions in the first few days of life
- Primary hepatic complex or caseating granuloma
- Documented TB infection of the placenta or endometrium
- Exclusion of TB by a career in the post natal period

With congenital TB, symptoms are usually seen in the second and third weeks of the infant's life and a definitive diagnosis rests on the culture of *M.Tuberculosis* from the tissues or fluids.[15] TST is unhelpful (takes 1-3 months to become positive). Virtually all infants have an abnormal chest radiograph with nearly half having a miliary pattern. If possible the placenta should be examined and cultured for tubercle bacilli.[54]

Management of the newborn

Mother to child transmission of TB my occur in utero as in congenital TB, in the intrapartum period through contact with infected amniotic fluid and in the postpartum period aerosol spread or through infected breast milk from an active tuberculous mastitis.[20] The diagnosis of TB in the newborn may be challenging as the early symptoms are often non specific and may be indistinguishable from other congenital infections.[15,24] If active disease is diagnosed, full treatment must be given.[20] There is consensus that breast feeding should not be discouraged for women treated with first line anti-tuberculosis drugs.[7,32,55,56] Pyridoxine supplementation should be considered if the breast feeding women is taking isoniazid to avoid pyridoxine deficiency seizures in the newborn.[7]

Separation of the infant from the mother is likely to be required if the mother has MDR-TB because of prolonged infectivity and the lack of an effective chemoprophylaxis regimen and should be considered if there is maternal non-compliance with treatment.[15] Infants exposed to a mother with infectious TB (sputum positive) and who has had less than 2 weeks treatment should be treated prophylactically with isoniazid (5-10 mg/day). TST should be performed at 6 weeks. If this is negative BCG vaccination should be given and chemoprophylaxis stopped. If TST is positive, congenital TB and perinatal infection should be excluded and isoniazid prophylaxis should be continued for a total period of six months.[7,15]

Conclusion

There has been a resurgence of TB both in the developing and developed countries over the past few years affecting women of childbearing age, so a large number of women can be expected to suffer from TB. Improved diagnosis and effective treatment are important to prevent adverse pregnancy outcome. Once suspected, TB should be diagnosed and treatment should be started regardless of gestational age. First line drugs are considered safe except streptomycin, but there is lack of sufficient information regarding the safety

of second line of drugs. HIV/TB co-infection can complicate the overall picture of pregnancy and tuberculosis and many areas of controversy exist. Better results are obtained in women known to have TB to have complete treatment before planning pregnancy. Oral contraceptive pills should be avoided in patients taking rifampicin.

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REVIEW ARTICLE

Best Practice Strategies for Prevention of Ventilator-Associated Pneumonia (VAP)

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Abstract

Pneumonia accounts for nearly 15% of all hospital acquired (nosocomial) infections and 24% to 27% of all those acquired in coronary care units and medical intensive care units (ICU) respectively. Ventilator-Associated Pneumonia (VAP) is a serious complication of mechanical ventilation which increases the patient's stay in the ICU and overall length of hospital stay and adds to overall costs. VAP is the most common of all nosocomial infections which contribute to death. In spite of extensive world-wide efforts to understand, prevent and treat this complication, a mortality rate of approximately 30% still exists. Several organizations and institutions have recommended strategies and approaches in an effort to address this problem. Evidence-Based Guidelines (EBGs) have been published, but there is still large variability in conformance by physicians and nurses.

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Definition of VAP

Ventilator-associated pneumonia is defined as pneumonia occurring more than 48 hr[1] after patients have been intubated and received mechanical ventilation. Diagnosing VAP requires a high clinical suspicion combined with bedside examination, radiographic examination, and microbiologic analysis of respiratory secretions. As early as 1972, studies have shown that the airway of mechanically ventilated patients quickly becomes colonized with gram-negative organisms.[2] At that time, it was thought that pathogens came from the ventilator equipment in use. However, as the problem was studied and evidence accumulated, it became evident that the origin of the VAP was from a source other than the ventilator equipment.[3,4,5] The primary route of VAP pathogenesis is a combination of two processes: bacterial colonization of the aero-digestive (upper airway + upper digestive) tract and the subsequent aspiration into the lower airway.[7,14]

Incidence

Diagnosis of VAP is difficult, therefore accurate determination of the incidence of VAP is also difficult,[17] and the diagnosis varies from study to study. In the United States, VAP rates are reported as cases per 1000 ventilator days. The mean VAP rate for burn patients in the US is 12.3. Neurosurgical patients have the highest rate at around 20 and pediatrics the lowest at 5.9.[17]

The overall percentages of nosocomial infections in US hospitals rank urinary as the highest (31%),

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pneumonia second (27%), and blood stream third (19%).[1] All three classes of infection are related to devices: urinary catheters, ventilators, and indwelling catheters, respectively.[1] Grossman reported that with each day of mechanical ventilation and intubation, the crude VAP rate increases by 1% to 3% and the death risk increases from two-fold to 10-fold.[19]

Traditional Signs and Symptoms of VAP[15]

- Chest X-ray showing new or progressive diffuse infiltrate which is not attributable to any other cause
- Onset of purulent sputum
- Fever greater than 38.5°C (101°F)
- Leukocytosis
- Positive sputum or blood cultures

Microbiology

VAP is a bacterial pneumonia which develops in patients receiving mechanical ventilatory support through an artificial airway. If the infection occurs within 48 to 72 hours, it is called "early-onset". Early-onset pneumonia is usually caused by one of the following bacteria:[7]

- Staphylococcus aureus (gram positive)
- Haemophilus influenzae (gram negative)
- Streptococcus pneumoniae (gram positive)

These are antibiotic sensitive strains which are common in the ICU.

Late-onset VAP is defined as pneumonia occurring after 72 hours of ventilation and is usually caused by:

- Methicillin Resistant Staphylococcus aureus (MRSA)
- Pseudomonas aeruginosa
- Acinetobacter or Enterobacter

In most patients, VAP is caused by multiple organisms.[16]

Mortality

Kollef quotes the crude mortality rate for VAP as 30%.[7] Craven lists the mortality to be between 27% and 43% with surgical ICU being higher than medical ICU.[16] It is important to note that as the number of days intubated increases, so does the mortality rate.

VAP Risk Factors

The single largest VAP risk factor is the endotracheal tube. Because mechanical ventilator support cannot be performed without the endotracheal tube (or other artificial airway), it is a necessary evil. The endotracheal tube provides a direct passageway into the lungs, bypassing many "natural protection" mechanisms. The endotracheal tube increases the risk for VAP by:

- preventing cough (the patients natural defense)
- preventing upper airway filtering
- preventing upper airway humidification
- inhibiting epiglottic and upper airway reflexes
- inhibiting cilliary transport by the epithelium
- acting as a direct conduit into the lungs for airborne pathogens
- potentially acting as a reservoir for pathogens by providing a place for biofilm to form
- having a cuff which provides a place for secretions to "pool" in the hypoglottic area
- initiating a foreign body reaction, interfering with the local immune

response Host or patient risk factors include:[17]

- age of 65 or more
- underlying chronic illness (e.g. Chronic Obstructive Pulmonary Disease (COPD), emphysema, asthma)
- immunosuppression
- depressed consciousness
- thoracic or abdominal surgery
- previous antibiotic therapy
- previous pneumonia or remote infection

Other device treatment and personnel related risk factors include:[4,7,12,17]

- nasogastric tube placement
- bolus enteral feeding
- gastric over-distension
- stress ulcer treatment
- supine patient position
- nasal intubation route
- instillation of normal saline
- understaffing
- nonconformance to handwashing protocol
- indiscriminate use of antibiotics
- lack of training in VAP prevention

Three Major VAP Prevention Principles

Ventilator associated pneumonia can be reduced with the implementation of a Best Practices program with these three factors or principles:

- Staff education
- Colonization reduction
- Aspiration avoidance

Staff Education

To change the VAP rate in any given ICU, a change in human behavior is needed. Like all behavioral changes, education and reinforcement is required. Education is therefore the first step in a VAP best practice program, followed by reduction of oropharyngeal colonization and reduction of aspiration. Education of the staff about VAP is absolutely necessary for a successful program. The implementation of all three strategies are required to maximally lower the VAP rate over the long term.[20]

Colonization Reduction

Colonized secretions reside in both the gastrointestinal tract and oropharynx.[21] Basic nursing care principles are the first line of defense.[17] Incorporating the following key points and practices can reduce colonization.

• Handwashing

The practice of handwashing and the wearing of gowns and gloves are basic and quite possibly the most important actions taken for reducing colonization. Methicillin Resistant Staphylococcus aureus (MRSA) is commonly spread by caregivers' hands.[12] Gloves and gowns have been shown to be effective in preventing the nosocomial spread of antibiotic resistant bacteria including Vancomycin-resistant enterococci (VRE) as well as MRSA.[7]

• Oral Hygiene

The importance of patient oral and nasal hygiene is often overlooked, although it is one of the most basic of nursing interventions. Sole found that less than half of the 27 surveyed sites (48%) had written policies for oral care of intubated patients, and even fewer (37%) had oral suction policies.[22] The use of closed suction systems (CSS) may contribute to the inattention paid to oral care in that oral suctioning is an integral part of traditional open suction procedures. Yet, it is widely recognized that the mouth is a virtual garden of normal bacterial flora and pathogenic organisms. Both Kollef[7] and Kunis[12] have advocated chlorhexidine oral rinse to reduce the oral bacterial load; however, its regular use may lead to chlorhexidine resistant organisms. Several studies have shown that oral decontamination is an effective method for reducing VAP.[23-25]

• Common Suction Protocol

Standardized, common endotracheal suction protocols, in which everyone suctions the same way, are of central importance in the reduction of colonization. The use of a CSS should be part of a VAP reduction program.[7,13] It has been shown that a focused education program using a common protocol actually lowered the infection rate and substantially reduced the associated costs and morbidity.[26]

• Closed Suction System

The CSS provides a barrier to separate the contaminated (colonized) catheter from the caregiver and other patients. One study has shown a significant reduction in the VAP rate with closed suctioning.[27] The recently revised clinical practice guideline published by the American Association for Respiratory Care (AARC)[13] recommends the use of the CSS as part of a VAP prevention strategy. In addition to reducing the risk of microbial contamination as compared to the open suctioning technique, closed suctioning permits continuous ventilation reducing respiratory stress and vulnerability.

Change out timing of CSS at 24 hours is presently being debated with at least two studies.[28,29] Another study has shown increased colonization when extending the use of the CSS longer than the recommendations stated on the label.[30] The length of time a CSS can be safely used beyond that which is indicated in the Directions for Use has not been determined.[13]

• Saline Lavage

Research does not support the use of saline lavage. Saline instillation in either the endotracheal tube or the tracheostomy tube is controversial[31] and may even be detrimental to the patient.[32] One study concludes that bacteria may be dislodged from the catheter and endotracheal tube into the lung[33] during the procedure while simultaneously causing oxygen desaturation.[31] However, some

textbooks still recommend the use of saline sparingly for thick secretions.[34]

• Closed Suction System Rinse Protocol

Saline instillation into the patient's artificial airway as discussed above is controversial and not supported by the literature, but this is not to say that saline rinsing the CSS after the suction episode should not be done. Thorough and complete rinsing of the CSS with sterile saline after the suction is of utmost importance when attempting to minimize colonization. Interestingly, Sole found that there is a difference in practice between nurses and respiratory therapists when rinsing the CSS.[22] The optimal method of cleansing the system is to follow the Directions for Use provided by the manufacturer.

• Maintain Closed Circuit

Obviously reducing the opportunity for contamination to occur from outside pathogens will reduce the colonization within the circuit; therefore, maintaining a closed circuit is emphasized by the AARC[13] and others.[35]

• Use Closed Condensation Traps

Condensation traps permit drainage without requiring the circuit to be opened, thus preventing external contamination. When using active humidification, the use of condensation traps in the ventilator circuit which do not require opening to be emptied is recommended by Zack.[26] This also reduces manipulation of the tubing thus reducing contaminated colonization dump into the airways. Opening the circuit for other procedures should be avoided.[13]

• Stress Ulcer Prophylaxis

All patients receiving mechanical ventilator support are susceptible to gastrointestinal hemorrhage (stress ulcer).[7] Prophylactic agents such as antacids and histamine type-2 antagonists are often used to protectively reduce peptic acidity. In this changed pH environment, the stomach may become colonized with pathogenic bacteria. As gastric volume is increased, micro-aspiration may also occur at any time. Both factors will increase the opportunity for VAP to occur. Alternatively, sulcralfate has been advocated[20] because it does not decrease the acidity or increase gastric volume and can prevent ble.

• Selective Decontamination of the Digestive Tract (SDD)

If microorganisms survive the peptic environment, regurgitation or reflux can place bacteria into the esophagus and upper airway. A procedure more widely used in Europe,[12] administration of topical antibiotics (Tobramycin, Polymixin B and others) via a paste or solution into the mouth and stomach with the goal of reducing the colonization and subsequent VAP, is controversial. However, neither of two meta-analyses of the research literature showed significant difference in mortality when the data was corrected for the systemic administration of antibiotics.[36] Furthermore, the use of SDD has been associated with emergence of antibiotic-resistant strains of bacteria — a worldwide problem which is on the increase.[36]

Aspiration Reduction or Prevention

The pathogenesis of VAP involves micro-aspiration of oropharyngeal and/or gastric secretions.[21] Any intervention which reduces the opportunity for aspiration will reduce the opportunity for VAP. Many of these interventions are simple and cost efficient. Key points for reducing or preventing aspiration include, but are not limited to, the following:

• Regular Oral Suction and Hygiene

As mentioned in the oral hygiene section above, oral care which includes suctioning is widely recognized as a major preventive strategy, yet actual practices vary widely and do not always reflect current research.[22,37] The CDC guideline, "Guidelines for Preventing Health-Care Associated Pneumonia, 2003", recommends oral suction as a routine prior to extubation.[8] In addition, Zack included oral hygiene in the educational program which reduced VAP by 57.6% in a hospital which has 5 intensive care units.[26]

• Subglottic Suction

The endotracheal tube prevents glottic closure. As a result, the patient is unable to cough and remove secretions in a natural way. However, accumulation or pooling of oropharyngeal secretions above the endotracheal tube cuff occurs and then these fluids can be aspirated. See Figure 1.

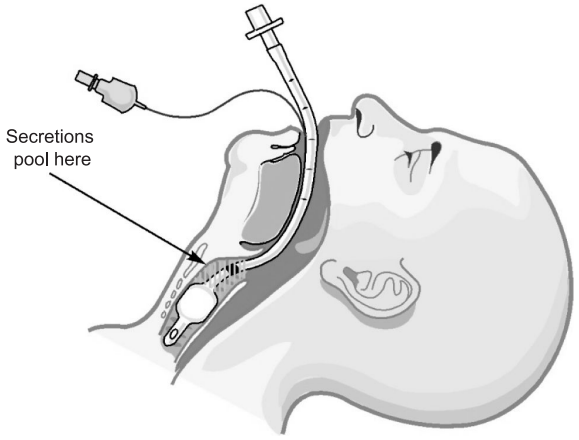

Figure 1

Secretions pool here

Removal of these secretions by suction can reduce the risk of aspiration and may be the most cost effective and safe intervention.[38] Four studies have shown subglottic suction to be safe and effective, [14, 38-40] while only one study showed no difference in colonization.[41] Figure 2 shows one method of performing subglottic suction with a separate suction catheter placed into the sub-glottic area.

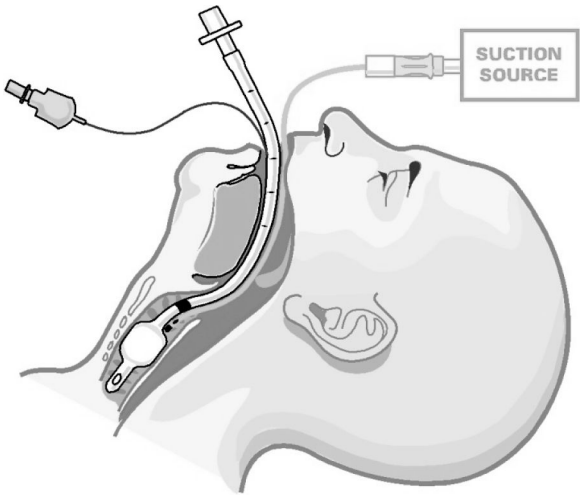

Figure 2

• Minimize Endotracheal Tube Manipulation and Maintain Cuff Pressure

Cuffed endotracheal tubes are essential in adults when positive pressure ventilation is used. The correct pressure within the cuff is critical to prevent aspiration around the cuff yet maintain ventilation and adequate capillary perfusion of the contacted mucosa.[42] The ideal cuff pressure has not been established; however, most authors agree that the cuff should be maintained at or below 20 mm/Hg as one study has shown that VAP is increased by 2.5 times if the cuff pressure is allowed to go below 20 mm/Hg.[22] Presumably, pathogenic laden secretions are able to migrate between the cuff and tracheal wall through minute channels which may be created when the pressure drops and the cuff is manipulated. Therefore, cuff pressure should be measured and recorded on a regular basis.[17,22,42] Also, when the tube is repositioned, oral care and subglottic suction should be performed to reduce disruption and aspiration of colonized bacteria.[17] Unnecessary manipulation of the tube should be avoided.

• Reverse Trendelenberg's (Head Up) Position

Supine body position is a risk factor for VAP. Elevation of the head of the bed to 30 degrees is strongly supported as a preventive strategy that lowers the risk of aspiration.[43] Semi-recumbent (elevation of head above 30 degrees) position is low cost, and effective.[44] Routine (standing) orders to keep all mechanically ventilated patients in the semi-recumbent position can be cost effective but will require an education program for both nurses and physicians to ensure compliance.[45]

• Post-pyloric Feeding

When gastric feeding tubes are placed, the gastroesophageal (cardiac) sphincter is violated which can cause or contribute to reflux. The feeding tube is yet another PVC tube transcending the oropharynx, which can provide a route for microbial access and colonization. Alternatively, delivering the feeding solution via percutaneous enteral gastric tube into the small bowel (post pyloric) has several advantages: reduction in gastroesophageal regurgitation, increased nutrient delivery, shorter feeding time, and a lower VAP rate.[46] In addition, continuous rather than bolus feeding is better tolerated by the patient to keep the stomach from becoming over distended and preserve peptic acidity at levels lethal to most bacteria.[17] The optimal approach for providing nutrition to mechanically ventilated patients is yet undefined; however, small bowel feeding is associated with an overall reduction of pneumonia.[20]

• Early Extubation

Because the occurrence of VAP increases with the length of mechanical ventilation,[4] it is important to wean the patient off the system as soon as clinically feasible.[7,17] Furthermore, premature or accidental extubation prevention strategies are important as reintubation will increase the risk of aspiration.

Conclusion

VAP is a serious complication of mechanical ventilation. It is the most common of all hospital acquired infections that contribute to patient death. VAP carries a mortality rate of approximately 30%. There are three basic strategies demonstrated to effectively reduce the prevalence of VAP. These include: 1) staff education; 2) implementation of specific recommendations for the reduction of microbial colonization; and 3) the prevention of microbial aspiration. Implementing these recommendations will save lives. They will also save hospital time and expense when compared to the alternative – caring for the VAP patient. Incorporating these strategies into the care of ventilated patients also demonstrates facility efforts to address patient safety initiatives.

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REVIEW ARTICLE

Anti-tubercular Drugs Induced Hepatotoxicity –An Update

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Abstract:

Drug-induced liver injury (DILI) is a problem of increasing significance but has been a long-standing concern in the treatment.The liver has a central role in drug metabolism and detoxification, and is consequently vulnerable to injury. The pathogenesis and types of DILI are presented, ranging from hepatic adaptation to hepatocellular injury. Knowledge of the metabolism of anti-TB medications and of the mechanisms of TB DILI is incomplete. Understanding of TB DILI has been hampered by differences in study populations, definitions of hepatotoxicity and monitoring and reporting practices. Available data regarding the incidence and severity of TB DILI overall, in selected demographic groups and in those co infected with HIV or hepatitis B or C virus are presented. Overall, drug induced hepatotoxicity in ATT patient was found to be higher than 34%, however, the age, sex,disease conditions, nutrition status, alcohol abuse and other possible confounding factors play statistically significant role. The reasons behind this higher level of drug induced hepatotoxicity are probably poverty, malnourishment, alcohol consumption, illiteracy of people and poor health management system with age playing a significant role.

Systematic steps for prevention and management of TB DILI are recommended. These include patient and regimen selection to optimize benefits over risks, effective staff and patient education, ready access to care for patients, good communication among providers and judicious use of clinical and biochemical monitoring. During treatment of latent TB infection (LTBI) alanine aminotransferase (ALT) monitoring is recommended for those who chronically consume alcohol, take concomitant hepatotoxic drugs, have viral hepatitis or other preexisting liver disease or abnormal baseline ALT, have experienced prior isoniazid hepatitis, are pregnant or are within 3 months postpartum. During treatment of TB disease, in addition to these individuals, patients with HIV infection should have ALT monitoring. Some experts recommend biochemical monitoring for those older

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than 35 years. Treatment should be interrupted and generally a modified or alternative regimen used for those with ALT elevation more than three times the upper limit of normal (ULN) in the presence of hepatitis symptoms and/or jaundice, or five times the ULN in the absence of symptoms.. For now, with an effective DOTS program accessible all over the country, a baseline laboratory testing criteria and monitoring system should be adopted before starting treatment to effectively reduce the treatment related morbidities. Along with this patient and staff education, appropriate selection of patients for treatment, careful regimen selection and monitoring will minimize the associated risk and adverse effects. The ability to adapt to changing medical landscape will be crucial to continue safe and effective treatment of TB.

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Introduction:

DRUG-INDUCED LIVER INJURY: GENERAL CONCEPTS

Definition

Drug-induced liver injury is ultimately a clinical diagnosis of exclusion. Histopathologic specimens of the liver are often not obtained. [1] Other causes of liver injury, such as acute viral hepatitis, should be methodically sought and their absence makes the diagnosis plausible. [2] Usually, the time of onset to acute injury is within months of initiating a drug. Rechallenge with the suspected offending agent with more than twofold serum alanine aminotransferase (ALT) elevation, and discontinuation leading to a fall in ALT is the strongest confirmation of the diagnosis. [3] Rechallenge may, in some instances, endanger the patient and is usually confined to essential drugs or used when multiple potentially hepatotoxic drugs have been administered concomitantly [4]. Tuberculosis remains one of the most challenging public health problems of the 21st century, particularly, in developing countries. The use of anti tuberculosis therapy (ATT) is associated with some adverse effects particularly hepatotoxicity which is a serious problem and main cause of treatment interruption during TB treatment course[5].

ATT induced hepatitis frequently occurs during first two months of therapy .It is reported that 1-28% of TB patients experience drug related hepatotoxicity following treatment. Reported incidence of hepatotoxic reaction in anti tuberculosis drug therapy 3% in USA 4% IN the UK,11% in Germany,9.9% in Argentina,13% in Hong Kong,36% in Japan,26% in Taiwan & 8-36% in India.[6]

Based on the definition severity of hepatotoxicity is considered as follows:

- Mild : ALT or AST < 2.5 times of the ULN,
- Moderate: ALT or AST 2.5 -5 times of the ULN,
- Severe: ALT or AST 5 -10 times of the UL N,
- Very Severe: ALT or AST >10 times of the ULN[7] ,

Risk Factors for ATT related Hepatotoxicity

- Age- Older patients may be more vulnerable.
- Sex- women especially pregnant one.
- Race: Asians are more vulnerable
- Alcoholism
- Underlying Liver Diseases
- Hepatitis B & C viruses
- HIV infection
- Extensive pulmonary parenchymal disease
- Hypoalbuminaemia
- Drugs.
- Malnutrition-BMI <18.5
- Acetylator Phenotype[8]

Anti-TB drugs responsible for Hepatotoxicity

- 1st line Anti–TB agents-
  - Pyrazinamide
  - Isoniazid
  - Rifampicin
- 2nd line Anti-TB agents
  - Fluroquinolones
  - Ethionamide
  - Prothionamide
  - PAS[9]

Hepatic Drug Metabolism: Transporters, Enzymes, and Excretion The splanchnic circulation carries ingested drugs directly into the liver, a phenomenon known as the "first pass" through the liver. Metabolic enzymes convert these chemicals through phase 1 pathways of oxidation, reduction, or hydrolysis, which are carried out principally by the cytochrome P450 class of enzymes[10]. Phase 2 pathways include glucuronidation, sulfation, acetylation and glutathione conjugation to form compounds that are readily excreted from the body. Other subsequent steps include deacetylation and deaminidation. Many drugs may be metabolized through alternative pathways, Their relative contributions may explain some differences in toxicity between individuals[11].

Pathogenesis of DILI

DILI may result from direct toxicity of the primary compound, a metabolite, or from an immunologically mediated response, affecting hepatocytes, biliary epithelial cells, and/or liver vasculature. In many cases, the exact mechanism and factors contributing to liver toxicity remain poorly understood. Unpredictable or idiosyncratic reactions comprise most types of DILI.[12] These hypersensitivity or metabolic reactions occur largely independent of dose and relatively rarely for each drug and may result in hepatocellular injury and/or cholestasis.Drugs that affect transport proteins at the canalicular membrane can interrupt bile flow. Certain drugs bind to or disable the bile salt export protein. This process causes cholestasis. [13]

Types of ATT induced Liver injuries

- Hepatic adaptation- evidenced by asymptomatic transient rise in ALT
- Drug induced acute hepatitis
- Granulomatous hepatitis-caused by hyper-sensitivity reactions eg Pyrazinamide. [14]

Normally isoniazid is cleared mostly by liver, primarily by acetylation by N-acetyl transferase2 (NAT-2). Acetyl-isoniazid is metabolized mainly to monoacetyl hydrazine (MAH). The reactive metabolites of monoacetyl hydrazine (MAH) are probably toxic to tissues through free radical generation. Incidence: 10 ~ 20% (asymptomatic) Liver enzymes ↑ 2 to 3 times: generally occur < first 8 weeks

Usually ↓ even if therapy is continued Hepatitis occurs in 0.4% patients. [15]

Mechanism of liver toxicity By Rifampicin:

Conjugated hyperbilirubinaemia probably is caused by inhibiting the major bile salt exporter pump.Rifampicin may occasionally cause dose depended interference with bilirubin uptake resulting in subclinical, unconjugated hyperbilirubinemia or jaundice without hepatocellular damage. Rarely DILI appears to be a hypersensitivity reaction. Prevalence is 10% to 15% usually as transient hepatic enzymes ↑ : usually within the first 8 weeks.Overt hepatotoxicity: < 1%[16]

Mechanism of liver toxicity by Pyrazinamide :It may exhibit both dose dependent and idiosyncratic hepato toxicity.It alters nicotinamide acetyldehydrogenase levels in liver which might result in generation of free radical species.

There may be shared mechanisms of injury for isoniazid and pyrazinamide, because of their some similarity in molecular structure. Patients who previously had hepatotoxic reactions with isoniazid have more severe reaction with rifampicin and pyrazinamide. The risk of drug-induced hepatitis is dosage dependent. Symptomatic hepatitis is 1% (combined with INH). [17]

Clinical Presentation of Hepatotoxicity: Some individuals may be asymptomatic, whereas others may experience symptomatic hepatotoxicity at varying serum transaminases concentrations. The followings are the sign and symptoms of DIH: Constitutional symptoms e.g malaise, fatigue,nausea, vomiting,abdominal pain,fever,rash,jaundice coagulopathy, Hypoalbuminemia.[18]

Differential diagnosis of Drug Induced Hepatitis

Acute viral hepatitis Granulomatous hepatitis (Disseminated TB) Chronic liver disease usually a clinical exclusion of other diseases (Histology not routinely done) [19]

Diagnosis:

A complete liver function profile including serum bilirubin, serum aminotransferases, total protein, serum albumin, serum alkaline phosphatase HBsAg, Anti HCV & Anti HAV. [20]

Management of DILI- If the diagnosis of drug-induced hepatitis is made, the anti TB drugs should be stopped. The drugs must be withheld until the jaundice or hepatic symptoms have resolved and liver function tests have returned to normal.If liver functions tests can not be done, then it is advisable to wait two weeks after the jaundice has disappeared clinically before recommencing anti TB treatment. [21] In most cases, the patient can be restarted with the same anti TB drugs without return of hepatitis. This can be done either gradually (one by one) or at once (if the hepatitis was mild).If the hepatitis produced severe jaundice, it is advisable to avoid PZA. [22] A severely ill TB patient with DIH may die without anti TB drugs and in this case the patient should be treated with two of theleast hepatotoxic drugs, streptomycin and ethambutol till jaundice subsides. A suggested regimen in such patients is 2SHE/10HE. [23] After the hepatitis has resolved, usual treatment should be restarted. In case of extensive TB, ofloxacin can be considered in conjunction with streptomycin and ethambutol. [24]

Conclusion:

Hepatotoxicity due to ATT is quite significant and common problem, being more prevalent in the elderly. A base line laboratory testing and monitoring system should be adopted before starting treatment which might help to reduce drug induced hepatitis in ATT patients. Patient education, awareness of health providers should be improved regarding anti TB drug induced hepatitis. [25]

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CASE REPORT

Bilateral Pleural Effusion- An Uncommon Case

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Abstract:

Pleural effusion due to sarcoidosis is not common presentation .Usually it is unilateral but bilateral effusion;though uncommon;can occur in sarcoicodosis.

A middle-aged lady presented in OPD with breathlessness on exertion, dry cough and weight loss. Her chest X-Ray showed moderate bilateral pleural effusion. She had enlarged right supraclavicular lymph node. Biopsy revealed necrotising granulomatous lymphadenitis. Hence with a diagnosis of tuberculosis adequate first line antituberculous therapy was given. But her symptoms worsened despite of six months regular antikochs.

After admission in this institute all necessary investigations were done where repeat biopsy of rt. supraclavicular lymph node revealed non- caseating granuloma .Her MT was negative and pleural biopsy also reveled non caseating granuloma and HRCT of chest showed bilateral hilar lymphadenopathy,bilateral moderate pleural effusion and interstitial fibrosis. Mycobacterial culture of biopsy tissue was negative. She was diagnosed as a case of sarcoidosis.

Cortico-steroid started in adequate dose.This results clinical and radiological improvement.Her cyanosis disappeared,dyspnoea releived and radiological clearance of effusion was evident on CXR with reduction in size of enlarged mediestinal lymph nodes were evident.

[Chest & Heart Journal 2011; 35(1) : 68-70]

Introduction:

Pleural effusion due to sarcoidosis is not a common presentation .Usually it is unilateral but bilateral effusion though uncommon may occur in sarcoidosis[1,2]. Sarcoidosis is a systemic granulomatous disease of unknown etiology which typically present in middle age and predominantly in female. The most commonly affected organs in this disease are lung and lymph nodes though any organ can be affected. The exact etiology of the disease is unknown and various factors are thought to be responsible for granulomatous inflammation. Patients may be asymptomatic but can present with symptoms on the basis of affected organ. Dyspnoea, tiredness which doesn't relief by rest and cough are common. Bilateral hilar lymphadenopathy and pulmonary parenchymal involvement are found.Pleural effusion,skin lesion,uveitis,parotitis and splenomegaly are also found. Anemia is common[3]. Corticosteroid can reverse the granulomatous process though their long term benefit remains unclear. Corticosteroids are recommended in unfavorable clinical situation. Alternative to corticosteroid are methotraxate,

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azathioprine, and hydrxy chloroquine.

Case Report:

A middle-aged lady presented with breathlessness on exertion, dry cough and weight loss. Her chest X-Ray showed moderate bilateral pleural effusion. She had enlarged right supraclavicular lymph node. Biopsy revealed necrotising granulomatous lymphadenitis. Hence with a diagnosis of tuberculosis adequate first line antituberculous therapy was given. But her symptoms worsened despite of six months regular antikochs

On examination, she was afebrile with tachypnea, tachycardia, central cyanosis, asterixis and bilateral pitting pedal oedema without elevation of JVP. She had three enlarged, firm, discrete, right supraclavicular lymph nodes. Chest examination revealed stony dullness on percussion Rest of the physical examination was unremarkable.

Hemogram and blood biochemistry were normal. Mantoux test was negative. ABG showed pH- 7.41, pCO_2 52.2 mmHg, pO_2 44.6 mmHg, HCO_3 32.6 mEq/l and saturation of 80.3%. Chest radiograph showed bilateral pleural effusion. HRCT scans [Figure - 1] revealed nodularity and marked thickening, predominantly along the central peribronchovascular interstitium. There was moderate bilateral pleural effusion. Subcarinal, paratracheal and anterior mediastinal nodes were enlarged, up to 12mm with some exhibiting areas of peripheral calcification [Figure - 2].

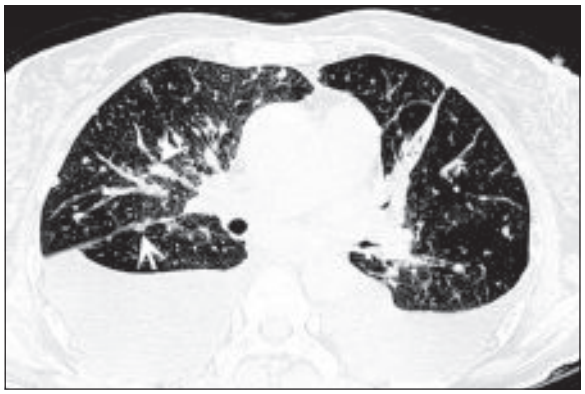

Fig.-1: *HRCT thorax, lung window, the image shows thickening of the peribronchovascular interstitium (arrowhead) and minimal fissural beading (arrow).*

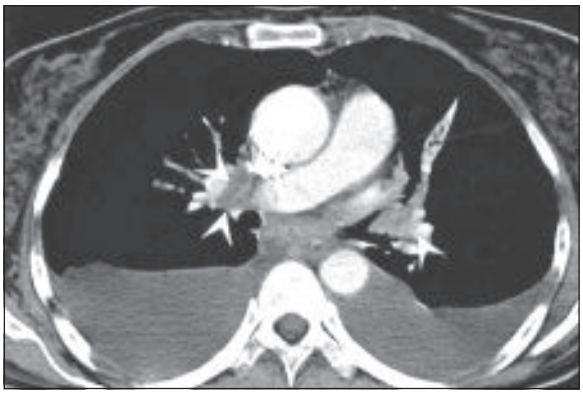

Fig.-2: *HRCT thorax, mediastinal window, image shows bilateral pleural effusion with mediastinal adenopathy (arrowheads)*

Pleural fluid analysis revealed an exudate with lymphocytic pleocytosis, bacterial, fungal and mycobacterial cultures were negative. Cytology was negative for malignant cells. Pleural biopsy revealed non-caseating granulomas and Mycobacterial culture of the pleural tissue was negative. Histology of right supraclavicular lymph node showed non-caseating granulomatous inflammation, and cultures were negative. Based on these clinico-radiologico-pathological features and non-response to anti-tuberculous therapy, she was diagnosed to have sarcoidosis.

She was initiated on corticosteroids and all antituberculous medications were discontinued. She had significant improvement of dyspnea and cyanosis disappeared. Repeat chest radiograph showed marked decrease in the effusion. Her follow up HRCT scans showed evidence of residual fibrosis with significant reduction in nodularity with regression of enlarged lymph node.

Discussion:

The presence of bilateral large effusions in sarcoidosis is unusual. The reported prevalence of pleural involvement in sarcoidosis varies from 0 to 5%[1] with unilateral, small effusions usually. Clinically significant bilateral effusions in sarcoidosis are rare. There are few other reports of sarcoidosis presenting with bilateral pleural effusions but the quantity of fluid was small and clinically insignificant.[2] The growth of one colony of *Mycobacterium tuberculosis* on culture from the lesion in our patient reiterate the possibility that

mycobacteria or some of its components may be capable of inducing the immune response and the pathologica lchanges of sarcoidosis.[3] Hence, sarcoidosis is an important treatable differential diagnosis to be considered in a patient with bilateral pleural effusions especially in the setting of associated pulmonary involvement, non-caseating granulomas[4,5] and non-response to antituberculous therapy.

Conclusion:

In country like Bangladesh where tuberculosis is very prevalent, tuberculosis comes as the first diagnosis of a granulomatous pleural effusion but one should always consider the differential diagnosis so that the less prevalent diseases like sarcoidosis will not go undiagnosed. As mentioned response to corticosteroid in this case is excellent. We kept the patient in follow-up for one year.

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CASE REPORT

Small Cell Carcinoma of Trachea – Report of a Rare Case

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Abstract:

Primary tracheal carcinoma is an uncommon malignancy of the respiratory tract. Small cell carcinoma of trachea is even more rare and only a few cases have been described. Clinical presentation reflects upper airway obstruction causing dyspnea, wheezing and stridor. CT scan of chest and bronchoscopy confirm diagnosis. A 45-years old female presented with severe dyspnea, cough and haemoptysis. Her breathlessness was associated with gradual increase in wheezing. CT scan of chest revealed tracheal tumour with luminal narrowing. This patient needed urgent surgical intervention for restoration of airway patency.

The rarity of the case and life saving restoration of airway patency by urgent surgical intervention inspired us to report this case.

[Chest & Heart Journal 2011; 35(1) : 71-73]

Introduction:

Primary tumours of trachea are rare with an incidence of less than 0.2 per 1,00,000 persons per year and a prevalence of 1 per 15,000 autopsies. The great majority of primary tumours in adults are malignant , whereas in children most are benign. Squamous cell carcinoma and adenoid cystic carcinoma are the most frequent histologic types encountered in the adult population; other tumours account for only occasional case reports.

More than 90% of primary tumours of the trachea and carina in the adult population are malignant. Squamous cell carcinoma and adenoid cystic carcinoma account for approximately two-thirds of primary tracheal malignancies[1]. Primary tracheal carcinoma is an uncommon malignancy of the respiratory tract, accounting for approximately 0.1% of such tumours. Small cell carcinoma of the trachea is even more rare[2], and only a few cases have been described. The clinical presentation of tracheal tumours may reflect upper airway obstruction (dyspnea, wheezing and stridor), mucosal irritation and ulceration (cough and haemoptysis), or direct invasion and involvement of contiguous structures (recurrent nerve palsy, dysphagia), or such tumours may be the result of distant metastasis[1]. Many patients are mis-diagnosed as asthma or chronic bronchitis.

Careful examination of the tracheal air shadow by standard roentgenography may help to detect the tumour but confirmation by computed tomography is required. Bronchoscopy is usually diagnostic and may even permit adequate tumour removal by forceps or with the aid of laser technology. Surgical resection, however, is treatment of choice[3].

Case Report:

A 45 years old female presented with severe respiratory distress, occasional cough and haemoptysis for two months. Breathlessness was associated with wheeze, which was gradually increasing in severity. Her cough was non-

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productive and haemoptysis was scanty. Since her illness she was treated with bronchodilators and antibiotics but with no improvement. She had no personal history of bronchial asthma or atopy; inhalation of foreign body , nor had the history of contact with TB patient. On examination she was alert with respiratory distress with prominence of accessory muscles of respiration. She was cyanosed and stridor was present. Breath sound wa^{2}s vesicular and of diminished intensity with occasional ronchi in both the lung fields. Urgent CT scan of the chest was recommended which revealed polypoid mass lesion (2.5 X 1.6 cm) in size within the lower trachea above the carina resulting luminal narrowing. The lesion was attached to the right posterior wall of the trachea which almost obliterated the tracheal lumen, however there was no evidence of any lung parenchymal lesion or mediastinal adenopathy. The impression was intra tracheal polypoid mass. Following the diagnosis patient was recommended urgent surgery.

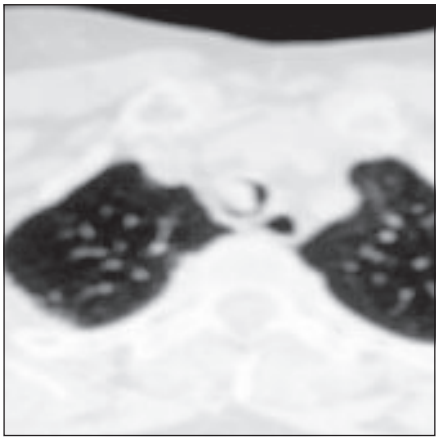

Fig-2: *CT Scan of Chest showing intra-tracheal tumour (coronal view)*

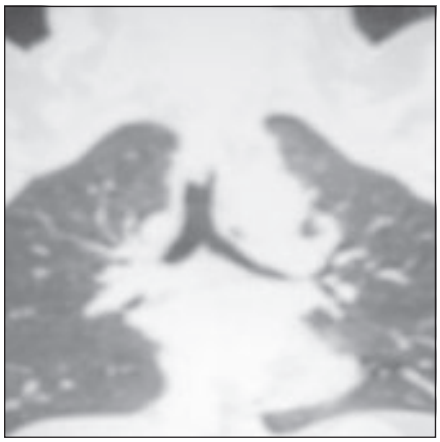

Fig-1: *CT Scan of Chest showing intra-tracheal tumour*

Surgical Procedure:

After induction, anaesthesia was maintained through proximal endotracheal intubation. A quick right posterolateral thoracotomy along third intercostal space was done. Right pleural space was entered. Mass was gently palpated in the trachea about 2cm above the carina. Trachea and right principal bronchus were mobilised. An opening was made in the lower trachea about 1cm above the carina with stay-suture through which intubation of left principal bronchus was performed for ventilation of left lung. Another such opening was made in right principal bronchus for ventilation of right lung. A vertical incision starting from lower tracheal opening was made over the trachea proximally for 3cm along the mass. The trachea was opened and a polypoid, sessile mass measuring about (3 X 1.6 cm), attached to right postero-lateral wall of the trachea was found. It was removed by piece-meal and by curettage. There was minimal bleeding which was controlled by temporarily placed adrenaline-soaked gauze. Trachea was repaired with interrupted prolene suture. Then intubation was switched over to endotracheal route. Distal tracheal opening was repaired with interrupted prolene suture after withdrawing of left endobronchial tube. Opening of the right principal bronchus was also repaired in the same manner. No air leakage was detected after submerging the repaired trachea and bronchus in normal saline in thorasic cavity. Chest was closed in layers keeping a chest drain. Post operative period was uneventful, lung was completely expanded, chest drain was removed on fourth post operative day. Histopathological diagnosis was small cell carcinoma. At present the lady is in good health having no respiratory distress.

Fig-3: *Specimen of the portion of Tracheal tumour*

Discussion:

Primary tracheal carcinoma is an uncommon malignancy of the respiratory tract, accounting for 0.1% of all such tumours[4]. The common symptoms of tracheal malignancies include breathlessness, cough, haemoptysis, dysphagia and stridor. Squamous cell carcinoma is the most common histology seen in primary tracheal carcinoma (60-90%), and is most frequently associated with smoking[4,5]. Other histologies described include adenoid cystic carcinoma, carcinoid, adenocarcinoma , carcinosarcoma, mucoepidermoid carcinoma, chondrosarcoma and small cell carcinoma[5]. Small cell carcinoma of the trachea is even more rare[4,5], and only a few cases have been described. CT scan of chest is highly diagnostic and bronchoscopy is essential in all cases and provides the simpliest and most reliable approach for biopsy and tissue diagnosis[1].

Conclusion:

Primary small cell carcinoma of the trachea is a rare malignancy and often diagnosis is delayed or even mis-diagnosed as asthma or chronic bronchitis. CT scan of the chest and bronchoscopy give valuable diagnostic yields. Airway obstruction in such cases may be life-threatening and needs urgent intervention. Maintenance of anesthesia and ventilation during operation requires special skills. Surgery is the best treatment option for such patients with post operative chemo-radiation.

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